UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2023

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM _____ TO _____**

Commission File Number 001-41551

Acrivon Therapeutics, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware	**82-5125532**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
480 Arsenal Way, Suite 100 Watertown, Massachusetts	**02472**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 207-8979

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	ACRV	Nasdaq Global Market

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		Emerging growth company	☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the voting and non-voting common stock held by non-affiliates of the registrant based on the closing price of the registrant's common stock as reported on the Nasdaq Global Market on June 30, 2023, was approximately $157.7 million. For purposes of this disclosure, shares of common stock held by each executive officer, director and stockholder known by the registrant to be affiliated with such individuals based on public filings and other information known to the registrant have been excluded since such persons may be deemed affiliates. This determination of executive officer or affiliate status is not necessarily a conclusive determination for other purposes.

The number of shares of Registrant's Common Stock outstanding as of March 25, 2024 was 22,636,951.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's definitive Proxy Statement, to be filed pursuant to Regulation 14A under the Securities Exchange Act of 1934, for its 2024 Annual Meeting of Stockholders are incorporated herein by reference in Part III.

Auditor Firm Id:	238	Auditor Name:	PricewaterhouseCoopers LLP	Auditor Location:	Boston, Massachusetts, United States

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Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K, or the Annual Report, contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 about us and our industry that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report, including statements regarding our future results of operations or financial condition, business strategy and plans and objectives of management for future operations, are forward-looking statements. In some cases, you can identify forward-looking statements because they contain words such as "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," or "would" or the negative of these words or other similar terms or expressions. These forward-looking statements include, but are not limited to, statements about the following:

- the timing, progress and results of our preclinical studies and clinical trials of our drug candidates, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available and our research and development programs;
- the timing of any Investigational New Drug, or IND, submissions, initiation of clinical trials and timing of expected clinical results for our lead drug candidate, ACR-368, ACR-2316, and our other future drug candidates;
- the timing of any submission of filings for regulatory approval of, and our ability to obtain and maintain regulatory approvals for, ACR-368, ACR-2316, and any other drug candidates for any indication;
- our ability to identify patients with the cancers treated by our drug candidates, and to enroll patients in trials;
- our expectations regarding the size of the patient populations, market acceptance and opportunity for and clinical utility of our drug candidates, if approved for commercial use;
- our manufacturing capabilities and strategy, including the scalability and commercial viability of our manufacturing methods and processes;
- our expectations regarding the scope of any approved indication for ACR-368, ACR-2316, or any other drug candidate;
- our ability to successfully commercialize our drug candidates;
- our ability to leverage our proprietary precision medicine platform, Acrivon Predictive Precision Proteomics, or AP3, to identify and develop future drug candidates;
- our estimates of our expenses, ongoing losses, future revenue, capital requirements and our need for or ability to obtain additional funding before we can expect to generate any revenue from drug sales;
- our ability to establish or maintain collaborations or strategic relationships;
- our ability to identify, recruit and retain key personnel;
- our reliance upon intellectual property licensed from third parties and our ability to obtain such licenses on commercially reasonable terms or at all;
- our ability to protect and enforce our intellectual property position for our drug candidates, and the scope of such protection;
- our financial performance;
- our use of proceeds from our initial public offering and the concurrent private placement;
- our competitive position and the development of and projections relating to our competitors or our industry;
- our estimates regarding future revenue, expenses and needs for additional financing;
- the impact of laws and regulations; and
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act.

You should not rely on forward-looking statements as predictions of future events. We have based the forward-looking statements contained in this Annual Report primarily on our current expectations and projections about future events and trends that we believe may affect our business, financial condition, and results of operations. The outcome of the events described in these forward-looking statements is subject to risks and uncertainties, including the factors described in "Part I, Item 1A. Risk Factors" and elsewhere in this Annual Report. Moreover, we operate in a very competitive and rapidly changing environment. New risks and uncertainties emerge from time to time, and it is not possible for us to predict all risks and uncertainties that could have an impact on the forward-looking statements contained in this Annual Report. The results, events, and circumstances reflected in the forward-looking statements may not

be achieved or occur, and actual results, events, or circumstances could differ materially from those described in the forward-looking statements.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based on information available to us as of the date of this Annual Report. While we believe that such information provides a reasonable basis for these statements, that information may be limited or incomplete. Our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all relevant information. These statements are inherently uncertain, and investors are cautioned not to unduly rely on these statements.

The forward-looking statements contained in this Annual Report relate only to events as of the date on which the statements are made. We undertake no obligation to update any forward-looking statements made in this Annual Report or to reflect new information or the occurrence of unanticipated events, except as required by law. We may not actually achieve the plans, intentions or expectations disclosed in or expressed by, and you should not place undue reliance on, our forward-looking statements. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures, or investments.

Unless the context otherwise requires, all references in this Annual Report to "we," "us," "our," "our company," and "Acrivon" refer to Acrivon Therapeutics, Inc. and its subsidiaries.

Summary Risk Factors

Investing in our common stock involves a high degree of risk because our business is subject to numerous risks and uncertainties, as more fully described in "Part I, Item 1A. Risk Factors" of this Annual Report on Form 10-K. Below are some of these risks, any one of which could materially adversely affect our business, financial condition, results of operations, and prospects:

- We are a clinical stage biopharmaceutical company and have incurred significant losses since our inception. We expect to incur losses over the next several years and may never achieve or maintain profitability.
- We have a limited operating history and no history of commercializing products, which may make it difficult for an investor to evaluate the success of our business to date and to assess our future viability.
- We will need additional funding to meet our financial obligations and to pursue our business objectives. If we are unable to raise capital when needed, we could be forced to curtail our planned longer-term operations and the pursuit of our growth strategy.
- Our business substantially depends upon the successful clinical development of drug candidates using our AP3 platform and OncoSignature™, or OncoSignature, companion diagnostics. If we are unable to obtain regulatory approval for, and successfully commercialize, drugs developed through the application of our AP3 platform and OncoSignature tests, our business may be materially harmed.
- We are highly dependent on the success of ACR-368 as this is our first drug candidate being developed for clinical development and regulatory approval. We may never obtain approval for ACR-368, ACR-2316, or any other drug candidate.
- The regulatory approval processes of the U.S. Food and Drug Administration, or FDA, and comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our drug candidates, on a timely basis or at all, our business will be substantially harmed.
- The successful clinical development of our drug candidates depends on the co-approval of the OncoSignature test as a companion diagnostic test. If we or our companion diagnostic collaborator are unable to obtain regulatory approval for our OncoSignature companion diagnostic tests for our drug candidates, we may not obtain regulatory approval and realize the commercial potential of our drug candidates.
- Our relationships with customers, healthcare providers, including physicians, and third-party payors are subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.
- Enacted and future legislation may increase the difficulty and cost for us, and any collaborators, to progress our clinical programs and obtain marketing approval or licensure of and commercialize our drug candidates and may affect the prices we, or they, may obtain.
- Even if we are able to commercialize any drug candidates, the products may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.
- We rely, and expect to continue to rely, on third parties, including independent clinical investigators, contracted laboratories and contract research organizations, or CROs, to conduct our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our drug candidates and our business could be substantially harmed.
- The precision oncology space is competitive, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.
- Our success depends in part on our ability to obtain intellectual property rights for our proprietary technologies and drug candidates, as well as our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.
- We depend on intellectual property licensed from a third party and termination of this license could result in the loss of significant rights, which would harm our business.

PART I

Item 1. Business.

Overview

We are a clinical stage biopharmaceutical company developing precision oncology medicines that we match to patients whose tumors are predicted to be sensitive to each specific medicine by utilizing our proprietary proteomics-based patient responder identification platform. Recently approved precision oncology treatments, such as kinase inhibitors, have transformed the cancer treatment landscape, and while the therapeutic benefit of these agents has provided significant benefit to patients, these precision oncology treatments unfortunately only address the less than 10% of patients with cancers that harbor certain easily-identifiable genetic mutations. Our approach is designed to overcome the limitations of genomics-based patient selection methods. We do this by using our proprietary precision medicine platform, Acrivon Predictive Precision Proteomics, or AP3, to develop our pipeline of oncology drug candidates. Our AP3 platform enables the creation of drug-specific proprietary OncoSignature companion diagnostics that are used to identify the patients most likely to benefit from our drug candidates, which we refer to as patient responders. We are currently advancing our lead candidate, ACR-368, a selective small molecule inhibitor which targets CHK1 and CHK2 at sub single-digit nM and single-digit nM potency in intact cells, respectively, in a potentially registrational Phase 2 trial across multiple solid tumor types. We are continuing enrollment and dosing of patients in this multi-center trial based on OncoSignature-predicted sensitivity to ACR-368 in patients with locally advanced or metastatic, recurrent platinum-resistant ovarian cancer, as well as endometrial adenocarcinoma or urothelial cancer, two tumor types predicted to be sensitive to ACR-368 through OncoSignature screening and not previously evaluated in past clinical trials. Our ACR-368 OncoSignature test, which has not yet obtained regulatory approval, has been extensively evaluated in preclinical studies, including in two separate, blinded, prospectively-designed studies on pretreatment tumor biopsies collected from patients with ovarian cancer treated with ACR-368 in past Phase 2 clinical trials conducted by Eli Lilly and Company, or Lilly, and at the National Cancer Institute, or NCI, providing evidence of robust enrichment of responders through our method.

The AP3 approach is proteomics-based and designed to enable identification and treatment of the patients whose tumors are sensitive to a specific drug or drug candidate based on direct protein measurement of critical tumor-driving mechanisms and independent of underlying genetic alterations. We believe our approach is applicable across stages of drug development and across therapeutic modalities. Accordingly, the AP3 method is not limited to the typically very small subset of cancers driven by single gene driver mutations or susceptible to a synthetic lethal approach. Rather, we believe our method is broadly applicable to the vast majority of cancers, in particular the majority of solid tumors, for which genetics-based approaches have proven insufficient to identify patient responders in many cases. In principle, we believe a much larger percentage of tumors can be addressed therapeutically using agents attuned to the specific biochemical signaling pathways found in these tumors, which our AP3 platform was purposefully designed to enable.

By applying our highly specific patient selection approach to drug development, we seek to both accelerate clinical development and significantly increase the probability of successful treatment outcomes for patients. Our pipeline includes the Phase 2 lead program, ACR-368, also known as prexasertib, a precision oncology asset that targets CHK1 and CHK2, or CHK1/2. Prior to the development of the OncoSignature test, ACR-368 was dosed in more than 400 patients at the recommended Phase 2 dose, or RP2D, with reported deep, durable responses, including complete responses, or CRs, in a proportion of patients with solid tumors in past single center and multi-center Phase 2 clinical trials in tumor indications with high unmet need. ACR-368 also demonstrated a generally favorable safety and tolerability profile with primarily reversible hematological toxicity and very limited non-hematological adverse events. We have received clearance from the U.S. Food and Drug Administration, or FDA, for an Investigational New Drug, or IND, application to advance ACR-368 in Phase 2 single arm clinical trials conducted under the FDA program known as the master protocol, which was developed to help expedite drug development in multiple tumor types for drugs with an established RP2D within the same overall trial structure. Initially, patients with platinum-resistant ovarian, endometrial, or bladder cancer will be treated in this trial. Patients will be stratified for treatment based on OncoSignature-predicted sensitivity to ACR-368 across multiple sites in the United States in this trial with registrational intent. Through the use of our OncoSignature test, we believe we can significantly increase the overall response rate, or ORR, observed in previous trials that were conducted without a prospective patient responder identification method.

We also plan to study ACR-368 in additional indications, such as human papilloma virus positive, or HPV^+, squamous cell carcinomas, including squamous cell cancer, or SCC, of head and neck, or SCCHN, anal, and cervical cancer, based on demonstrated clinical single-agent activity in SCCHN and anal cancer and OncoSignature-based prediction of sensitivity to ACR-368 in a proportion of patients in past clinical trials. In addition to ACR-368, Acrivon is also leveraging its proprietary AP3 precision medicine platform for developing its co-crystallography-driven, internally-discovered preclinical stage pipeline programs, including its development candidate, ACR-2316, a selective, dual WEE1/PKMYT1 inhibitor designed for superior single agent activity as demonstrated in preclinical studies against benchmark inhibitors, and a cell cycle program with a yet undisclosed target.

We were founded and are led by pioneers in oncogenic signaling, oncology precision medicine and the use of proteomic technology to uncover intracellular biochemical signaling pathways with the goal of applying this knowledge to develop drug candidates

and clinical diagnostics. Our founders have established proof-of-concept, including clinical implementation, for the underlying technologies in our AP3 platform. Our scientific advisors are thought leaders from leading global cancer and academic centers and are actively involved in our drug development process.

Our AP3 Platform

Our proprietary AP3 platform is engineered to measure compound-specific effects on the entire tumor cell protein signaling network and drug-induced resistance mechanisms in an unbiased manner at very high resolution and throughput. As such, all drug-regulated effects on the disease-driving, upregulated pathways and active proteins are revealed for each compound that we profile. We apply these distinctive capabilities of AP3's for drug design optimization for monotherapy activity, the identification of rational drug combinations, and the creation of drug-specific proprietary OncoSignature companion diagnostics that are used to identify the patients most likely to benefit from Acrivon's drug candidates.

One of the key applications of our AP3 platform are our proprietary response-predictive clinical tests that we refer to as OncoSignature tests. These are drug-tailored, automated, quantitative proteomic tissue imaging tests applied to pretreatment tumor biopsies as a companion diagnostic, or CDx, to select and treat the patients predicted to benefit from the drug candidate. Our OncoSignature test, which has not yet obtained regulatory approval, is being developed with Akoya Biosciences, Inc., or Akoya, pursuant to a companion diagnostic agreement. Our OncoSignature tests encompass a signature of three classes of functionally-defined protein biomarkers assembled into a single signature assay. The quantitative levels for each of the three biomarkers are defined to determine whether a patient's individual tumor has upregulated the biochemical signaling mechanisms that the drug modulates and that the tumor depends on for growth and/or survival. Our company name, Acrivon, is derived from Greek for "accurate." We chose it to embody how our OncoSignature tests are designed to accurately match our therapies with patients who will benefit.

The tumor-agnostic application of OncoSignature tests enables us to identify and focus on tumor types for which a high unmet need for a treatment exists and that are predicted to be highly sensitive to our drug candidates. We achieve this by deploying our OncoSignature screening of human cancer samples across various tumor types. Through this process, we can identify new tumor types predicted to be sensitive to a drug candidate and even estimate the percentage of predicted responders before entering clinical trials. For example, we have identified endometrial cancer and bladder cancer as two highly sensitive cancer types for ACR-368, and therefore will include patients with these tumor types in our Phase 2 trials. Moreover, we have found through this approach that a proportion of patients with HPV^{+} cancers are predicted to be responsive to ACR-368, consistent with previously demonstrated clinical activity in a proportion of patients with SCCHN and anal cancer. Furthermore, we predicted that patients with squamous non-small cell lung cancer, or sqNSCLC, would not respond to ACR-368, consistent with an observed objective response rate, or ORR, of 0% in patients with this tumor type in a past trial with ACR-368. Hence, through our OncoSignature screening approach, we can specifically avoid running clinical trials in cancer types predicted to have limited sensitivity to our drug candidate.

We are not only using our AP3 platform to generate drug-tailored, response-predictive clinical OncoSignature tests, but we also use our AP3 platform to provide unbiased, quantitative analyses of off-target effects on intracellular signaling using phosphoproteomic profiling, potentially enabling us to discover inhibitors that are both highly potent and highly selective.

We believe that by leveraging our AP3 platform and clinical OncoSignature tests, we will profoundly alter precision oncology drug development and the treatment landscape of patients suffering from cancer.

Our Pipeline

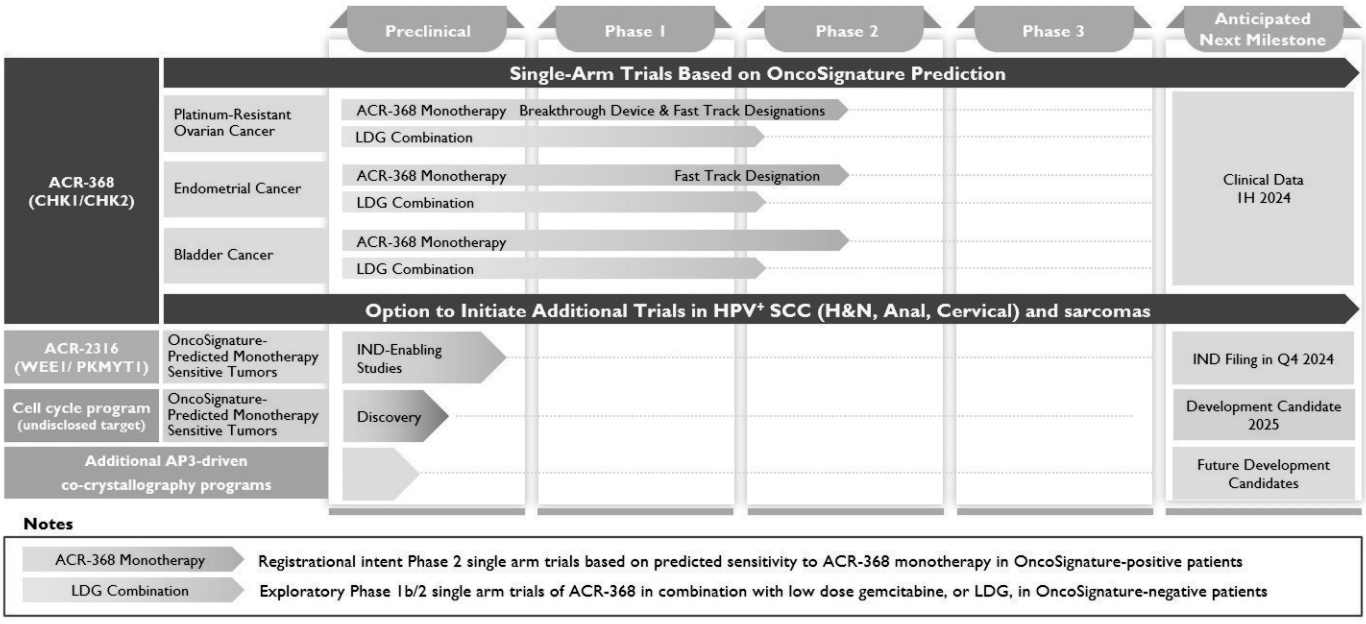


Figure 1. Acrivon's internal pipeline including the clinically advanced ACR-368 and two preclinical programs.

Our Lead Clinical Candidate ACR-368

ACR-368 is a selective small molecule inhibitor targeting CHK1/2. CHK1/2 are key regulators of the cell cycle and of DDR and inhibition of CHK1/2 has been demonstrated to have anti-tumor activity in multiple preclinical models as well as in clinical trials in humans. Several CHK1/2 inhibitors including ACR-368, also known as prexasertib, have been investigated in the clinic; however, none have been approved by the FDA. ACR-368 has shown deep, durable single agent clinical activity, including CRs and partial responses, or PRs, in a proportion of patients with solid tumors with high unmet need for a treatment, such as platinum-resistant ovarian cancer, and SCCs, including SCCHN and anal cancer. More than 400 patients with these tumors have been treated with ACR-368 monotherapy at the RP2D in advanced single- and multi-center clinical trials conducted by Lilly, NCI, and at MD Anderson Cancer Center, or MDACC. The confirmed ORR in these trials without a predictive biomarker was 29% at the single center Phase 2 ovarian cancer trial at NCI in the intent to treat, or ITT, population, and approximately 12% across the platinum-resistant ovarian cancer cohorts in the large Phase 2 multi-center international trial sponsored by Lilly. The median duration of response, or mDoR, at the RP2D across trials to date have ranged from almost six months to 12 months, and ACR-368 monotherapy demonstrated a generally favorable safety and tolerability profile with primarily reversible hematological toxicity and very limited non-hematological toxicity. Based on these two trials, encompassing over 200 patients with ovarian cancer, primarily platinum-resistant, we believe the unenriched background ORR in a larger patient population of platinum-resistant ovarian cancer is somewhere between 15% and 20%.

Using our AP3 platform, we have developed a predictive OncoSignature test for ACR-368, called ACR-368 OncoSignature, that we believe can predict patient response to ACR-368 monotherapy and therefore substantially improve the clinical ORR and, furthermore, that we believe, has the potential to enable expedited drug development. Predicted patient responders are referred to as ACR-368 OncoSignature-positive and predicted non-responders are referred to as ACR-368 OncoSignature-negative. The ACR-368 OncoSignature test has been extensively evaluated in preclinical studies in both patient-derived xenograft, or PDX, mouse tumor models as well as in two separate blinded, prospectively designed preclinical studies of pre-treatment tumor biopsies collected from patients with ovarian cancer that received ACR-368 in previous clinical trials. Based on the preclinical study results, we believe the ORR in the ACR-368 OncoSignature-positive patients will be increased significantly when compared to the unenriched ORR observed in previous trials.

By applying our ACR-368 OncoSignature test for indication finding and expansion across human cancer types, as described below, we have found that approximately 30% of samples from patients with ovarian cancer are ACR-368 OncoSignature-positive. Moreover, we observed that between 30% and 40% of patients with endometrial and bladder cancer are predicted to be highly sensitive to ACR-368. Patients with these two types of cancer were not previously treated in ACR-368 clinical trials. All three tumor types are therefore included in our ongoing Phase 2 clinical trial.

We have also used our AP3 platform to identify resistance mechanisms to ACR-368. Through phospho-proteomic profiling of human tumor cell lines that are either highly sensitive or highly resistant to ACR-368, we uncovered key resistance mechanisms and found that very low dose gemcitabine, or LDG, could be used to overcome resistance and further sensitize human tumor cells to ACR-368 through inducing increased DDR stress. Moreover, the use of LDG was observed to enhance sensitivity to ACR-368 in the already sensitive cells. We expect this may enable ACR-368 in combination with LDG to be an important treatment for ACR-368 OncoSignature-negative patients who would otherwise be excluded from ACR-368 treatment.

Based on these results, we are conducting a Phase 2 clinical trial where we are treating patients with all three tumor types: platinum-resistant ovarian, endometrial, and bladder cancer. ACR-368 OncoSignature-positive patients, which we believe will represent 30% to 40% of patients of each tumor type, receive ACR-368 monotherapy in a single arm Phase 2b trial for each of the three tumor types. The ACR-368 OncoSignature-negative patients with one of these three tumor types receive ACR-368 combined with LDG at the RP2D of ACR-368 and RP2D established in the study which is 10 mg/m^2 in the exploratory Phase 2 dose expansion portion of the trial. As a result, all patients with these tumor types that have been biopsied will be eligible to receive therapy. Akoya procures and manufactures the necessary supplies to perform the OncoSignature tests. Based on our communications with the FDA to date, we believe the monotherapy trial, if successful, has the potential to be registrational for ACR-368 in each of the three tumor types.

We are carrying out our trial under the auspices of the master protocol guidance issued by the FDA in March 2022 to enable expedited drug development. This guidance provides sponsors of drugs or biologics for the treatment of cancer and for which the RP2D has been established in prior studies, the opportunity to simultaneously evaluate more than one investigational drug and/or multiple cancer subpopulations within the same overall trial structure under master protocol in adult and pediatric cancers.

We believe that use of our ACR-368 OncoSignature test to select patients predicted to be sensitive to ACR-368 for treatment will significantly increase the ORR, which has the potential to lead to accelerated approval for multiple cancers while avoiding treatment of patients with tumors that are not likely to respond. However, we cannot guarantee that the FDA will permit us to utilize an accelerated approval process or that our intended approach will be sufficient for regulatory approval. We are planning to file one or more IND application amendments to add one or more additional cancer types under the same or a similar trial protocol design at a later time, including head and neck cancer, anal cancer, and cervical cancer.

Our Preclinical Programs

We also have wholly-owned, internally developed preclinical drug programs uniquely enabled by our AP3 platform and its ability to rationally design compounds with optimal target selectivity properties aiming to achieve potent single agent activity through elimination of dominant resistance mechanisms. These programs are also structure-guided with rational medicinal chemistry efforts based on co-crystallography of lead series with their respective targets to ensure high selectivity.

ACR-2316 is the first of these and is currently advancing in IND-enabling studies. It is a novel, dual WEE1 and PKMYT1 inhibitor small molecule development candidate, rationally designed through advanced co-crystallography and the AP3 platform to achieve optimal target potency and selectivity, delivering potent single agent anti-tumor activity across in vitro and in vivo preclinical studies, compared to benchmark WEE1 and PKMYT1 inhibitors. Clinical WEE1 inhibitors have demonstrated promising anti-tumor activity in early clinical trials conducted by competitors; however, their clinical activity has been hindered by a narrow therapeutic index and WEE1 inhibitor-induced resistance mechanisms. ACR-2316 was specifically designed using AP3 to address these limitations through very high selectivity to limit adverse events to mechanism-based, on-target, and to simultaneously inhibit PKMYT1, a closely related protein serine/threonine kinase also serving critical functions in the cell cycle and DDR pathways, that accounts for a major part of WEE1 inhibitor-induced resistance, as revealed by AP3. Based on mechanism of action and confirmed in our preclinical studies, balanced inhibition of PKMYT1 results in more potent single agent activity. Currently one company has advanced a selective PKMYT1 inhibitor into phase 1 clinical trials.

We believe there is a need for novel patient selection methods to overcome the challenges with genetics-based patient selection methods, and that using AP3 will enable us to identify drug-sensitive indications and individual patients predicted sensitive to WEE1 and PKMYT1 inhibitors. Using AP3 for unbiased quantitative high-resolution measurement of the effects of ACR-2316 on the human tumor cell phosphoproteome, this compound has been optimized for potent induction of mitotic catastrophe, which is key to its strong single agent activity in preclinical models and potentially favorable clinical profile for monotherapy development. ACR-2316 was discovered by AP3-based SAR, facilitated by co-crystallography, and designed by AP3 to overcome WEE1-induced resistance mechanisms. The preclinical data generated so far demonstrate a very potent single agent activity so we believe patient selection might not be needed in the most sensitive tumor indications. Nevertheless, we plan to generate an OncoSignature to be used for identifying the sensitive tumor indications prior to anticipated start of clinical trials and to enable drug target engagement-based dose optimization using the OncoSignature assay. The ACR-2316 program is currently rapidly advancing in IND-enabling studies and is anticipated to be ready for IND-submission by the fourth quarter of 2024. We also have a cell cycle program with an undisclosed target for which we anticipate nominating a development candidate in 2025.

AP3 Potential for Broad Clinical Impact

Our AP3 platform is based on two integrated technology pillars, mass spectrometry-based proteomic profiling and our automated tumor imaging biomarker platform. Mass spectrometry, or MS, enables a systematic, unbiased quantitative analysis of the proteins inside a cell or entire tissues and is used to identify our biomarker candidates. These are validated using our biomarker platform which is also used to run our OncoSignature tests. AP3 is designed to generate multiple clinically-actionable, valuable outputs:

- Predictive biomarkers and patient responder identification: Our OncoSignature tests are designed to enable identification and treatment of patients predicted to be sensitive to the drug candidate, while avoiding treatment of patients predicted not to benefit.
- Indication finding and expansion: OncoSignature screening of human patient tumor samples is used to predict what proportion of various tumor types are expected to be highly sensitive to our drug candidates. This enables indication expansion and could potentially increase the response rates in clinical trials.
- Identification of resistance mechanisms: AP3 is a powerful technology to identify either pre-existing (intrinsic) resistance or acquired (therapy-induced) resistance to drugs demonstrated in prior studies. We intend to apply this technology to develop combination therapy candidates that target the druggable resistance mechanisms and re-sensitize tumors and to prevent resistance development.
- Identification of rational drug combinations: Through our AP3 platform, we uncover the entire protein signaling pathways underlying resistance. The druggable targets on such pathways are a basis for rational drug combinations and we believe can efficiently overcome resistance demonstrated in multiple prior studies. We intend to apply this for indication expansion and confirmatory trials for our drug candidate pipeline.
- Unbiased drug target engagement and pharmacodynamic biomarker discovery: Through our high resolution phosphoproteomic drug profiling, we uncover thousands of on- and off-target interactions and drug-regulated pharmacodynamic, or PD, biomarkers for each drug candidate. These can be used to guide selectivity optimization of preclinical lead series and to measure drug target engagement in patient tumor tissues during clinical trials, and hence guide dose optimization.

Our AP3 platform deploys high resolution, high throughput MS resulting in large datasets reflecting differentially drug-regulated phosphorylation sites and signaling pathways inside sensitive and resistant cells for each drug candidate we profile. The data are highly structured and amenable to machine learning, which has enabled us to create a streamlined process and to integrate all the analytical steps into a single workflow. We intend to apply our AP3 platform to both our existing and future pipeline of drug candidates addressing prevalent, high unmet need cancers and where patient responder identification has proven challenging, as further described below.

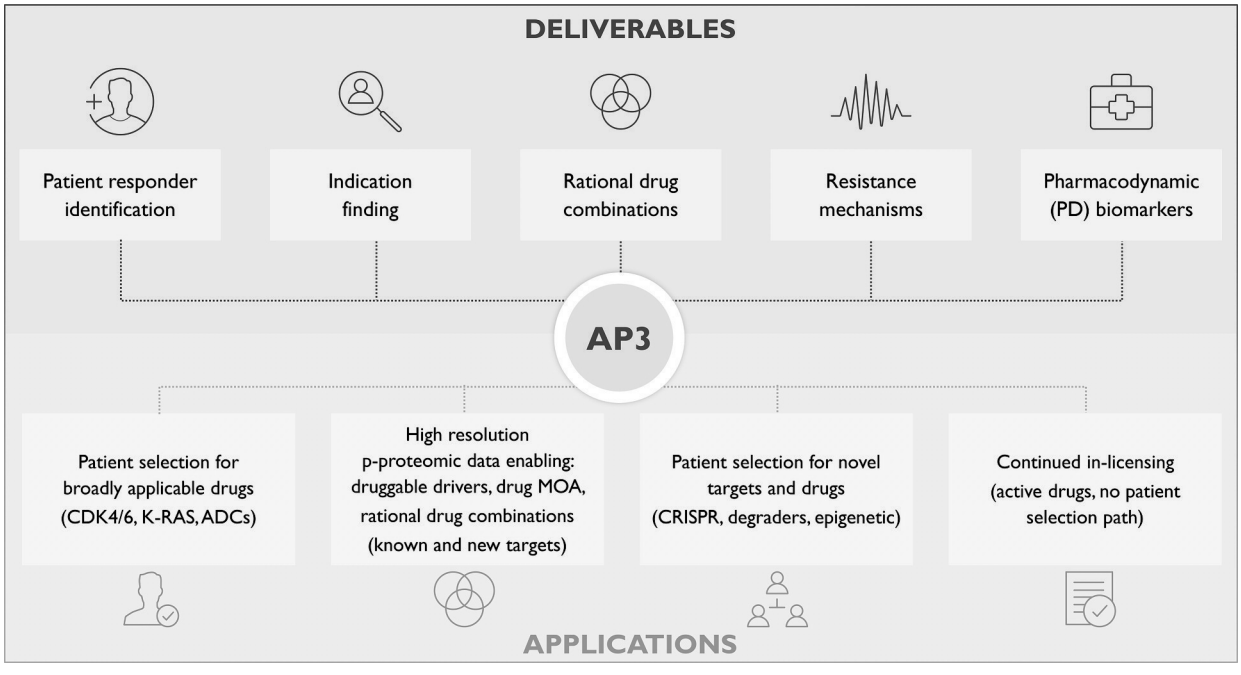


Figure 2. AP3 has potential for broad impact across the drug discovery and development process.

Our Team

We were founded in 2018 and are led by pioneers in oncogenic signaling, oncology precision medicine, and the use of proteomic technology to uncover intracellular biochemical signaling pathways and to apply this knowledge to develop drug candidates and clinical diagnostics. Peter Blume-Jensen, MD, PhD, our co-founder, President and Chief Executive Officer, is the inventor of our AP3 platform and OncoSignature patient selection method. He has extensive experience in oncology drug discovery and development at leading pharmaceutical companies including Serono, Merck & Co. and Daiichi Sanyo. While Chief Scientific Officer at Metamark Genetics, Dr. Blume-Jensen led the development of an automated, proteomics-based predictive clinical diagnostic for prostate cancer which was validated through blinded clinical trials and included as the only stand-alone test under National Comprehensive Cancer Network, or NCCN, guidelines and reimbursement in 2015. Kristina Masson, PhD, co-founder, Executive Vice President, Business Operations and head of our discovery research site in Sweden, previously founded and operated OncoSignature AB, a biotech company which established the phosphoproteomics and drug discovery infrastructure and which we subsequently acquired. Jesper Olsen, PhD, our academic co-founder, is Professor of Quantitative Proteomics at the University of Copenhagen and Vice Director of the Novo Nordisk Foundation for Protein Research and a recognized pioneer of MS-based quantitative phosphoproteomics. Rasmus Holm-Jorgensen, our Chief Financial Officer, has over 20 years of experience in the biopharmaceutical industry, most recently as Chief Strategy & Portfolio Officer and part of the founding team at Kiniksa Pharmaceuticals. Erick Gamelin, MD, PhD, our Chief Development Officer, has led over 100 Phase 1 through Phase 3 oncology clinical trials and most recently served as Chief Medical Officer of Step Pharma. Eric Devroe, PhD, our Chief Operating Officer, has extensive experience in operations and business development leadership from his time at Metamark Genetics, MDACC, and several start-up companies. Jean-Marie Cuillerot, MD, our Chief Medical Officer, was most recently Chief Medical Officer at Dragonfly Therapeutics and Agenus. He has extensive experience in leading clinical programs in immune-oncology from pre-IND through global submissions, including development of Avelumab at EMD-Serono, the first drug approved to treat Merkel cell carcinoma and second-line bladder cancer, as well as multiple Phase 2 and Phase 3 clinical trials at Bristol Myers Squibb for Ipilimumab across indications.

Our founders have pioneered and established proof-of-concept, including clinical implementation, for the underlying technologies in our AP3 platform. Our scientific advisors are thought leaders from leading global cancer and academic centers and are actively involved in our drug development process.

Our Strategy

Our goal is to be the leading biopharmaceutical company leveraging proteomic and phosphoproteomic data, which we access through our proprietary AP3 platform, to unlock insights superior to those from traditional genomic-based approaches and discover and efficiently develop medicines to benefit patients with cancer.

While our AP3 approach is broadly applicable across disease areas, we are initially committed to oncology. Our goal is to treat patients with cancer with clinically active therapeutics that have a high likelihood of success based on predicted sensitivity to our drug candidates. Oncology is an area of high unmet clinical need, in which only a small fraction of patients currently benefit from existing predictive biomarkers, such as next-generation sequencing, or NGS. We are currently applying the AP3 technology to both in-licensed clinical stage and to internally developed drug candidates for tumors that do not harbor single gene driver mutations, which is estimated to be more than 90% of all human cancers. The relevant drug target classes in these tumors that we believe are well-suited for our AP3 approach include but are not limited to DDR pathways, DNA replication stress, super enhancers, and cell cycle and transcriptional regulators. We are initially focused on expedited clinical development of our clinically advanced asset ACR-368, in our upcoming Phase 2 trial in patients with platinum-resistant ovarian, endometrial, or bladder cancers, followed by staggered development of ACR-368 in HPV^+ cancers. This trial is based on OncoSignature-predicted sensitivity to ACR-368 and has recently been cleared by the FDA to be conducted under a master protocol. In addition, we intend to continue to leverage AP3 for our internally developed preclinical programs targeting WEE1/PKMYT1 and a cell cycle program. The key elements of our strategy summarized below are to:

- **Advance ACR-368, our CHK1/2 inhibitor, through clinical development in ovarian, bladder, and endometrial cancer by enrolling ACR-368 OncoSignature-positive patients**. Our lead program, ACR-368, has already demonstrated deep, durable anti-tumor activity, including CRs, in patients with ovarian cancer in past clinical trials. Based on our robust preclinical data, including in two blinded, prospective studies on pretreatment tumor biopsies from past ovarian cancer trials with ACR-368, we believe that our ACR-368 OncoSignature test will lead to significant improvement in ORRs in ovarian cancer as compared to the ORR seen in the previous trials. Based on human tumor sample profiling, we expect around 30% of patients with ovarian cancer to be ACR-368 OncoSignature-positive and these patients will receive ACR-368 monotherapy in a single arm Phase 2 clinical trial. Additionally, through screening with our ACR-368 OncoSignature test we predict that patients with other solid tumor types of high clinical unmet need, including 30% to 40% of patients with endometrial and bladder cancer, could benefit from ACR-368 monotherapy. We have further confirmed this prediction in preclinical studies on PDX models of these two tumor types where we observed that these tumors were highly sensitive to ACR-368, and that our ACR-368 OncoSignature test was able to prospectively identify which models are the most sensitive. We have begun enrolling and dosing patients in Phase 2 clinical trials in these tumor types, reported

encouraging initial clinical observations in November 2023, and expect to report more mature clinical data during the first half of 2024. In the OncoSignature-positive patients, after completion of the Simon Stage 1 and pending the results and discussions with the FDA, we intend to enter the registrational phase during 2024.

- **Selectively pursue AP3 identified rational drug combinations with our drug candidates in OncoSignature-negative patients, initially ACR-368 with LDG**. Our AP3 platform is able to elucidate pathways of underlying tumor resistance mechanisms, both pre-existing (intrinsic) and acquired (therapy-induced). This allows us to identify rational drug combinations that can re-sensitize ACR-368 OncoSignature-negative patients to our drug candidates in resistant tumors. For example, we have shown that LDG was highly synergistic with ACR-368 in resistant human tumor cell lines and was able to re-sensitize ACR-368 resistant tumors to ACR-368, in ovarian, bladder, and endometrial cancers. Based on these findings, we are conducting a Phase 1b/2 clinical trial with ACR-368 in combination with LDG for patients that are ACR-368 OncoSignature-negative within these tumor types. Work is now proceeding to advance into the exploratory Phase 2 dose expansion portion of the study utilizing the newly established RP2D for low dose gemcitabine and the previously established RP2D for ACR-368 for all three tumor types - ovarian cancer, endometrial adenocarcinoma and urothelial cancer. We reported encouraging initial clinical observations in November 2023, and expect to report more mature clinical data during the first half of 2024.

- **Discover and develop a pipeline of proprietary drug candidates by leveraging our AP3 platform and predictive OncoSignature tests**. We are applying our AP3 platform in multiple ways to build and advance a pipeline of structure-guided, wholly owned precision oncology drug candidates. The first of these, ACR-2316, is a novel dual WEE1 and PKMYT1 inhibitor small molecule development candidate, rationally designed through advanced co-crystallography and the AP3 platform to achieve optimal target potency and selectivity, delivering potent single agent anti-tumor activity across in vitro and in vivo preclinical studies, compared to benchmark WEE1 and PKMYT1 inhibitors. While WEE1 inhibitors have shown single agent clinical activity across patients with solid tumors of high unmet need, the ORR so far has been insufficient for approval and, despite significant efforts in identifying patient responders, these efforts have not been fruitful to date. We believe that with our AP3 platform and OncoSignature patient selection strategy, we can significantly enrich the ORR for responders sufficient for approval. The ACR-2316 program is currently in IND-enabling studies and is anticipated to be ready for IND-submission by the fourth quarter of 2024. We also have a cell cycle program for which we anticipate nominating a development candidate in 2025. All of our internally derived drug candidates will leverage AP3 phosphoproteomic drug candidate profiling to guide and optimize drug potency and selectivity. We believe that this approach will help ensure that our drug candidates directly affect the pathways of interest while minimizing off-target effects, an approach that is highly differentiated from traditional drug discovery programs. Additionally, by developing OncoSignature tests tailored for our pipeline drug candidates we believe we can identify patients with highly sensitive tumor types of high unmet clinical need for treatment before initiation of our clinical trials.

- **Acquire rights to drug candidates for which we believe our OncoSignature tests can increase the likelihood of clinical success**. We in-licensed ACR-368 after successfully developing a predictive ACR-368 OncoSignature test to increase the probability of clinical success. We intend to take a similar approach and in-license other attractive drug candidates where genetics-based patient selection is challenging or impossible, and develop drug-tailored OncoSignature tests for these drug candidates. We intend to pursue only the opportunities that, similar to ACR-368, have high clinical potential and where we believe we can successfully select patients who are likely to respond to such specific drug candidates, based on our proprietary OncoSignature tests.

- **Opportunistically enter into strategic co-development partnerships around predictive OncoSignature tests to maximize the full potential of our AP3 platform**. We believe that there are opportunities to partner with organizations that have approved drugs or drug candidates in development under competitive pressure and where the availability of a highly predictive OncoSignature test to achieve high ORRs can potentially provide an advantage in obtaining regulatory approval and market share. Moreover, we believe that identification of rational drug combinations for such drugs to improve ORR and clinical benefit are of high value to prospective partners. We intend to pursue such partnerships where we can realize the value that OncoSignature and our AP3 platform can bring to the drug candidate through early co-development.

Urgent Need for Precision Oncology Approaches that Transcend the Limitations of Genomics

Cancer is a disease of dysregulated protein activity, which occurs as a result of underlying genetic changes. The majority of precision medicine efforts in oncology have been focused on identifying patients who are most likely to respond based either on genetic changes in their tumors, such as specific mutations, gene amplifications, and gene translocations, or on the patient's own genetic background. The availability of genomic sequences from tens of thousands of tumors has begun to transform oncology treatment away from the use of broad cytotoxic drugs approved based on tumor location towards precision medicines that address tumors with specific genetic alterations. However, while this approach has led to the recent approval of a number of targeted therapies, their use is limited to a very small fraction of patients with these mutations. It is estimated that only 9% of all patients with cancer have tumors with genetic profiles that make them eligible for an available precision oncology medicine, so-called genetically-defined cancers, and only 5% of all patients with cancer are likely to benefit from available therapies.

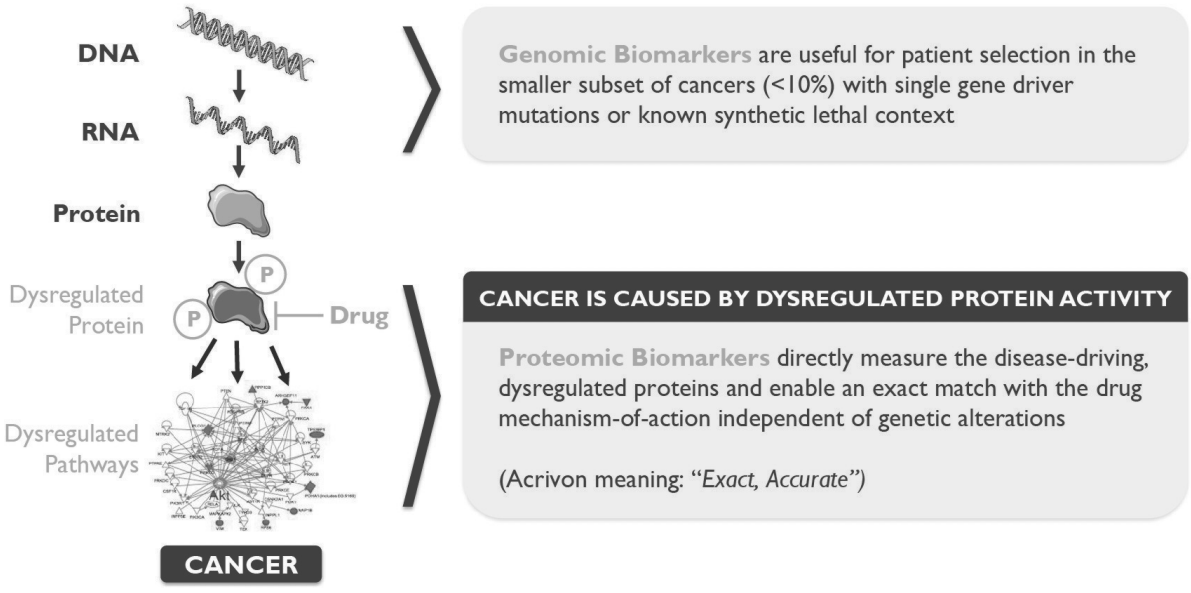


Figure 3. Proteomic biomarkers have the potential to be broadly applicable across the vast majority of cancers.

Proteomic biomarkers have the potential to be broadly applicable for the vast majority of cancers where more traditional genetics-based approaches have proven challenging. In this small subset of genetically defined cancers, most often the alterations in the gene lead to drug target protein dysregulation that drives the cancer, which are potential targets of cancer therapies. There are three main types of such recurrent single driver gain-of-function, or GOF, gene alterations known in human cancer: point mutations, gene fusions, and amplifications, which represents less than 10% of all cancers. These most easily addressable GOF mutation-driven cancers have been the obvious focus of drug discovery and development for more than two decades. Examples of such approved drugs include Vemurafenib for B-RAF-V600E-mutant melanoma, Imatinib for KIT and PDGFR-alpha mutant GIST, Crizotinib for EML4-ALK+ lung cancer, Trastuzumab for HER2 amplified breast cancer, Larotrectinib for solid tumors with N-TRK fusions, and most recently, Retevmo for patients with RET-mutated tumors. However, more than 90% of cancers have tumor-driving targets that do not harbor underlying single genetic alterations. Such tumor-driving drug targets are activated through post-translational modifications, including phosphorylation, due to complex genetic alterations elsewhere in the genome of tumor cells, rather than in the drug target itself. Successful clinical development of inhibitors for these targets is highly challenging as prevailing predictive methods such as NGS, polymerase chain reaction, or PCR, fluorescent *in-situ* hybridization, or FISH, immunohistochemistry, or IHC, and transcriptomics have not been successful in identifying patients that would significantly benefit from the drug.

Accordingly, while a powerful tool to uncover underlying mechanisms of disease, the utility of genomics for patient selection is limited when it comes to drug response prediction in oncology. Additionally, the lack of therapeutic efficacy for a given drug, due to inability to identify patient responders, is still a top attrition factor in drug development. The vast majority of cancers contain multiple, complex genomic alterations resulting in the dysregulated, tumor-driving protein activity. Relatively few genetic alterations are common to a broad percentage of patients with cancer, such as mutations in the K-RAS or p53 genes. However, precision medicines against these targets have been difficult to develop and, because of the complex genetic alterations often co-existing in tumors, treatment often does not elicit expected clinical benefit.

The AP3 Solution: Matching Drug Action to the Disease-driving Mechanisms in Patients' Tumors

Our AP3 platform has been developed over the last decade to be an efficient process and workflow to determine sensitivity to drugs based on the biological signaling pathways that are activated in diseased cells and are required for their survival. Our AP3 platform leverages proteomic biomarkers which enable direct measurement of disease-driving mechanisms independent of target gene alterations, and allow for accurate matching with the mechanism of action of a particular drug. For example, in the case of ACR-368, which is a selective CHK1/2 inhibitor, the three biomarkers we quantify with our ACR-368 OncoSignature assay measure the level of activated DNA repair downstream of the activated drug targets and whether the tumor likely depends on it. One biomarker is a specific phosphorylation site in the drug target and another is a specific phosphorylation site in a key DNA repair protein, which together inform us about their functional activity. The third is a protein that drives premature DNA replication, which implies that the tumor is dependent on the upregulated DNA repair measured by the two other biomarkers. We have designed our proprietary AP3 platform to be agnostic to the underlying genetic alterations in the genome and enable identification and treatment of patients based on direct measurement of the disease-driving mechanisms that are regulated by and sensitive to the drug. Hence, in contrast to measuring genetic alterations in a patient's tumor, which is only a surrogate read-out for protein dysregulation, and having to infer whether the drug will act on the inferred protein dysregulation, the AP3 method directly reveals the dysregulated proteins and pathways driving the tumor that the drug acts on. The AP3 method is drug-tailored, and we believe enables an accurate match *(*Acrivon is derived from Greek for "accurate") between the mechanism of the drug action with the disease-driving mechanisms in the patient's tumor.

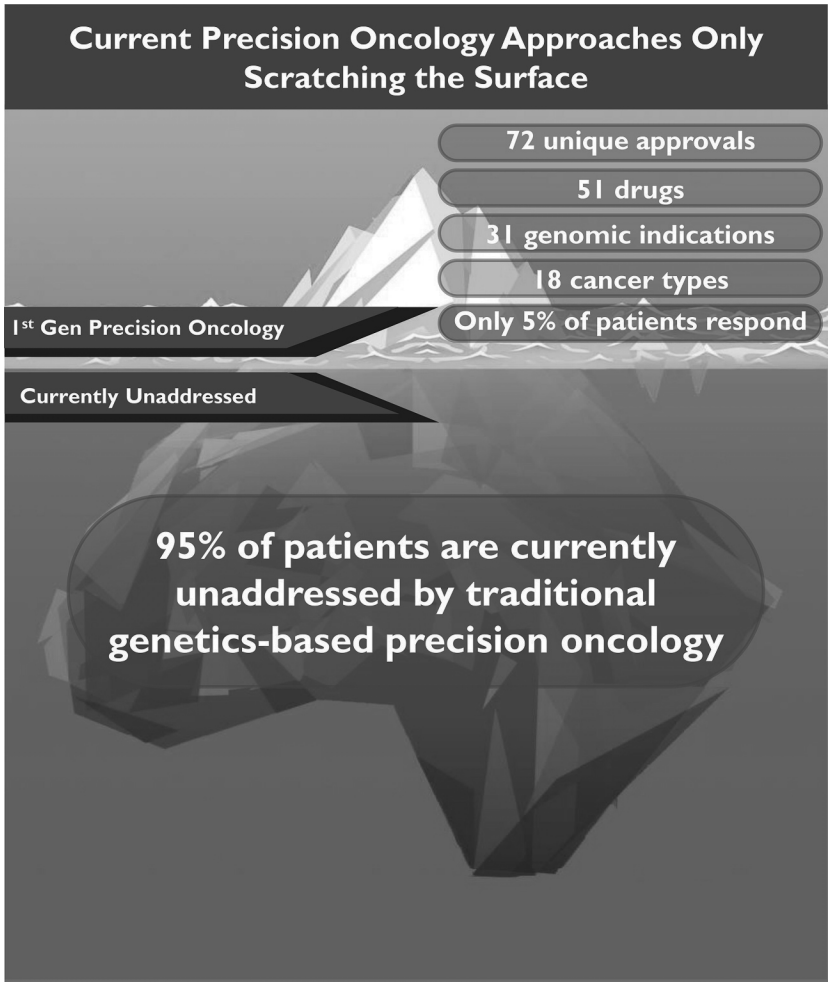


Figure 4. We are applying AP3 to develop drug candidates with the potential to serve the high unmet clinical needs of the 95% of patients currently unaddressed by precision oncology.

Our AP3 platform is fundamentally different from genetics-based methods to identify patient responders and we believe it is particularly applicable to the majority of cancers without genetic alterations in the drug target itself. It specifically focuses on the proteins and pathways that drive tumor growth and survival and enable drug action, rather than exploring complex biology and accumulated genetic alterations that have proven very difficult to connect to drug response.

While the principles and technology behind AP3 are not limited to cancer, we are initially committed to oncology, where we are applying AP3 to develop drug candidates with the potential to transform the treatment of solid tumors of high unmet clinical need. Strategically, we are applying AP3 to drug classes where genetics has proven difficult or insufficient for response prediction, and that are active in major fractions of solid tumors, but where the ORR is insufficient for approval without a prospective patient responder identification method. In addition to DDR pathway inhibitors such as ATR, ATM, WEE1, and CHK1/2, examples of drug classes that we believe would benefit from our AP3 platform include cell cycle regulators (such as CDK2, 4, 6), mitotic regulators (such as Aurora kinases), transcriptional regulators, DNA replication modulators, such as CDC7, super enhancer kinases (such as CDK7, 9, 12), and inhibitors of mutated forms of K-RAS. We believe our ability to apply AP3 to these drug classes allows us to open up the potential of precision medicine approaches to a much larger fraction of patients than has been possible using exclusively genetics-based approaches. We are initially progressing a pipeline of DDR and cell cycle drug candidates, but intend to broaden our pipeline to some of these other drug classes and targets through OncoSignature patient responder identification.

Our AP3 platform is based on two underlying technology pillars typically executed in two sequential steps: the first step, a high-resolution MS for biomarker identification which is integrated with, the second step, our automated tumor biopsy-imaging biomarker platform that enables biomarker validation and which is also used to run our OncoSignature tests.

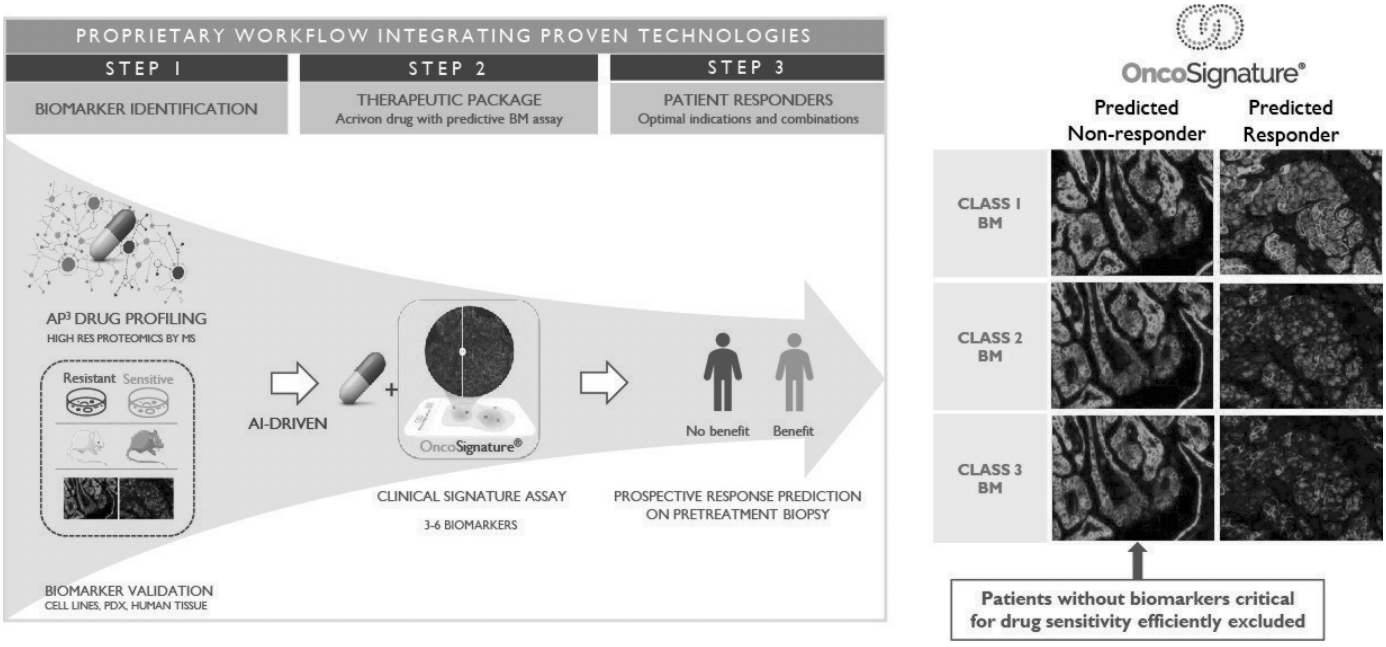


Figure 5. Our AP3 platform is based on unbiased biomarker identification using global phosphoproteomic profiling by MS and an automated biomarker platform for our clinical OncoSignature tests.

MS enables a systematic, unbiased quantitative measurement and analysis of the proteins inside a cell or entire tissues. We specifically use it to identify and measure in an unbiased manner the effects of any given drug or drug candidate on the activity state of the protein signaling networks inside a cell through analysis of the phosphorylation state and levels of proteins inside a tumor cell. Phosphorylation is the best-studied, allosteric on-off switch regulatory mechanism for protein activity involved in all forms of intracellular signaling. Analysis of the entire phospho-proteome before and after drug treatment, so-called phosphoproteomic drug profiling, enables us to objectively identify the global effect of any drug on the activity state of the protein signaling network.

Our MS efforts allow us to identify attractive drug-regulated biomarker candidates, which include identifying changes in overall protein levels as well as in post-translational modifications of proteins, such as those that involve phosphorylation and are involved in activation or inhibition of protein function in biological signaling pathways. Our data-independent acquisition, label-free phosphoproteomic methods provide for very high resolution. Starting with lists of thousands of potential biomarker candidates that correlate with drug sensitivity and resistance, our proprietary algorithms and workflows distill biomarker candidates into three functionally defined classes. The biomarkers are further validated in tumor models and through quantitative measurements on PDX models as well as on patient tumor samples and, when available, clinical trial biopsies, as we have done with ACR-368.

Use of our AP3 platform to develop drug-tailored, predictive OncoSignature tests

One of the key outputs of our AP3 platform are our drug-tailored OncoSignature tests, which are based on an assembly of biomarkers from each of the three classes selected by the process described above, resulting in a single, quantitative signature test. They are automated, quantitative protein imaging tests designed to be applied to pretreatment tumor biopsies as a CDx to select and treat the patients predicted to benefit from the specific drug candidate for which they are developed. The tests are developed for routine-processed, paraffin-fixed biopsy tissue and stained with fluorescently labeled antibodies against the OncoSignature biomarkers. Digital images of these stained tissues are then processed by proprietary software that identifies both tumor cells and tumor cell nuclei. They are quantitatively measured in only defined tumor tissue regions of a patient biopsy where they function, called the "region-of-interest," or ROI. A proprietary algorithm assesses the quantitative level of each biomarker and combines them to predict the likely response to a drug or drug candidate.

The AP3 approach is designed to provide a streamlined, rationale-driven workflow to identify and validate biomarkers. Every OncoSignature test is drug-tailored. Our process to generate an OncoSignature test, including technical biomarker validation, can be completed in approximately two to three months. It measures three functionally defined classes of biomarkers that in combination are predictive of sensitivity to the particular drug. Each biomarker class can contain more than one biomarker, but we typically measure only one in each class for a total of three biomarkers. A key rationale is that patients whose tumors do not harbor the specific protein disease-driving mechanisms that are sensitive to the drug are predicted to be unlikely to respond to a particular drug or drug candidate and hence can be excluded from treatment.

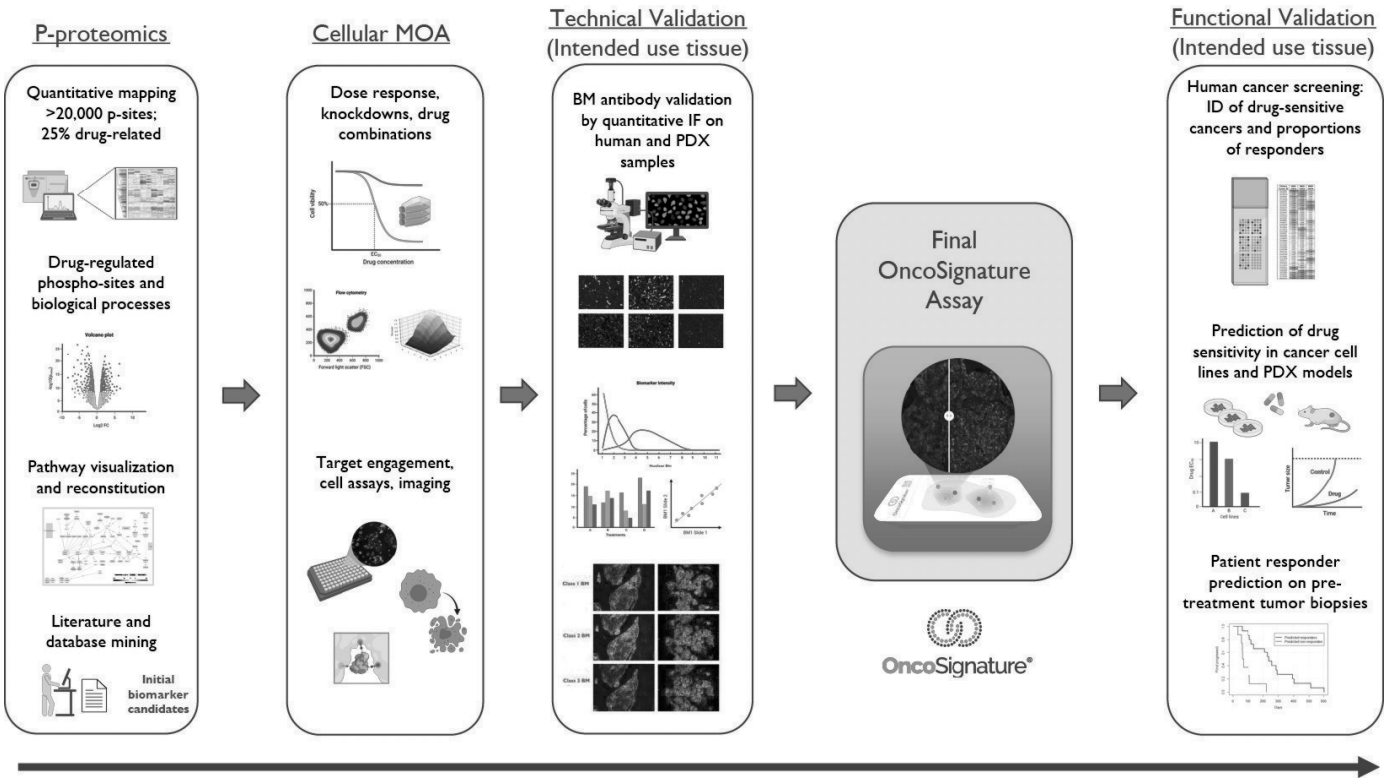


Figure 6. AP3 approach for streamlined development and validation of predictive OncoSignature tests.

In order to create an OncoSignature test that can be readily performed on clinical samples, we qualify monoclonal antibodies for the prioritized set of three biomarkers. These antibodies are chosen based on our systematic evaluation of their specificity and sensitivity including correlation in changes in biomarker levels with drug sensitivity in cell lines and, most importantly, their technical performance on human intended use FFPE-processed cancer tissues as well. This technical validation ensures specificity (that it only recognizes the biomarker of interest), dynamic range (the fold changes of the biomarker level across tumor samples), and proper intensity. The technically qualified antibodies are then assembled into a final drug-tailored predictive OncoSignature test that is functionally validated in a blinded, prospectively designed manner in various preclinical studies. These include prediction of drug sensitivity across human tumor cell lines, in PDX models, and across human tumor samples, and, when available, on pretreatment tumor biopsies collected from past trials with the drug or drug candidate. Using our AP3 platform workflow, we have developed and evaluated in preclinical studies an OncoSignature predictive test for ACR-368, as further described below. We have also developed and done preliminary validation for two prototype OncoSignature tests for two other clinical stage assets, a CDK7 and a CDC7 inhibitor, for which genetics-based patient selection has also proven challenging.

The ACR-368 OncoSignature test has been transferred as a clinical trial assay under an exclusive license to our external companion diagnostic partner, who is running our test during our ongoing clinical trial, and developing it into a companion diagnostic test which they will also commercialize, pending regulatory approval. The tests are performed on a standard, routine processed pre-treatment tumor biopsy with an anticipated turnaround time of five to seven business days. We intend to protect all our drug-tailored OncoSignature tests via patents for their tumor-agnostic usage across cancers.

Figure 7. Our OncoSignature tests are applied to pretreatment tumor biopsies and will be offered by our CDx partner with an anticipated turn-around time of five to seven business days.

Enablement of AP3 through our team's expertise

The enablement of the AP3 approach as a means to realize the potential of proteomic drug profiling and protein signature tests in precision medicine is the result of the vision of our founders and their long-standing expertise in the field, including pioneering the underlying AP3 technologies and implementation experience. Three critical aspects behind AP3 are:

- **Founding concept and vision**. Our founders are leaders and respected authorities in the understanding of oncogenic kinase signaling, protein dysregulation through tyrosine phosphorylation, and the relationship of each to human cancer. Our vision was embedded in the 2001 *Nature* review article, "Oncogenic kinase signaling," by our founder Peter Blume-Jensen, which became a citation classic in the field of medicine. It described how cancer and other diseases are inevitably driven by dysregulated protein signaling resulting from either very simple or complex underlying genetic alterations. The paper linked simple GOF mutations in a class of proteins called tyrosine kinases with their disease-driving dysregulation and involvement in a certain small subset of human cancers. Our founding vision is that proteomic biomarkers enable direct measurement of the disease-driving mechanisms and allow for accurate matching with drug action, independent of underlying genetic alterations.

- **Technical expertise and implementation experience**. The two underlying technologies used in a stepwise manner in our AP3 platform, (1) high resolution MS for quantitative protein and protein phosphorylation analysis and (2) the automated biomarker platform, have been pioneered and established by our founders and team and integrated into a content system and approach. Jesper Olsen, our academic co-founder, is a recognized world leader in the use of MS-based phosphoproteomics, or the study of protein phosphorylation and its impact on biology. Dr. Olsen is one of the most highly cited authors in this field. Our co-founder, Kristina Masson, has established the entire infrastructure for phosphoproteomics at our subsidiary in Medicon Village, Lund, Sweden in close proximity with Dr. Olsen's laboratory in Copenhagen, Denmark. Our OncoSignature technology is enabled by this comprehensive proteomics infrastructure and demonstrated proof-of-concept for the first unbiased MS step in the AP3 approach, resulting in identification of resistance mechanisms and rational drug combinations with the potential to be tested in controlled clinical trials with the drug selinexor in acute myeloid leukemia. This work was published in *Cell Reports* on August 9, 2022.

Peter Blume-Jensen led the first proof-of-concept for unbiased identification of drug-regulated PD biomarkers for PI3'K pathway-targeted agents through an MS-based phosphoproteomics approach. Under his leadership, our team also led the establishment of our automated biomarker platform and the research and development of ProMark, a proteomics eight biomarker imaging test for prostate cancer outcome prediction launched by Metamark. That test was validated in a blinded trial and was subsequently included in the NCCN Clinical Practice Guidelines. Through this experience, we understand the technical and regulatory challenges involved in developing and implementing a clinically meaningful proteomic test, and we fully leverage and factor these insights into the design of our OncoSignature tests.

ACR-368, Our Phase 2 Lead Candidate

Our lead drug candidate, ACR-368, also known as prexasertib, is a selective inhibitor with sub single-digit potency against CHK1 and single-digit potency against CHK2. ACR-368 was originally discovered by Array BioPharma and acquired by Lilly, who evaluated the compound in over 1,000 patients across 18 clinical trials, where it demonstrated deep, durable single agent activity, including CRs, in a proportion of patients across several Phase 2 studies of platinum-resistant ovarian cancer and other solid tumors. Despite the demonstrated clinical activity in a proportion of patients, there was no obvious patient selection strategy to improve responses sufficient for approval. We chose to in-license ACR-368, prioritizing it over other carefully evaluated candidates, based on multiple criteria, including its proven clinical single agent activity, extensive safety data set and extensive comparison work and in-house AP3 profiling.

We have begun enrolling and dosing patients in our Phase 2 trial of ACR-368 in patients with ovarian, endometrial, or bladder cancer based on OncoSignature-predicted sensitivity to ACR-368. We reported encouraging initial clinical observations from this trial in November 2023 and expect to report more mature clinical data during the first half of 2024. Patients who test ACR-368 OncoSignature-positive receive ACR-368 monotherapy in a single arm Phase 2b trial, while ACR-368 OncoSignature-negative patients receive ACR-368 in combination with LDG in the Phase 1b/2 single arm trial. In the OncoSignature-positive patients, after completion of the Simon Stage 1 and pending the results and discussions with the FDA, we intend to enter the registrational phase during 2024. We also plan to study ACR-368 in one or more additional indications, such as HPV^+ squamous cell carcinomas, including SCCHN, anal, and cervical cancer, based on demonstrated clinical single agent activity in SCCHN and anal cancer and OncoSignature-based prediction of sensitivity to ACR-368 in a proportion of patients. Akoya is procuring and manufacturing the necessary supplies to perform the OncoSignature tests used in our Phase 2 clinical trial.

ACR-368, a selective inhibitor of CHK1 and CHK2, key DDR regulators

CHK1 and CHK2 are checkpoint proteins that prevent cell replication when DNA damage is present. In the absence of DNA damage, CHK1 and CHK2 are largely inactive. Most normal tissues, other than certain dividing cells such as those in bone marrow, are not reliant on DDR mechanisms such as CHK1 and CHK2, and hence not subject to the negative side effects from such inhibitors. In contrast, inhibition of the kinase activity of these proteins or knockdown of their expression by RNA interference in certain G1/S checkpoint-deficient tumor cells has been shown to prevent repair of double-strand DNA breaks resulting in cell death. Treatment of cells with DNA damaging agents or inhibitors of other proteins involved in the DDR, sensitizes them to cell killing by CHK1 and CHK2 inhibitors.

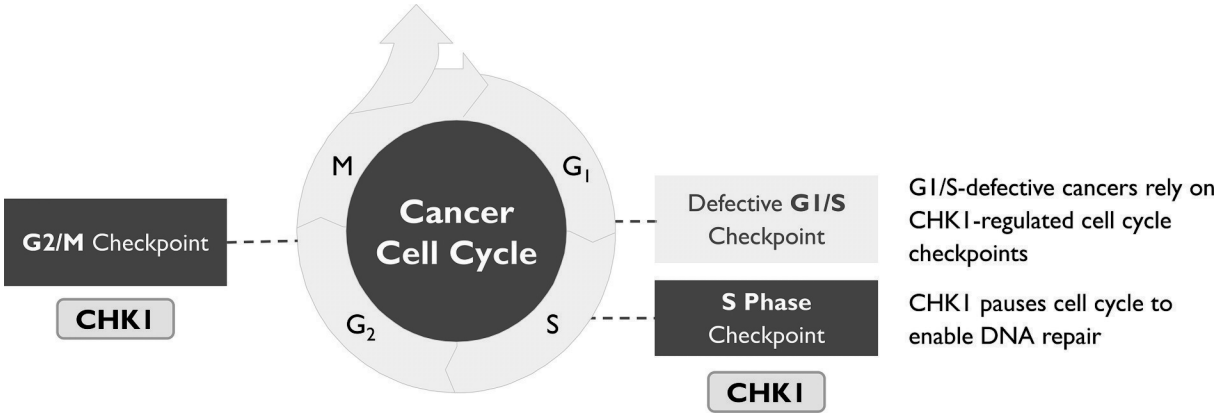


Figure 8. CHK1 functions as a cell cycle checkpoint to inhibit DNA replication when DNA damage is present.

ACR-368 is a selective CHK1/2 inhibitor with a potency of less than 1 nM against CHK1 and 8 nM against CHK2. In preclinical studies, ACR-368 inhibited growth with a potency of less than 100 nM in over 75% of 600 cancer cell lines screened, including a potency of less than 50 nM in 16 of 23 tested ovarian cancer cell lines. ACR-368 as a single agent led to complete tumor regression in approximately 40% of 38 ovarian cancer PDX models tested. Significant anti-tumor activity was also observed in other tumor models such as sarcomas and neuroblastoma. The anti-tumor activity of ACR-368 was enhanced in preclinical models when it was combined with DNA damaging agents such as cisplatin and gemcitabine.

Clinical development of ACR-368 for patients with ovarian and other solid cancers of high unmet treatment need

We are developing ACR-368 for the treatment of patients with advanced solid tumors including ovarian, endometrial, and bladder cancers. ACR-368 has demonstrated deep, durable single agent anti-tumor clinical activity, including CRs, in a proportion of more than 400 patients treated at RP2D in past clinical trials conducted by Lilly, its previous sponsor, and in several investigator-initiated trials, including at the NCI and at MDACC. Importantly, ACR-368 was well-tolerated in these trials, exhibiting primarily reversible, manageable hematological adverse events and limited dose-limiting non-hematological adverse events. Accordingly, there have been no clinical or regulatory holds reported and less than 2% drug-related discontinuations across all trials to date. Without the use of the OncoSignature test, the ORR in the single center Phase 2 study at NCI was 29%, and the confirmed ORR in a 169-patient Phase 2 trial conducted in 46 centers across eight countries in platinum-resistant ovarian cancer was approximately 12%. By pairing ACR-368 with our compound-specific OncoSignature test, we believe we can significantly increase the ORR by targeting treatment to the patients that are predicted to be most dependent on CHK1/2, and therefore more likely to respond.

Based on our preclinical studies, which include blinded, prospective studies of ACR-368 OncoSignature test on pretreatment tumor biopsies collected from patients treated with ACR-368 in the past ovarian trials, we expect 30% to 40% of patients in our three lead indications, platinum-resistant ovarian, endometrial, and bladder cancer, will be ACR-368 OncoSignature-positive. We expect the ORR to be significantly amplified and, if the data are sufficient, we will aim for single-agent, single-arm approval. These patients are treated with ACR-368 in a Phase 2 trial at the RP2D. The remaining 60% to 70% of ACR-368 OncoSignature-negative patients receive ACR-368 at the RP2D with LDG, which we have found to be highly synergistic with ACR-368 using our AP3 platform in preclinical studies. We are currently enrolling and dosing patients in the ongoing study in these three tumor types; initial clinical observations, as reported in November 2023, are encouraging and support the ongoing trials. We expect to report more mature clinical data from the ongoing Phase 2 ACR-368 monotherapy single-arm trials and the Phase 1b/2 ACR-368 and LDG combination single-arm trials during the first half of 2024.

Ovarian cancer background

Ovarian cancer is the fifth deadliest cancer in women, accounting for more deaths than any other cancer of the female reproductive system. An estimated 19,710 women in the United States are projected to be diagnosed with ovarian cancer and approximately 13,270 will die from this disease in 2023 based on projections from the American Cancer Society. The overall five-year survival rate in patients with ovarian cancer is 50% but drops to 31% in patients with metastatic disease.

Surgery and cytotoxic chemotherapies are widely used to treat patients with ovarian cancer. One of the primary chemotherapies involves the use of platinum containing regimens such as carboplatin or cisplatin. Approximately 85% to 90% of patients with high-grade ovarian carcinoma initially respond to these drugs, but in over 80% of cases, these cancers return and are considered platinum-sensitive as long there is more than 6 months between the last cycle of platinum and recurrence. However, most of them will ultimately progress within 6 months after the last exposure to carboplatin and will then be considered platinum resistant. For these patients, there are few remaining treatment options, including bevacizumab with chemotherapy or PARP inhibitor as maintenance therapy for some patients. On November 14, 2022, Mirvetuximab soravtansine has received FDA conditional accelerated approval with a black-box warning (severe ocular toxicities), for patients with folate receptor alpha-high who have been previously treated with 1 to 3 prior systemic treatments. Currently, only about 12% of platinum-resistant patients achieve tumor shrinkage with standard of care chemotherapy and, on average, survive for no longer than a year.

Endometrial cancer background

Endometrial cancer is a cancer of the lining of the uterus that primarily affects post-menopausal women. The American Cancer Society estimates that in the United States there will be 66,200 new cases of endometrial cancer and approximately 13,030 patients will die of this disease in 2023. First-line treatment for patients with localized, early-stage disease is surgery with radiation therapy. Patients with more advanced disease, stages III or IV, especially high-grade, are treated with chemotherapy, typically with platinum-based drugs. Approximately 60% of patients with endometrial cancer initially respond to these treatments; however, similar to ovarian cancer, resistance develops to these drugs. These patients with platinum-resistant disease are treated with immune checkpoint inhibitor PD-1/PD-L1 combined with lenvatinib, a pleiotropic receptor tyrosine kinase inhibitor. There is no standard of care in later lines or therapy. Five-year survival for patients with metastatic endometrial cancer is approximately 20%.

Bladder cancer background

Bladder cancer is the most common malignancy involving the urinary system, and 90% of bladder cancer cases are urothelial carcinomas. The five-year survival for patients with early-stage disease is 96%; however, for patients with advanced metastatic disease the five-year survival drops sharply to less than 10%. The American Cancer Society estimates that there will be 82,290 new cases of bladder cancer and 16,710 deaths in the United States in 2022.

The most common treatment for patients diagnosed with advanced or metastatic bladder cancer is chemotherapy with platinum-based drugs such as cisplatin or carboplatin, or, if cisplatin-ineligible, chemotherapy in combination with gemcitabine. Patients with metastatic disease that progress during or after platinum-based chemotherapy are increasingly being treated with immune checkpoint inhibitor therapy. A number of PD-1 and PD-L1 checkpoint inhibitors have been approved by the FDA for use in refractory bladder cancer. Objective ORRs in clinical trials with checkpoint inhibitors have been approximately 15%. On July 9, 2021, enfortumab vedotin, a nectin-4-directed antibody drug conjugate was approved for patients that have progressed after treatment with immune checkpoint inhibitors PD-1/PD-L1 and a platinum-containing chemotherapy. The ORR is about 40%, but eventually the disease progresses, and the median overall survival is approximately 12 months. On December 20, 2022, the FDA granted priority review for enfortumab vedotin and prembrolizumab in locally advanced or metastatic disease for patients who are ineligible to receive cisplatin-based chemotherapy. In December 2023, enfortumab vedotin received full approval in combination with pembrolizumab, for the treatment of adult patients with locally advanced or metastatic urothelial cancer. As single agent, it is indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma who have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor and platinum-containing chemotherapy, or are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy.

Only an estimated 20% of patients with bladder cancer have alterations in the FGFR2 or FGFR3 genes. In clinical testing, erdafitinib, an FGFR-targeted drug, has demonstrated a 32% ORR with 2% of patients achieving CRs. On January 19, 2024, the FDA approved erdafitinib for patients with locally advanced or metastatic urothelial carcinoma with susceptible FGFR3 genetic alterations, as determined by an FDA-approved companion diagnostic test. Despite the availability of these therapies, the prognosis for patients with metastatic bladder cancer is still poor with a five-year survival rate of only 8%.

HPV+ squamous cell carcinoma background

Squamous cell carcinomas are cancers that develop in the squamous cells that make up the outermost layer of the mucosa. More than 90% of anal cancers and cervical cancers and about 70% of SCCHN (the oral/oropharyngeal sub-group) are linked to infections with HPV. There are over 46,000 HPV+-associated cancers diagnosed in the United States each year and up to 5% of cancers worldwide are potentially caused by HPV+ infections.

Unlike many cancers, HPV+ cancers are not typically driven by high levels of genomic instability but rather by alterations in cell cycle regulation, including upregulation of DDR pathways. Certain HPV+ cancers, primarily SCCHN and cervical cancer, respond to PD-1 or PD-L1 immune checkpoint inhibitor therapy with ORR of approximately 20%, as single agent or in combination with chemotherapy, depending on the line of therapy and the level of PD-L1 expression in the tumor. Several PD-1/L1 inhibitors have received FDA approval for use in patients with metastatic or unresectable recurrent head and neck squamous cell carcinoma, in combination with platinum and fluorouracil or as a single agent for patients whose tumors express PD-L1 as determined by an FDA-approved test. On October 13, 2021, the FDA approved pembrolizumab in combination with chemotherapy, with or without bevacizumab, for patients with persistent, recurrent or metastatic cervical cancer whose tumors express PD-L1, as determined by an FDA-approved test. FDA also granted regular approval to pembrolizumab as a single agent for patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumors express PD-L1 as determined by an FDA-approved test.

Sarcoma background

In addition to previously demonstrated clinical activity in the above tumor types as monotherapy, ACR-368 has also shown clinical activity in patients with certain sarcoma subtypes in combination with various chemotherapeutic agents. Patients with sarcomas have very limited treatment options, primarily surgery, chemotherapy, and radiation, depending on the subtype. The five-year survival for patients with metastatic soft tissue sarcomas is approximately 17%.

Previous clinical trials of ACR-368 have demonstrated compelling, durable single agent activity in a proportion of patients with various tumor types

In previous clinical trials, conducted prior to the development of the ACR-368 OncoSignature test, ACR-368 has demonstrated deep, durable single agent activity, including CRs, in a proportion of more than 400 patients with high-grade serous, primarily platinum-resistant, ovarian cancer and SCC treated at RP2D. Overall, ACR-368 has been tested in 18 clinical trials as monotherapy or in combination with both targeted agents and chemotherapy in over 1,000 patients across primarily solid tumor types and has shown a generally favorable safety profile.

Phase 1a/b trial in squamous cell carcinoma established single agent clinical activity and the RP2D

A 146-patient Phase 1 multicenter trial was conducted in patients with refractory or recurrent squamous cell carcinoma and led by Dr. David Hong at MDACC. The trial included patients with SCCHN, sqNSCLC, and anal cancer. The primary objective of the Phase 1b expansion cohorts was to determine the safety, toxicity, and RP2D of ACR-368. In addition, the ORR according to Response Evaluation Criteria in Solid Tumors, or RECIST, version 1.1 for patients with specific types of SCC was recorded.

The RP2D was established at 105 mg/m^2 given as an intravenous infusion every 14 days, and used in the expansion phase for 101 patients. The study demonstrated clinical monotherapy activity of ACR-368, with a 5% ORR in SCCHN and 15% ORR in anal cancer. The mDoR was seven months and over 12 months, respectively, including a CR in anal cancer. Based on these results and the lack of highly effective treatments, ACR-368 has been granted FDA Orphan Drug Designation, or ODD, for the treatment of anal cancer.

Of note, approximately half of the patients with SCCHN were HPV+ and showed a significantly higher ORR of 19% in response to ACR-368—a similar finding to the ORR recorded in patients with anal cancer, which is almost obligate HPV+. This was reflected in

a markedly longer progression-free survival, or PFS, in HPV$^+$ compared to HPV-negative, or HPV$^-$, patients, with some HPV$^+$ patients benefiting from therapy well over 12 months while no HPV$^-$ patients had benefit beyond five months (Fig. 9.).

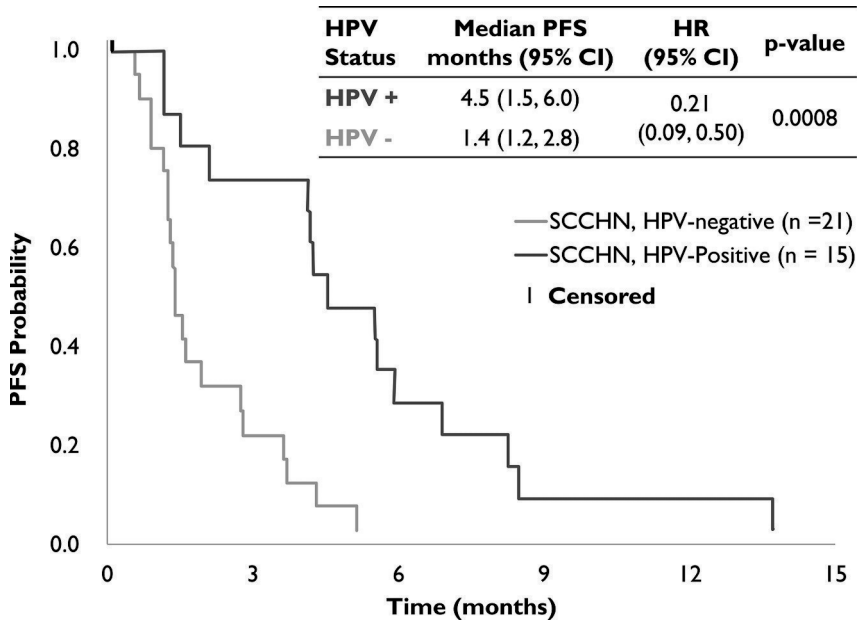


Figure 9. ACR-368 treatment resulted in a significant improvement in progression-free survival in patients with HPV$^+$ SCCHN compared to patients with HPV$^-$ SCCHN.

In this trial, as in most of the other clinical trials with ACR-368, an attempt was made to identify biomarkers predictive for response to ACR-368 in pretreatment tissue samples by NGS. In an analysis of genetic changes in 24 genes involved in DDR or increased replication stress, no obvious correlation with clinical response was observed. This lack of correlation between genetic changes and clinical response underscores the need for an alternative patient responder identification method, such as AP3.

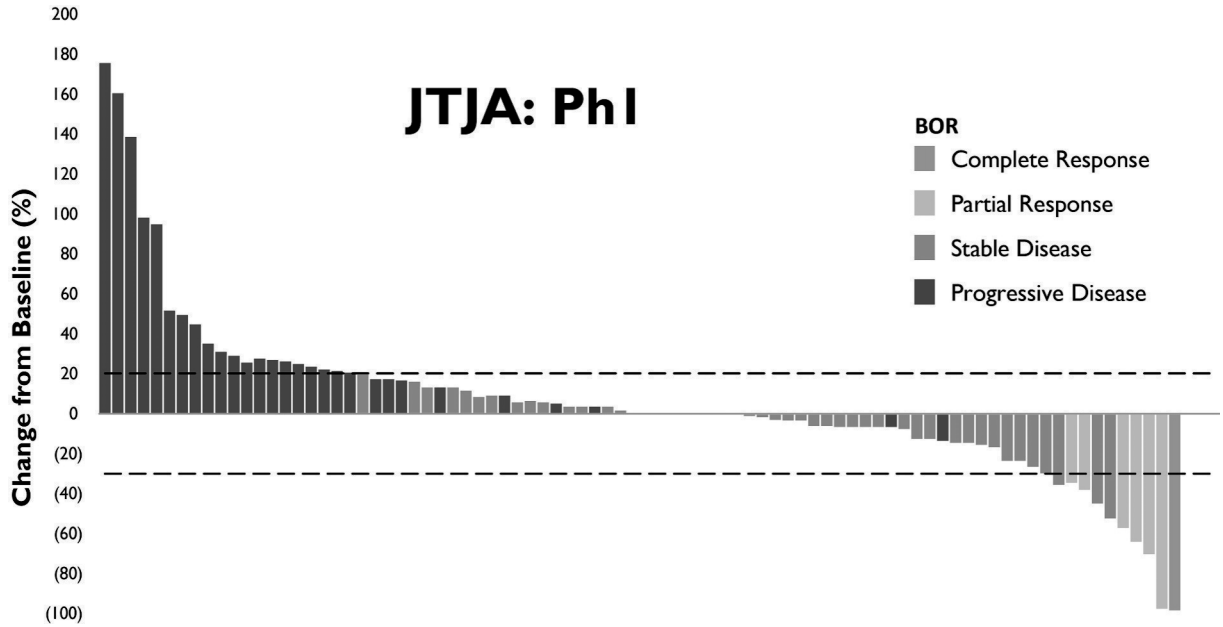


Figure 10. Maximal percentage change in tumor size from baseline by best ORR across all expansion cohorts.

Phase 2, single center NCI trial in patients with high-grade serous ovarian cancer

A Phase 2 trial of ACR-368, led by Dr. Lee at NCI, enrolled 28 women with high-grade serous ovarian cancer. ACR-368 was administered at the RP2D every 14 days until disease progression, an event of unacceptable toxicity, or withdrawal of consent. Twenty-four women had evaluable responses after three withdrew consent because of travel inconvenience and one developed an intervening illness that prevented radiological evaluation of tumor progression. All patients in this trial had failed at least one round of prior cytotoxic chemotherapy and three quarters of the patients had failed three or more prior lines of therapy. The primary endpoint in this single center trial was investigator assessed tumor response based on RECIST v1.1.

In the analysis of the ITT population of 28 patients, an ORR of 29% was achieved. For the 21 patients in the ITT population with platinum-resistant disease, an ORR of 29% was achieved. The mean duration of response in patients with platinum-resistant ovarian cancer was over ten months, with some patients remaining on ACR-368 therapy for over 16 months (Fig. 11).

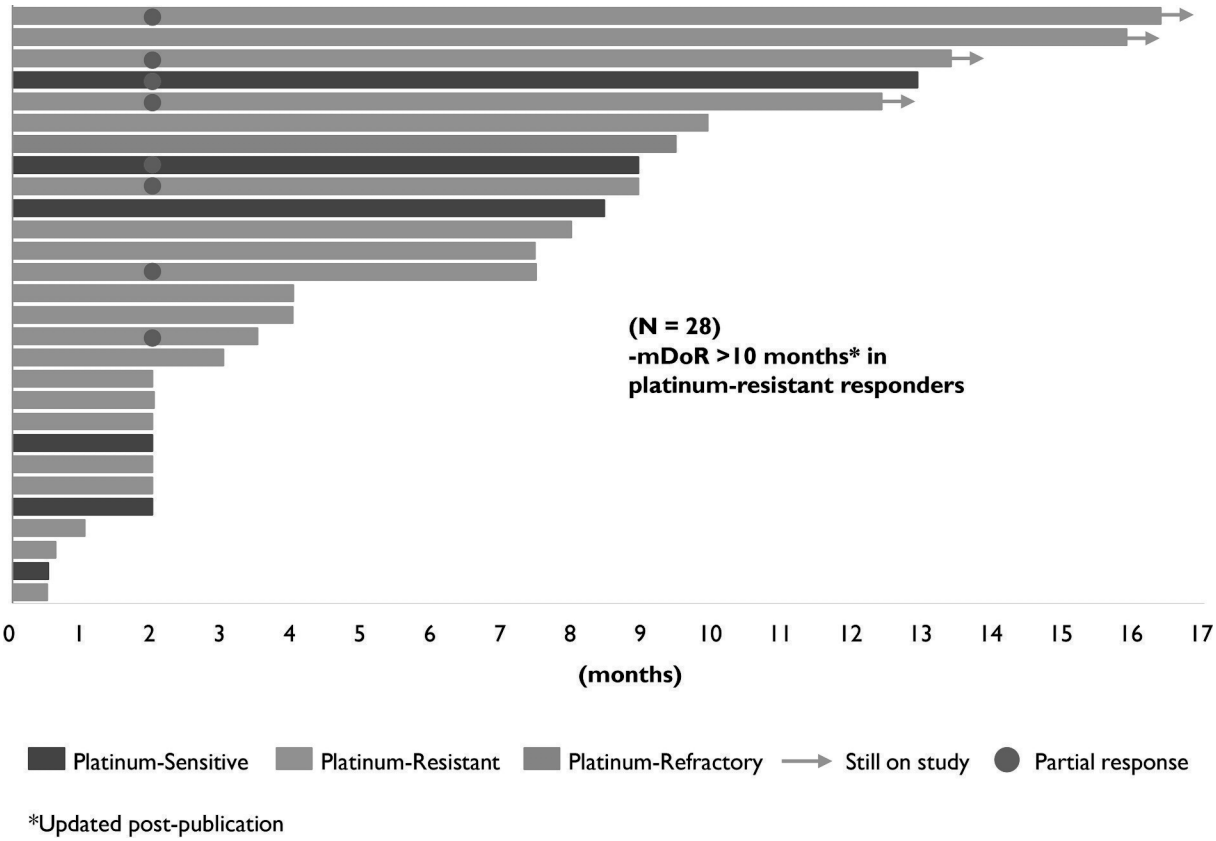


Figure 11. Duration of response with ACR-368 in a 28-patient ovarian cancer Phase 2 trial.

Similar to the findings reported for ACR-368 in SCC, there was no correlation observed between clinical response and alterations or the expression of potential biomarker genes (Fig. 12).

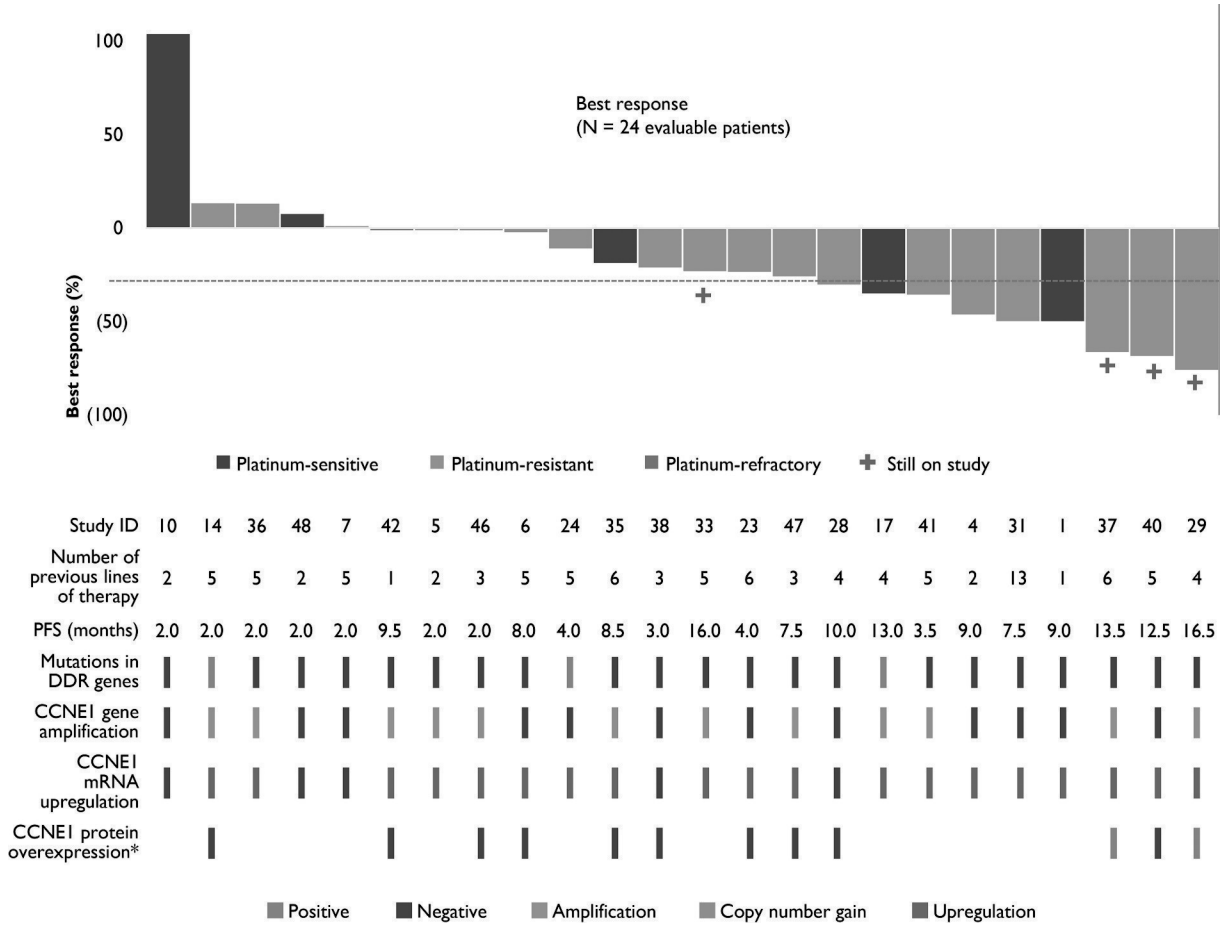


Figure 12. No correlation was observed between ACR-368 response and genetic alterations or potential biomarker expression in patients with ovarian cancer.

Phase 2 multicenter trial in advanced, high-grade serous ovarian cancer by Lilly

A large Phase 2 trial of ACR-368 in patients with platinum-resistant and platinum-refractory ovarian cancer sponsored by Lilly was conducted in 46 centers across eight countries. The 169 patients enrolled in this trial had failed two to four prior systemic therapies and 90% of patients had stage III or stage IV disease. The trial included patients with either an altered BRCA1 or BRCA2 gene, or BRCA-positive, or unaltered BRCA1 or BRCA2 gene, or BRCA-negative, ovarian cancer and was divided into four cohorts.

- Cohort 1: patients with platinum-resistant, BRCA negative ovarian cancer with at least three lines of prior therapy
- Cohort 2: patients with BRCA negative platinum-resistant ovarian cancer with no more than two lines of prior therapy
- Cohort 3: patients with platinum-resistant BRCA mutant ovarian cancer with any line of prior therapy, but with obligatory prior PARP inhibitor therapy
- Cohort 4: patients with platinum-refractory BRCA negative or BRCA mutant ovarian cancer and any line of prior therapy.

N= 169 Patients	Cohort Description	Percent Confirmed ORR (95% Confidence Interval	Percent Disease Control Rate (95% Confidence Interval)
Cohort 1 (53)	Plat resistant BRCA wt ≥3 lines of prior therapy	11.3 (4.3 to 23.0)	45.3 (31.6 to 59.6)
Cohort 2 (46)	Plat resistant BRCA wt < 3 lines of prior therapy	13.0 (4.9 to 26.3)	32.6 (19.5 to 48.0)
Cohort 3 (41)	Plat resistant BRCA mt, any line of therapy (must include prior PARPi)	12.2 (4.1 to 26.2)	31.7 (18.1 to 48.1)
Cohort 4 (29)	Plat refractory any BRCA any line of prior therapy	6.9 (0.8 to 22.8)	31.0 (15.3 to 50.8)

Figure 13. ORR and Disease Control Rate in each of the four cohorts of patients with platinum-resistant and platinum-refractory ovarian cancer.

The primary outcome in this study was ORR. Results from this trial showed that a subset of patients with ovarian cancer treated with ACR-368 across all four cohorts achieved durable PRs. The ORR in the 140 patients with platinum-resistant ovarian cancer was 12.1%, not including unconfirmed responders.

Secondary outcomes included Disease Control Rate, or DCR, which is the percentage of patients with a best overall response of CR, PR, or stable disease, or SD, for at least four months. The DCR was over 30% across all four cohorts, varying from 31% in patients with platinum-refractory disease to 45% in patients with platinum-resistant disease with at least three lines of prior failed therapies. In the three cohorts of patients with platinum-resistant disease, the median duration of response was 5.6 months (95% confidence interval: 3.9 months; 7.6 months), and the median duration of overall survival was 11.9 months (95% confidence interval: 9.9 months; 14 months).

Consistent with previous observations, retrospective analyses of patient pretreatment tumor samples by both NGS and by IHC failed to identify biomarkers that strongly correlated with clinical response. Despite the demonstrated clinical activity, these data underscore the need for an effective patient responder enrichment method.

ACR-368 has been generally well-tolerated with manageable side effects

There have been eight Lilly-sponsored clinical trials with ACR-368. In these trials, ACR-368 was administered to a total of 681 subjects, to 479 subjects as monotherapy and to 202 subjects in combination with other treatments. In addition, there have been 10 Investigator-Initiated Trials, or IITs, where ACR-368 was administered to a total of 283 patients as either monotherapy or in combination. The primary adverse events observed in these trials were hematological, including transient neutropenia and thrombocytopenia, both of which were generally reversible and manageable. The neutropenia and thrombocytopenia are thought to be part of the mechanism-based suppression of cells in the bone marrow, or myelosuppression, which is also seen with other DDR inhibitors. However, by dosing ACR-368 at the established RP2D once every 14 days it was found that in most patients who experienced drug-related hematologic toxicities such as neutropenia had already begun to recover by the 14th day after dosing. Hence, granulocyte colony-stimulating factor and platelet infusions to correct for neutropenia and thrombocytopenia, respectively, were not mandated but were used at the discretion of the treating physicians in these trials. Nonhematologic toxicities deemed related to ACR-368 treatment occurred at a much lower frequency and severity as summarized below, with fatigue, nausea, and diarrhea being the mostly commonly observed events. In addition, in a few patients, an association was identified between increasing ACR-368 plasma concentration following monotherapy and transient QTcF prolongation. None of these episodes led to clinical manifestations. Accordingly, drug-related discontinuations were between only 1% to 2% across all patients. A proportion of patients experienced very durable responses, and in a few cases remained on therapy for several years.

Summary of adverse events from published reports on clinical trials with ACR-368 monotherapy dosed at RP2D

Study Number NCT Number Status	Study Design Monotherapy	ACR-368 Dosing Regimen and Schedule	Number of Subjects	Summary of Safety Data*
Ovarian Carcinoma				
NCI Phase 2 single center study in platinum-resistant or refractory recurrent ovarian cancer	Single arm study in BRCA-negative, primarily platinum-resistant, recurrent high-grade serous or high-grade endometrioid ovarian carcinoma (Lee et al, Lancet Oncology, 2018)	RP2D: 105 mg/m^2 every 14 days	28 intent to treat platinum resistant (N=21), platinum-sensitive (N=6), and platinum-refractory (N=1) patients.	Most frequent treatment related AEs ≥ Grade 3: neutropenia measured at day 8, 26 (93%), leukopenia 23 (82%), thrombocytopenia 7 (25%), anemia 3 (11%), febrile neutropenia 2 (7%); most frequent treatment related non hematological AEs ≥ Grade 3: fatigue 2 (7%), vomiting 1 (4%), diarrhea 2 (7%). No deaths and no treatment discontinuation due to AEs reported. Note: in this trial, neutropenia and thrombocytopenia were measured at day 8 after infusion, which is nadir for neutropenia, to specifically assess highest degree of neutropenia, not at end of each dosing cycle, which is standard clinical practice.
Other Cancer Types				
I4D-MC-JTJA (JTJA) NCT01115790 Completed Phase 1 open-label, multicenter	Non randomized, cohort expansion in subjects advanced squamous cell carcinomas (Hong et al, Clin Cancer Res 2018)	RP2D: 105 mg/m^2 every 14 days	Total: 101 Anus: 26 H&N: 57 NSCLC: 16 + 2 subjects skin and vaginal	Most frequent treatment related AEs ≥ Grade 3: 93/101 (92%) subjects; neutropenia at day 8, 90 (89%), leukopenia 26 (26%), thrombocytopenia 16 (16%), febrile neutropenia 12 (12%), anemia 14 (14%). Most frequent treatment related non-hematological AEs ≥ Grade 3: fatigue 2 (2%), and headache 1(1%). Dose reductions in 10 subjects (10%) and dose delays in 22 (22%) due to neutropenia. No deaths and no treatment discontinuation due to AEs reported. Note: in this trial, neutropenia and thrombocytopenia were measured at day 8 after infusion, which is nadir for neutropenia, to specifically assess highest degree of neutropenia, not at end of each dosing cycle, which is standard clinical practice.
I4D-MC-JTJH (JTJH) NCT02735980 Phase 2 multicenter, nonrandomized	Parallel cohort study in subjects with extensive-Small Cell Lung Cancer who had either platinum-sensitive or platinum-resistant/refractory disease (Byers et al, Clin Lung Cancer 2021)	Cohort 1: platinum-sensitive Cohort 2: platinum-resistant/refractory RP2D: 105 mg/m^2 every 14 days	Total: 116 Cohort 1: 58 Cohort 2: 60	Treatment related AEs ≥ Grade 3: 89/116 (76.7%) subjects; neutropenia 75 (64.7%), leukopenia 30 (25.9%), thrombocytopenia 30 (25.9%), febrile neutropenia 12 (10.3%), anemia 14 (12.1%). Non-heme AEs: fatigue 5 (4.3%), and decreased appetite 2 (1.7%). Dose reductions in 8 subjects (13.3%). Dose delays in 19 (31%) due to neutropenia or thrombocytopenia, and 2 possibly drug related treatment discontinuations due to Gr3 pneumonia and Gr2 leukopenia. Mean relative dose-intensity 98.26%. Three deaths (5.4%) in cohort 1 deemed possibly related to study treatment.

* Adverse events greater than or equal to Grade 3 are considered serious adverse events

Using Our ACR-368 OncoSignature Test For Prediction of Sensitivity to ACR-368 in Our Ongoing Phase 2 Trial

Using the AP3 streamlined process as described above, we have developed a predictive OncoSignature test for ACR-368, called ACR-368 OncoSignature. We are using this in our ongoing Phase 2 trial to treat patients with ovarian, endometrial, or bladder cancer based on predicted sensitivity to ACR-368. We have extensively evaluated our ACR-368 OncoSignature test in various preclinical studies and models demonstrating the ability to predict sensitivity to ACR-368.

Prediction of sensitivity to ACR-368 across multiple human ovarian tumor samples

Two key questions facing companies entering clinical trials is whether the chosen tumor types in a particular trial will be sensitive to the drug candidate and, if so, what percentage of patients with each of these tumor types are expected to be sensitive to the drug candidate. To acquire this important information, we use our OncoSignature tests to screen across human patient tumor samples and multiple tumor types to predict not only which tumors are sensitive to our drug candidates, but also what percentage of patients with these tumor types are predicted to respond. We have used our ACR-368 OncoSignature test in this manner to screen across commercially available human patient tumor samples and across tumors that have been routine-processed by formalin-fixation and paraffin embedding, or FFPE, just like the pretreatment tumor biopsies collected from patient tumors are being processed in our ongoing clinical trial.

Using automated image acquisition software, the biomarkers in our ACR-368 OncoSignature tests are measured quantitatively within the ROI, which is where they are informative and exert their biological function. Patient tumor samples with a minimal predictive threshold of each of the three biomarkers present predicts sensitivity to ACR-368. Conversely, patients without presence of any of the three biomarkers are predicted to not benefit from ACR-368 and are being excluded from the monotherapy arm in our ongoing clinical trial.

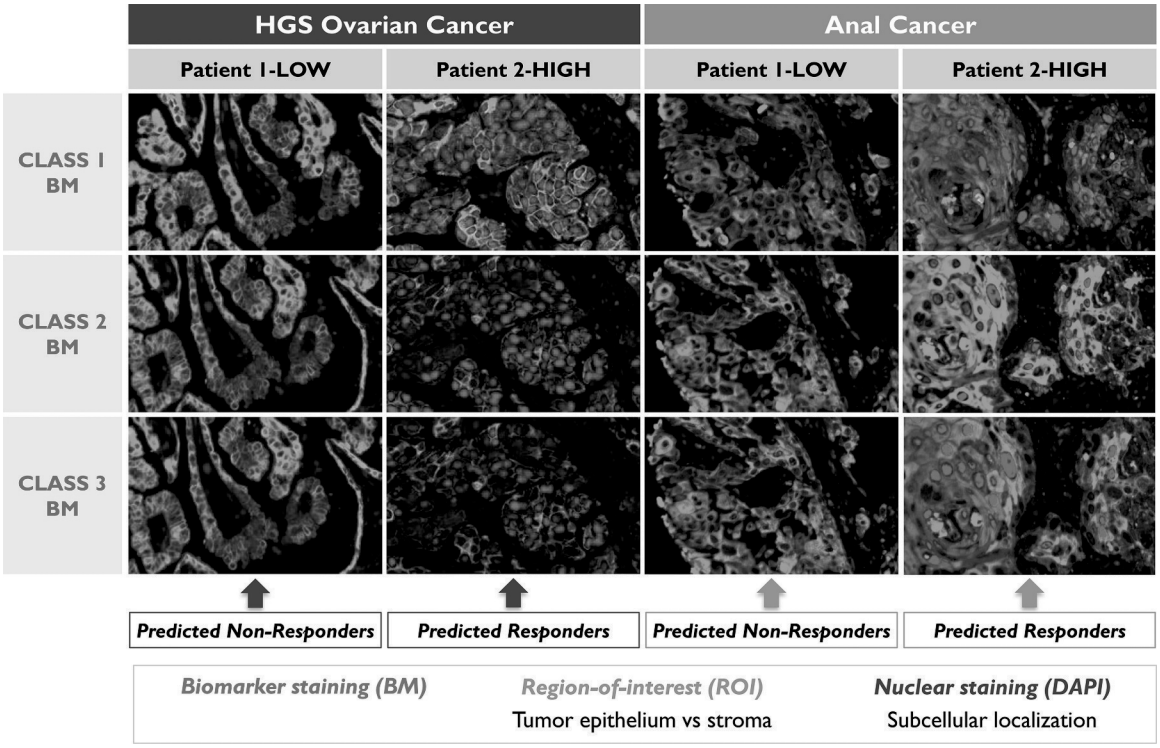
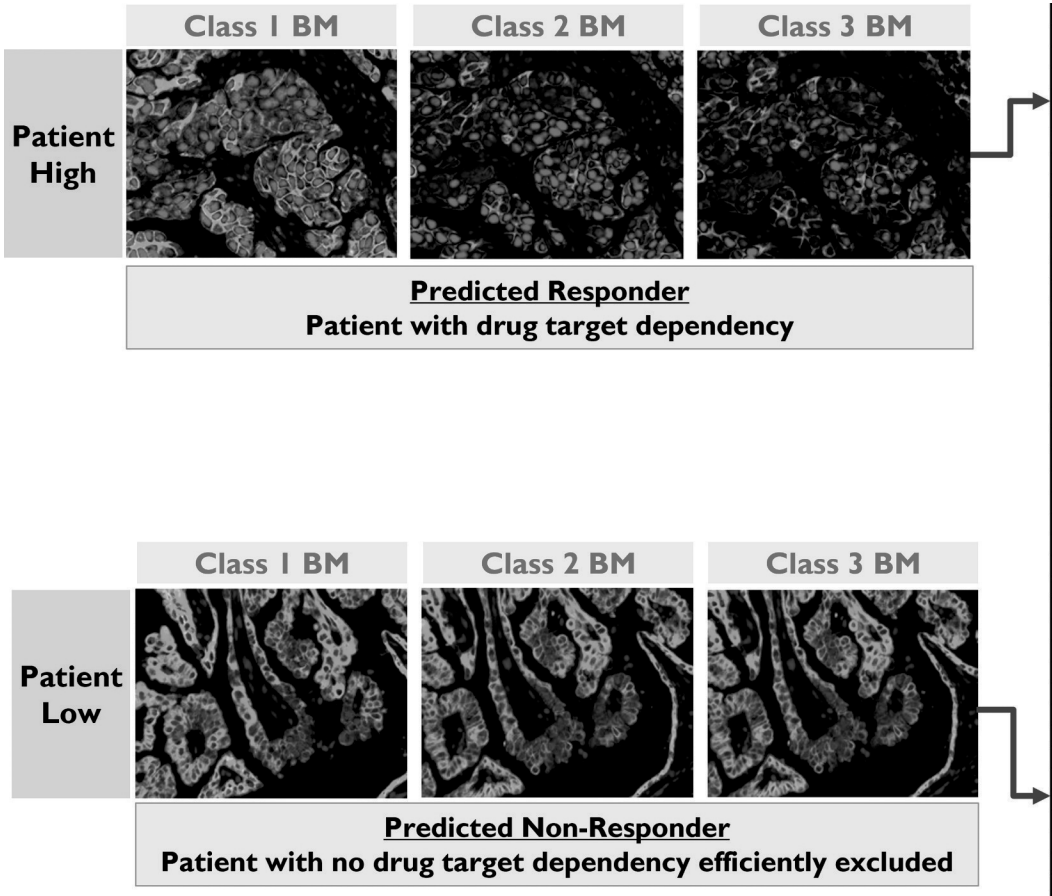


Figure 14. Screening with our ACR-368 OncoSignature across human patient tumor samples is used to predict which patients are believed to be sensitive and resistant to ACR-368, in this example using human ovarian and anal tumor samples.

Through our analysis of patient tumor samples acquired from biorepositories, we have found that in high-grade serous ovarian cancer approximately 30% of all patient tumor samples have each of the three biomarkers present above the minimal predictive threshold. This result, combined with the results described below, suggests that approximately 30% of patients could potentially benefit from treatment with ACR-368 monotherapy.

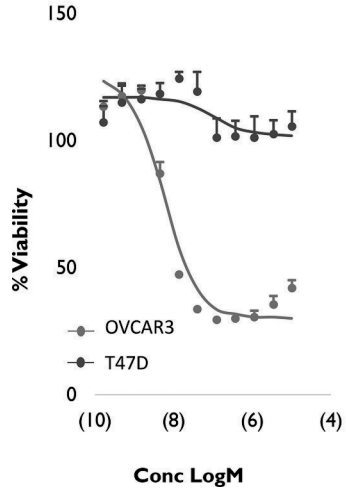


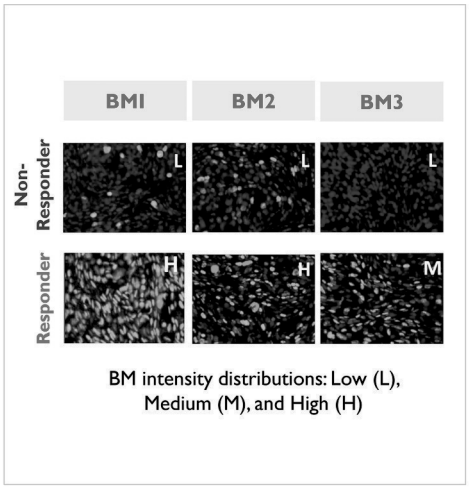
Tissue ID.	BM1	BM2	BM3
Fov060265	0.69	0.79	0.73
Fov050855	0.94	0.71	0.67
Fov041300	0.89	0.23	0.55
Fov060380	0.95	0.62	0.51
Fov060050	0.85	0.23	0.51
Fov041285	0.69	0.19	0.5
Fov100142	0.47	0.76	0.47
Fov050764	0.82	0.22	0.47
Fov041267	0.4	0.36	0.36
Fov100146	0.84	0.57	0.26
Fov060382	0.44	0.45	0.22
Fov041269	0.37	0.21	0.2
Fov060302	0.29	0.22	0.15
Fov020067	0.89	0.38	0.09
Fov100003	0.9	0.89	0.08
Fov050700	0.17	0.17	0.07
Fov050139	0.63	0.66	0.05
Fov041138	0.36	0.11	0.05
Fov060152	0.24	0.3	0.03
Fov030062	0.57	0.14	0.02
Fov060133	0.94	0.43	0.01
Fov050666	0.93	0.38	0.01
Fov060371	0.88	0.93	0
Fov020497	0.61	0.43	0
Fov010706	0.54	0.14	0
Fov020386	0.11	0.09	0.12
Fov050734	0.11	0.06	0.08
Fov040872	0.23	0.04	0.36
Fov050659	0.29	0.01	0.02
Fov060293	0.42	0	0
Fov060210	0.1	0.1	0
Fov050840	0.07	0.29	0.01
Fov040855	0.05	0	0.22
Fov050816	0.04	0.33	0.12
Fov060355	0.04	0.27	0
Fov010252	0.03	0.17	0.02
Fov010682	0.03	0.03	0
Fov060553	0.03	0.02	0.03
71768C3	0.02	0	0
Fov150230	0	0.36	0.12
Fov060308	0	0	0

Figure 15. Our ACR-368 OncoSignature provides quantitative scores that we use to objectively predict tumor response. Patient tumor samples with all three biomarkers above a certain minimum level on the heatmap are predicted to benefit from ACR-368 therapy.

Prediction of sensitivity to ACR-368 in human tumor cell lines

Human tumor cell lines are very different from human intact tumor tissue, but are still widely used to assess anti-tumor efficacy. To date, it has been very challenging to predict sensitivity to DDR inhibitors with prevailing genetics-based methods in human tumor cell lines. However, by applying our ACR-368 OncoSignature to a small panel of human tumor cell lines, we demonstrated our ability to predict sensitivity to ACR-368 with a high degree of certainty. The presence of all three biomarkers above a minimal level predicted sensitivity to ACR-368 in all cells that are highly sensitive to ACR-368 in viability assays, except for one.





ACR-368		
Human Tumor Cell Line	EC50 (uM)	Prediction
Line 1	0.01	**NR**
Line 2	0.02	R
Line 3	0.02	R
Line 4	0.02	R
Line 5	0.08	R
Line 6	>10	R
Line 7	>10	**NR**
Line 8	>10	**NR**
Line 9	>10	**NR**
Line 10	>10	**NR**
Line 11	>10	**NR**

Figure 16. Prediction of ACR-368 sensitivity across human tumor cell lines.

EC_{50}: concentration of ACR-368 resulting in 50% inhibition of tumor cell survival.

R = predicted responder and NR = predicted non-responder.

Prediction of sensitivity to ACR-368 in ovarian PDX models

To demonstrate that we can also predict responders to ACR-368 in PDX models, we obtained untreated tumor tissue samples from 20 PDX models of ovarian cancer and generated quantitative biomarker scores with our ACR-368 OncoSignature test. Using the same approach, we assessed whether the tumor samples with a minimal level of each of the three biomarkers would predict sensitivity to ACR-368. We found that our ACR-368 OncoSignature was able to capture 80% of responders in PDX models while improving the ORR to approximately 55% compared to an approximated 20% baseline response rate.

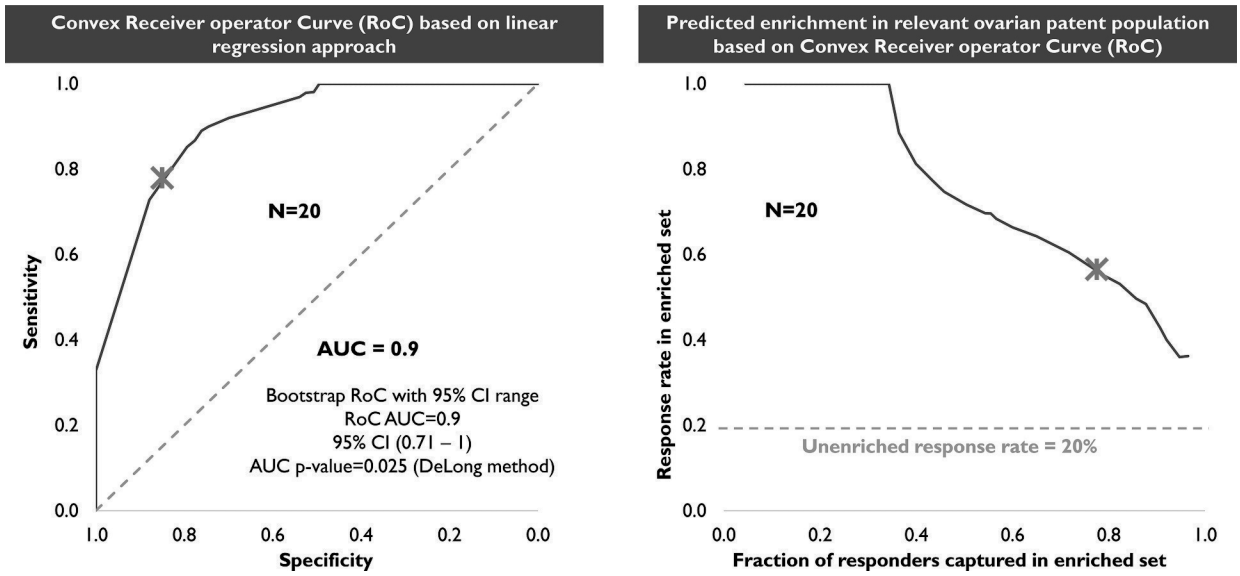


Figure 17. Our ACR-368 OncoSignature accurately distinguished responders from non-responders in PDX models; sensitivity and specificity plotted as an area under receiver operator curve, or AUC.

Blinded, prospectively designed prediction of ACR-368 sensitivity in two separate studies of pretreatment tumor biopsies from past Phase 2 trials with ACR-368 in patients with high grade serous ovarian cancer

Our OncoSignature tests are developed using only tumor cells independent of any input from clinical results. The tests are dictated by a mechanistic, functional definition of each of the three classes of biomarkers based on a strong scientific and clinical rationale as well as on our insights into biological signaling. Based on our approach, we believe we can predict that if all three classes of biomarkers are present at a minimal level in a tumor sample, the tumor depends on upregulation of the drug target signaling axis for its growth and survival. Moreover, from our phosphoproteomic drug profiling of tumor cells, we have found that this upregulated signaling axis is modulated by the drug candidate.

To test our ACR-368 OncoSignature for its ability to identify the patients that benefit from monotherapy with ACR-368, we conducted two separate studies on pretreatment tumor biopsy samples collected from patients treated with ACR-368 in past trials. Importantly, the studies were blinded to any treatment outcome annotation, the analyses were prospectively defined, and results were analyzed by an independent third-party statistician.

We were able to obtain pre-treatment biopsy samples from a subset of patients with ovarian cancer treated with ACR-368 in the prior clinical Phase 2 trials: patients treated at NCI and in the multi-center trial sponsored by Lilly. We generated OncoSignature scores on these biopsy samples blinded to treatment outcome and handed these over to the third-party biostatistician, who received the treatment outcome annotation separately. The results of both of these studies showed that use of our tumor-agnostic ACR-368 OncoSignature test was able to significantly improve the response rate, to 47% and 58%, respectively. Moreover, the results also demonstrated that a negative ACR-368 OncoSignature largely eliminated patients who are less responsive to ACR-368, hence sparing these patients from a ACR-368 single-agent treatment from which they would not benefit.

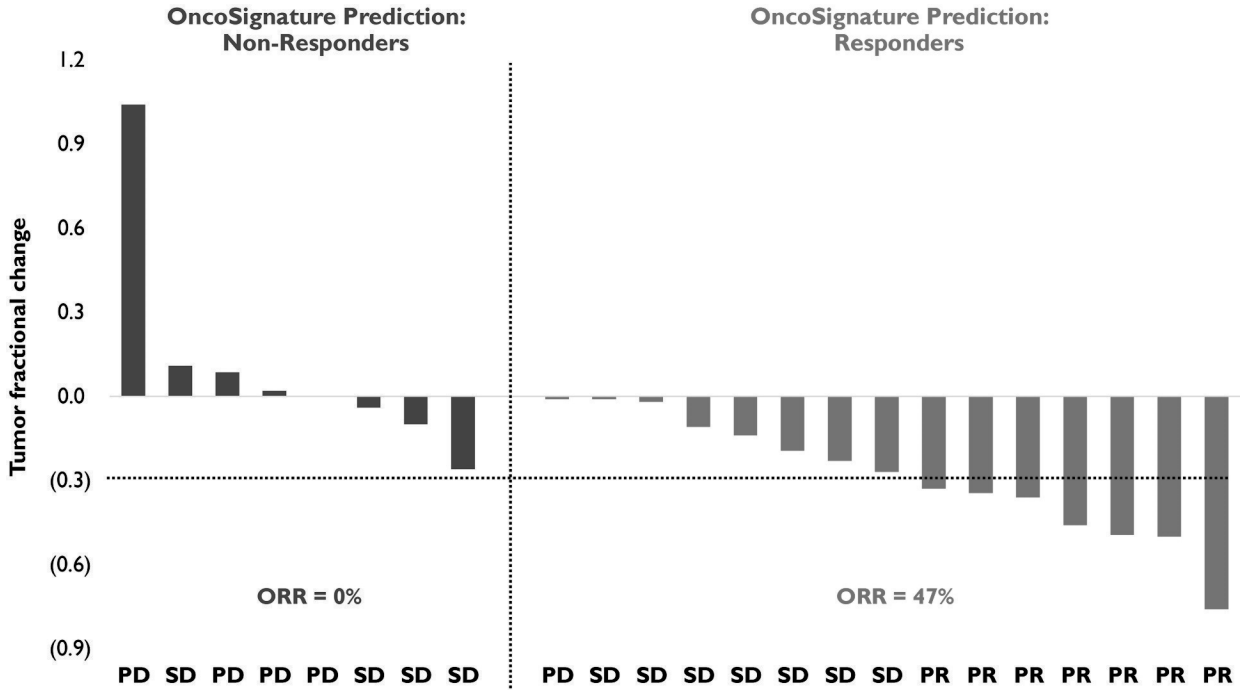


Figure 18. Blinded OncoSignature scoring of pre-treatment tumor biopsies from prior clinical trials of ACR-368 was able to segregate responders from non-responders.

Patients predicted to be sensitive to ACR-368 had a median PFS, or mPFS, of 7.9 months compared to 2.2 months for those predicted to be non-responders. This reflects the fact that not only the patients with PR or CR, but also with SD predicted by ACR-368 OncoSignature to be responders to ACR-368 treatment did indeed benefit for longer periods of time than the predicted non-responders. This could be valuable for confirmatory trials where mPFS is typically a primary endpoint.

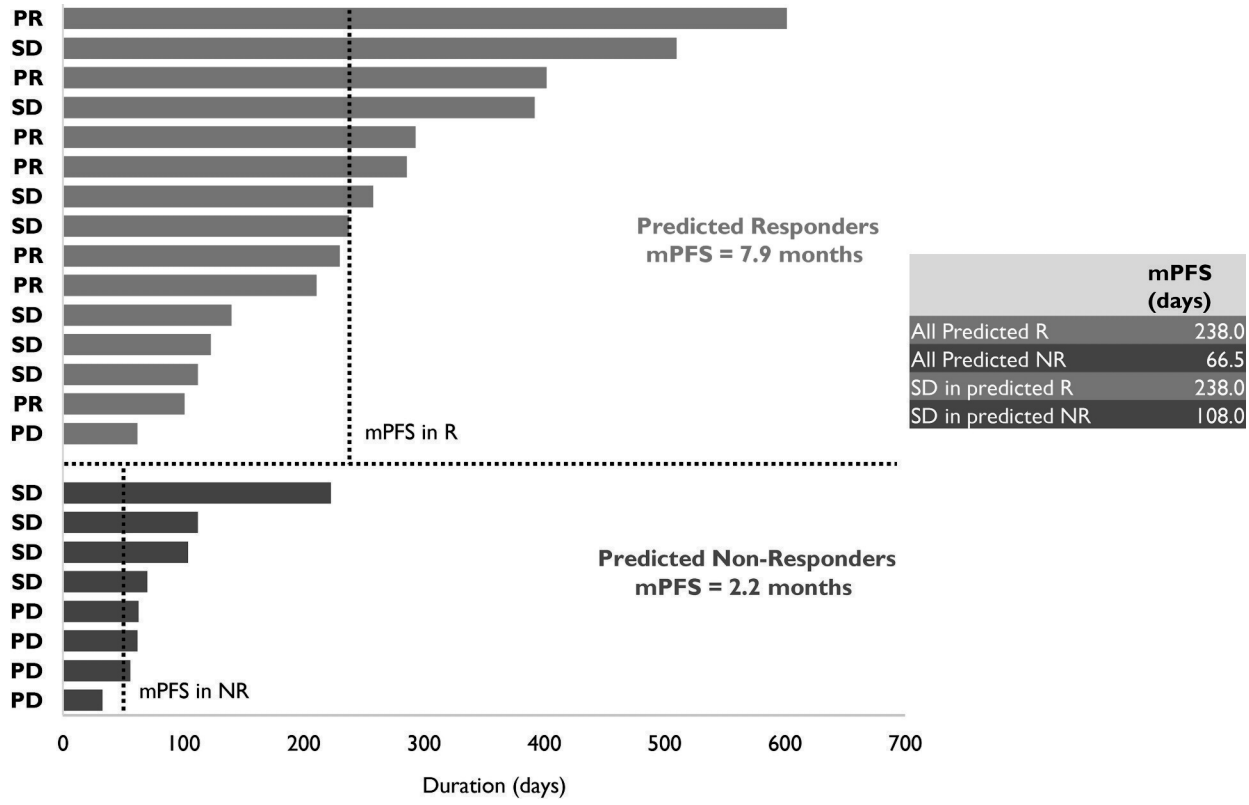


Figure 19. Patients with OncoSignature positive scores had improved PFS compared to OncoSignature negative patients.

Prediction of ACR-368 clinical activity in additional cancer indications

To identify tumor types predicted to be sensitive to ACR-368, we used our ACR-368 OncoSignature test to screen across large numbers of human patient tumor samples across tumor types obtained from biorepositories. Through this tumor-agnostic usage of ACR-368 OncoSignature we found that between 30% and 40% of samples from patients with endometrial cancer and bladder cancer were predicted to be sensitive to ACR-368. In addition to confirming the positive predictive value of our ACR-368 OncoSignature test, we have also demonstrated the high negative predictive value of our ACR-368 OncoSignature test. For example, in sqNSCLC our ACR-368 OncoSignature test predicted that none of the patient samples would be sensitive to ACR-368, which is consistent with the Phase 1 trial that was conducted in SCC types and described above, which showed an ORR of 0% in sqNSCLC. Based on these findings, which were further confirmed in PDX models of endometrial and bladder cancer, as described below, we predict that a significant proportion of patients with endometrial and bladder cancer will also be sensitive to ACR-368 monotherapy, and these two tumor types are therefore included together with ovarian cancer in our upcoming Phase 2 trial. In the limited number of patients evaluated by imaging to date, preliminary evidence of clinical activity has been observed in OncoSignature-positive patients across all three tumor types, including the two AP3-predicted tumor types endometrial and bladder cancer, treated with single agent ACR-368 at RP2D.

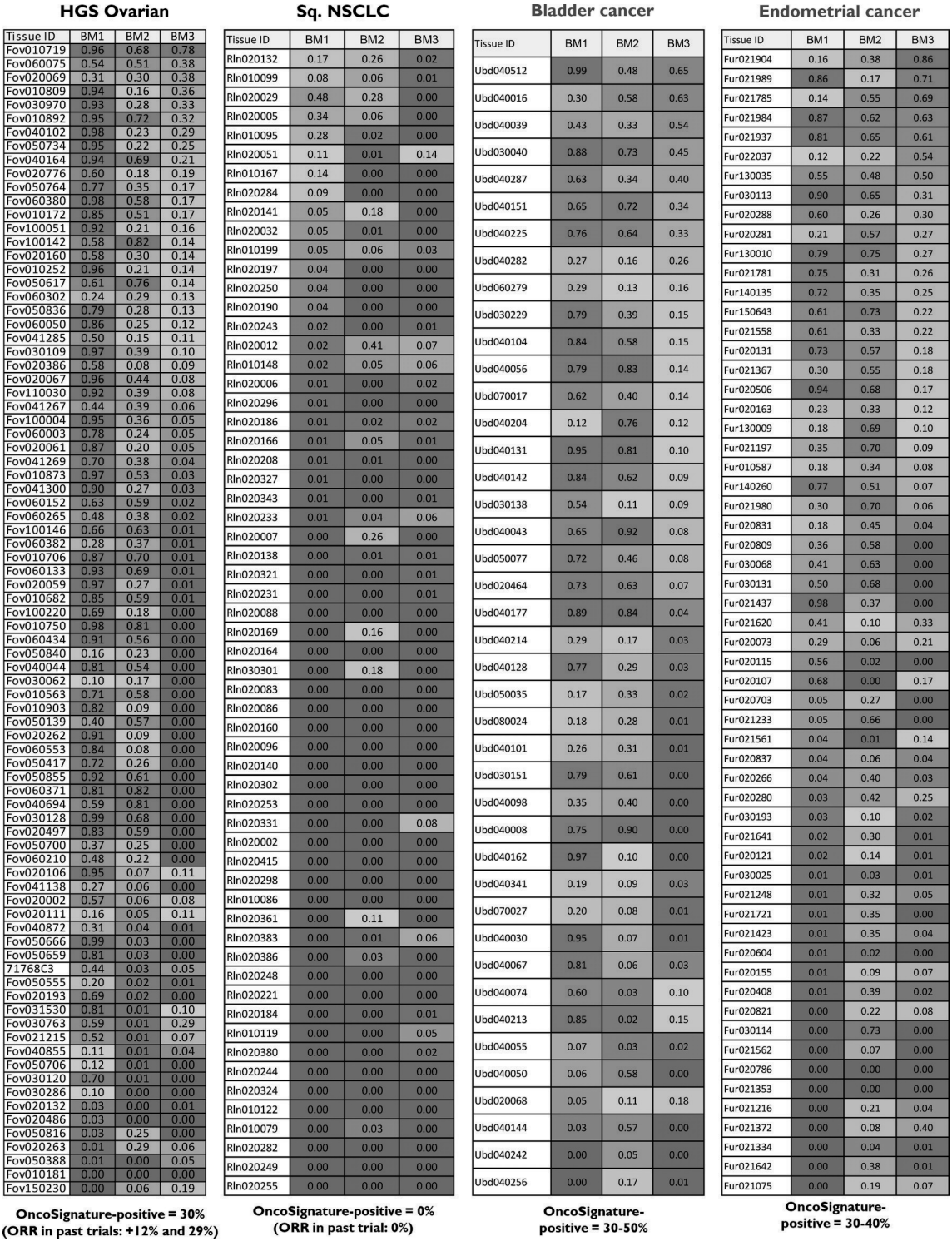


Figure 20. ACR-368 OncoSignature screening across human routine-processed FFPE patient tumor samples predicts which tumor types and what proportion thereof are sensitive to ACR-368. Each line in the four heat maps for each of the four tumor types—ovarian cancer, sqNSCLC, endometrial cancer, and bladder cancer—represents an individual tumor sample and the three columns from left to right represent the quantitative level of each of the three biomarkers in the OncoSignature test, BM1, BM2, and BM3.

Confirmation of activity in PDX models of predicted tumor types

In order to confirm our prediction based on screening of human patient tumor samples that a proportion of patients with bladder and endometrial cancer are sensitive to ACR-368 monotherapy, we generated PDX models of these two tumor types and assessed anti-tumor activity of ACR-368 in these tumors. Fresh tumor tissues from mice bearing established primary human endometrial and bladder cancer tissues from 20 and 18 patients, respectively, were harvested and small pieces inoculated into mice randomized into two groups, receiving vehicle control and ACR-368, respectively, as well as a PD group used to predict ACR-368 sensitivity on the tumor tissue prior to treatment.

Mice were treated in a three-days-on, four-days-off weekly schedule for four weeks at 10 mg/kg. Mice were sacrificed either four days after last dosing or when the tumor volume in one of the arms reached 2,000 mm, whichever came first. ACR-368 demonstrated anti-tumor single agent activity in a proportion of models while others were less sensitive, consistent with the prediction obtained from screening of human patient tumor samples. This result in these preclinical studies confirmed the predicted single agent activity of ACR-368 in endometrial and bladder cancer.

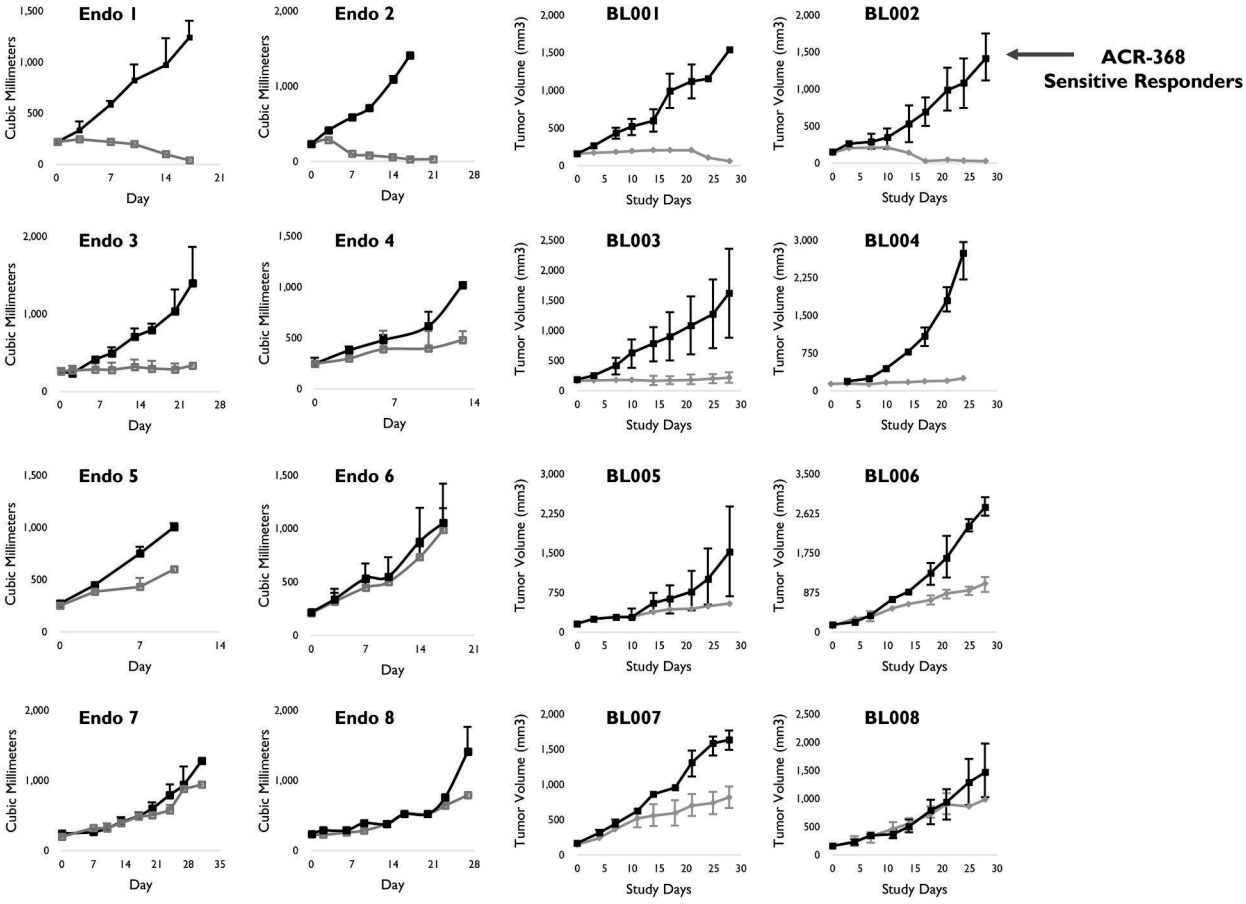


Figure 21. Assessment of anti-tumor activity of ACR-368 in PDX models of endometrial cancer (left two columns) and bladder cancer (right two columns) confirm that a proportion are indeed highly sensitive to ACR-368.

Blinded, prospectively designed prediction of sensitivity to ACR-368 in endometrial PDX models

To further demonstrate the predictive power of our ACR-368 OncoSignature test, we were able to obtain de-identified FFPE tissue samples from the PD arm of the endometrial cancer PDX model study. ACR-368 OncoSignature biomarker scores were generated for 18 out of 20 PDX models, as two PDX models lacked cytokeratin expression.

Using the same minimal biomarker levels established and evaluated in all our other studies summarized above, we found that eight PDX models were ACR-368 OncoSignature-positive and predicted to be sensitive to ACR-368. After unblinding of the data and analysis by a third-party biostatistician, we showed that these models all were sensitive and experienced tumor growth inhibition, or TGI, in response to treatment with ACR-368. The ACR-368 OncoSignature-negative models, which are predicted less sensitive to ACR-368, contained all the non-responsive PDX models as well as some models with overall less pronounced TGI. The segregation of non-responders from responders was statistically significant, and a sensitivity and specificity analysis demonstrated an AUC of 0.88. Despite the well-known observation that PDX models in general tend to show a much higher percentage of responders compared to human patients, as also demonstrated in our ovarian PDX model study above, this result nevertheless confirmed the ability of our ACR-368 OncoSignature test to segregate the most sensitive from non-sensitive PDX models in a blinded, prospectively designed manner.

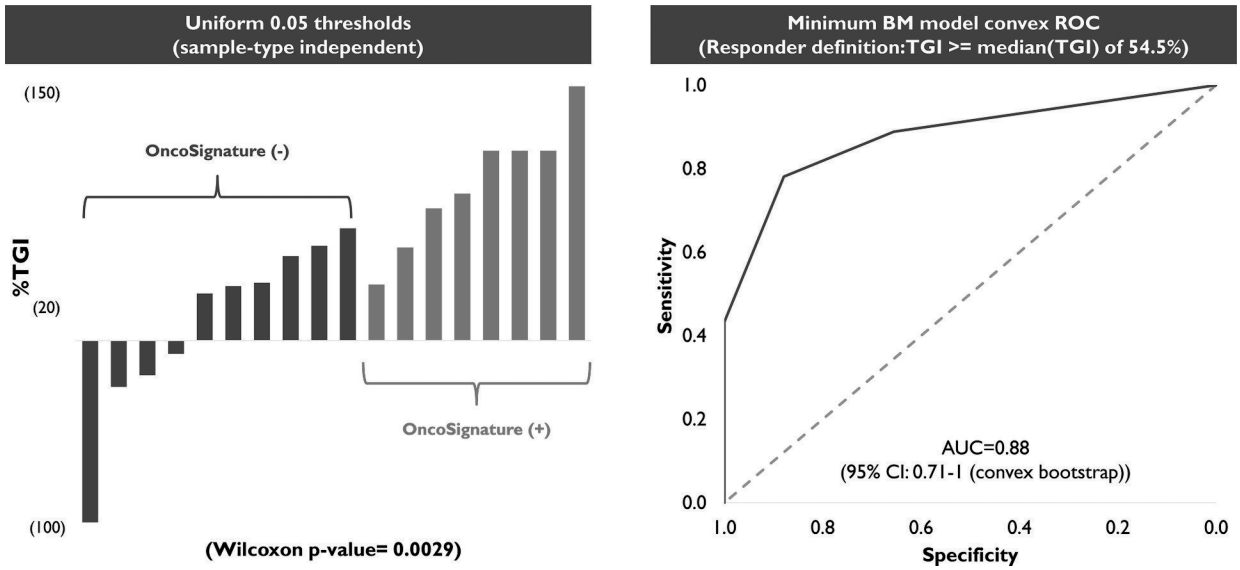


Figure 22. Blinded, prospectively designed prediction of ACR-368 sensitivity with our OncoSignature test demonstrates segregation of responders and non-responders with a p-value = 0.003 and an AUC of 0.88.

AP3 Platform Prediction of LDG as a Rational Combination to Circumvent ACR-368 Resistance

Not all tumors are sensitive to ACR-368, and those that are sensitive can develop resistance to treatment. We used our AP3 platform to identify pathways that drive resistance to ACR-368 and to propose potential combination therapies to circumvent these resistance pathways.

As an example, we generated ACR-368-resistant ovarian cancer cell lines by growing five different human tumor cell lines, including OVCAR3, that are normally sensitive to ACR-368 in the presence of a clinically relevant dose (50 nM) of ACR-368 for over ten weeks. While most cells died, a few cells developed resistance to ACR-368 and were able to grow in the presence of the drug candidate. In general, resistant cells were at least 1,000-fold less sensitive to ACR-368 than the parental cell lines. Removal of ACR-368 for up to two months in the cell lines did not alter this level of resistance, and resistance was maintained in the presence of drug efflux inhibitors, suggesting that the resistance was not due to drug efflux from the cells, but rather permanent change in cell signaling in these cell lines drove the development of resistance.

Using AP3, we conducted global proteomic analyses comparing ACR-368 sensitive and resistant OVCAR3 cells, identifying thousands of differentially expressed proteins and phosphoproteins in these cells. Pathway mapping and analyses of these proteins and phosphoproteins showed that the activity state of proteins involved in DNA damage repair were significantly downregulated, with a compensatory upregulation of proteins involved in cell cycle progression. These changes demonstrate a low level of active DNA damage repair and hence we believe that they allowed these ACR-368 resistant cells to continue to progress through the cell cycle regardless of the presence of the drug. Furthermore, we found that cells treated with low doses of gemcitabine led to reversal of these changes, upregulating the activity of the core DNA damage repair pathways, consistent with potentially identifying a means of reversing ACR-368 resistance. This was in line with our quantitative phosphoproteomic data, which showed that treatment of ACR-368 resistant cells with LDG resulted in an upregulation of the three OncoSignature biomarkers, rendering the tumor cells more ACR-368 OncoSignature-positive after treatment with LDG.

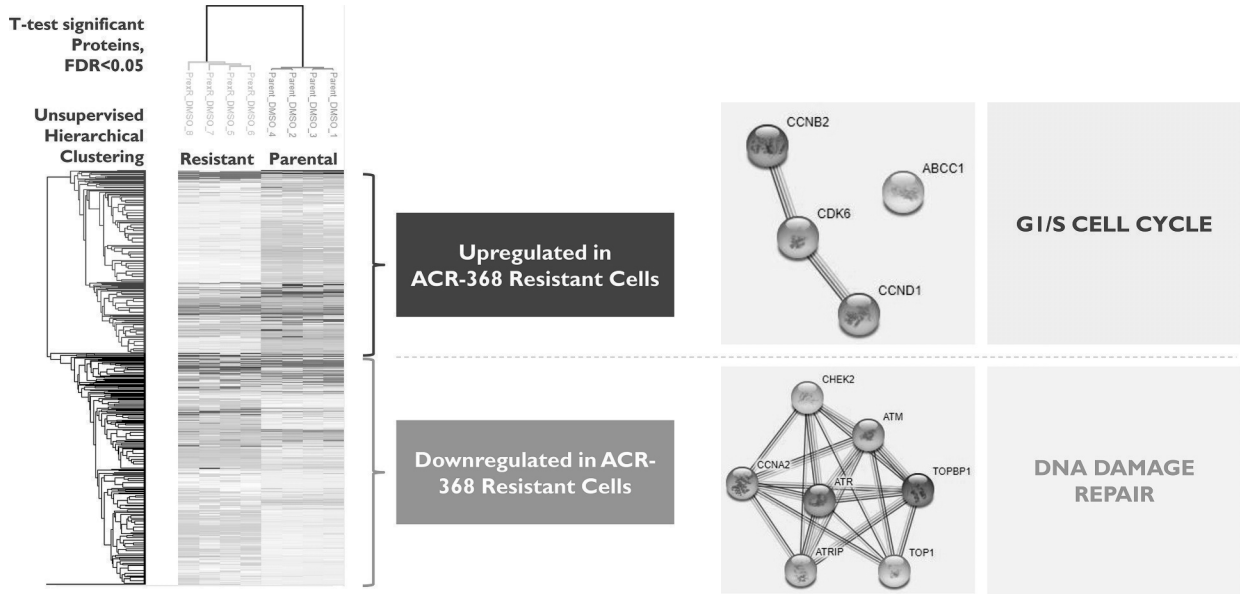


Figure 23. Proteomic analyses of ACR-368 sensitive and resistant ovarian cell lines identified activation of proteins that regulate cell cycle progression and inactivation of proteins in the DNA damage repair pathways.

These findings suggested that tumor cells that are resistant to ACR-368 should be sensitized by treatments such as gemcitabine that function by disrupting cell cycle progression. We tested this hypothesis in cell-killing assays. The five parental human ovarian tumor cell lines were highly sensitive to ACR-368 killing with a concentration required for 50% inhibition, or EC_{50} between ten to 30 nM. The EC_{50} for OVCAR3 was 15 nM ACR-368. By contrast, the resistant OVCAR3 cells had an EC_{50} of over 10 μM, which means they were over 1,000-fold less sensitive to ACR-368. Treatment of these cells with 0.53 nM gemcitabine, lowered the EC_{50} for ACR-368 to 100 nM. A further increase in gemcitabine concentration to 2.7 nM lowered the EC_{50} for ACR-368 to 6 nM. Likewise, treatment of the parental cells with the same low doses of gemcitabine increased the sensitivity to ACR-368. Treatment of these cells with 0.53 nM gemcitabine lowered the EC50 for ACR-368 to 2.7 nM. A further increase in gemcitabine concentration to 2.7 nM lowered the EC50 for ACR-368 to 0.2 nM. These findings of synergy between ACR-368 and LDG were extended into other human tumor cell lines, including endometrial and bladder.

Support for the synergistic action of ACR-368 and gemcitabine comes from the observation that gemcitabine alone does not induce potent cell death in OVCAR3 cells: at 0.53 and at 2.7 nM of gemcitabine there was no effect on cell survival, and more than half of treated cells survived at concentrations exceeding 30 μM.

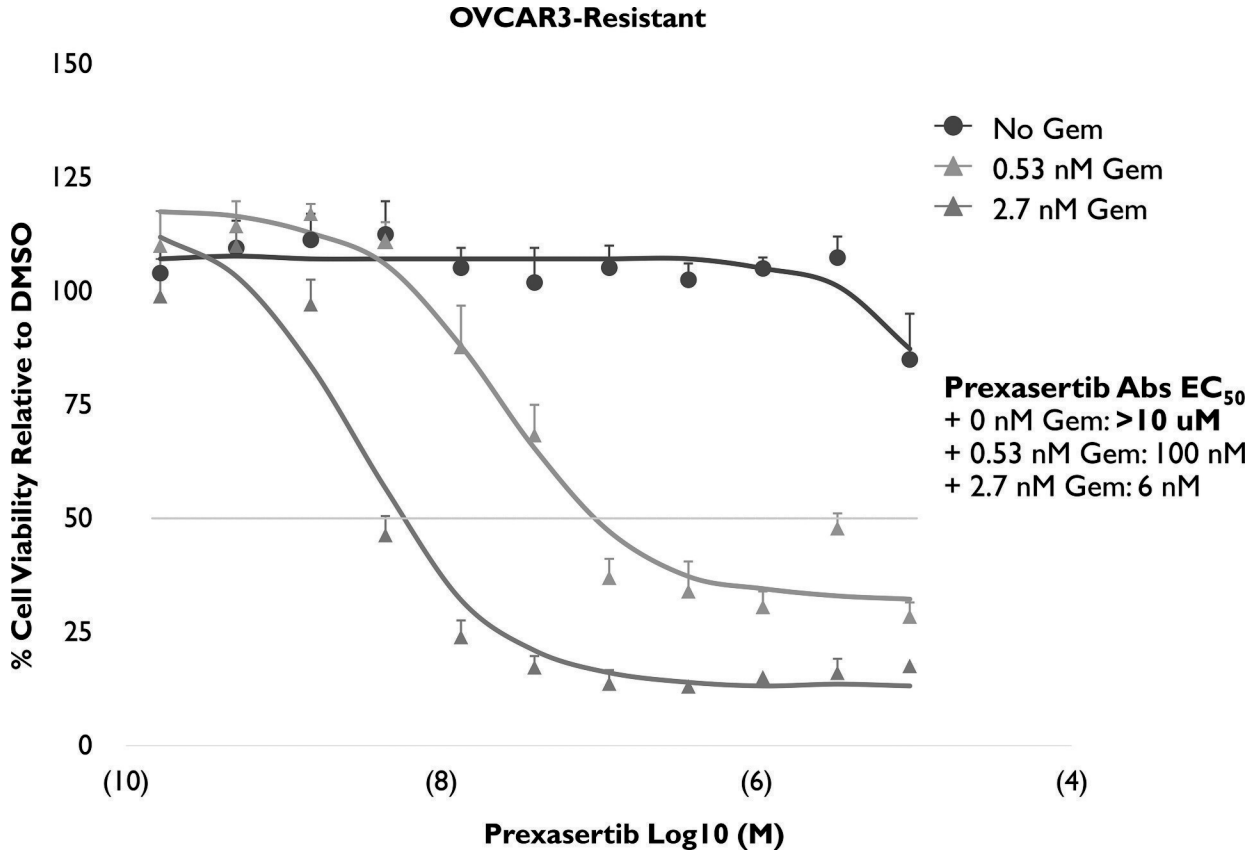


Figure 24. Low concentrations of gemcitabine sensitize a highly resistant ovarian cancer cell line to ACR-368.

Based on these results, we are treating patients who are predicted to be resistant to ACR-368 in our clinical trials with LDG in combination with ACR-368 to potentially overcome resistance to ACR-368.

Our Ongoing Phase 2 Clinical Trials of ACR-368 Based on ACR-368 OncoSignature-predicted Drug Sensitivity

The IND for our Phase 2 clinical trial of ACR-368 with cohorts of patients with advanced or metastatic recurrent platinum-resistant high-grade ovarian, endometrial, and bladder cancers has cleared. The trial is being conducted under the master protocol guidance by the FDA published in March 2022, which aims to enable expedited drug development in multiple cancer types of drugs for which the RP2D has been established in prior studies. The Phase 2 trial is based on ACR-368 OncoSignature prediction of sensitivity to ACR-368 monotherapy on freshly sampled pretreatment tumor biopsies. Patients with ACR-368 OncoSignature-positive tumors of all three tumor types are being enrolled in an arm to be treated with ACR-368 monotherapy at RP2D in a Simon two-stage, single arm design. Patients who have OncoSignature negative tumors of all three tumor types are predicted not to be highly sensitive to ACR-368 monotherapy. These patients are being treated with ACR-368 at RP2D plus LDG in a single arm design based on our expectation that LDG will increase ACR-368 sensitivity in a proportion of these ACR-368 OncoSignature-negative patients.

In the ACR-368 OncoSignature-positive arm, up to 23 patients of each of the three tumor types will receive ACR-368 monotherapy at RP2D. The trial incorporates an opportunity to refine the OncoSignature biomarker patient selection threshold based on the first 12 patients treated with ACR-368 monotherapy. An interim futility analysis will be used to exclude the non-interesting response rate and assess the ORR. Based on this result, the study is designed to enroll up to an additional 48 patients with these tumor types with a registrational intent. We have completed the Phase 1b portion of the study exploring ACR-368 and LDG combination in OncoSignature-negative patients and work is now proceeding to advance into the exploratory Phase 2 expansion portion of the study utilizing the newly established RP2D for LDG at 10 mg/m^2 with the previously established RP2D for ACR-368 for all three tumor types - ovarian cancer, endometrial adenocarcinoma and urothelial cancer. Anti-tumor activity will be assessed by RECIST. Consistent with AP3-predicted tumor sensitivity, early imaging-based evidence of clinical activity across all three tumor types has been observed in OncoSignature-negative patients treated with ACR-368 at RP2D and LDG during the dose escalation phase.

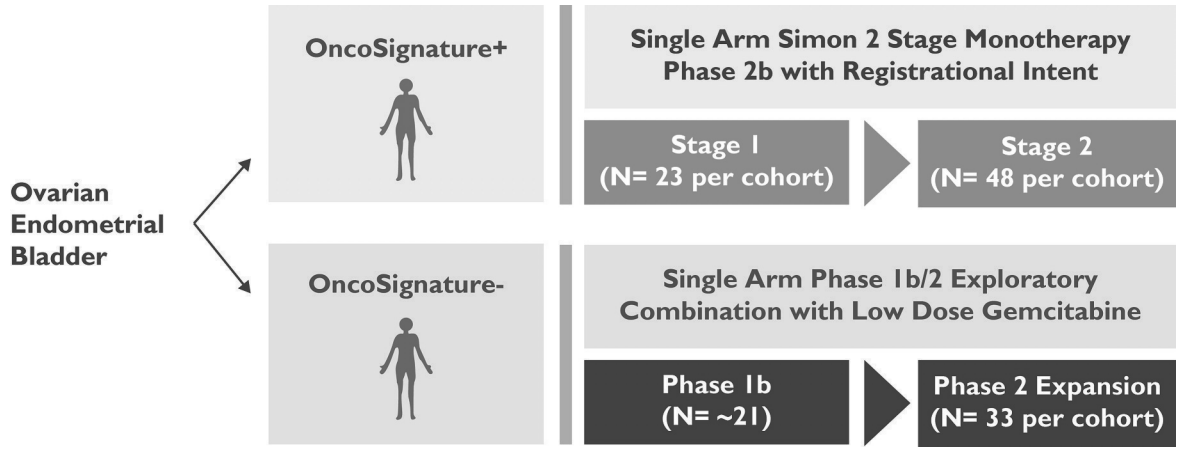


Figure 25. Design of the single arm Phase 2 ACR-368 monotherapy and single arm Phase 1b/2 ACR-368 with LDG combination trials.

We intend to expand our master protocol, at a later point to include patients with HPV$^+$ squamous cell carcinomas, including SCCHN, anal, and cervical cancer. The prior studies in SCCHN and anal cancer, described above, have demonstrated an unenriched ORR of 19% in patients with HPV$^+$ SCCHN, and 15% in patients with anal cancer. Moreover, the mDoR was seven months for SCCHN and above 12 months in anal cancer. The FDA has granted ODD for ACR-368 for anal cancer. Preclinical screening on human patient tumor samples suggests that approximately 25% of cases of these cancers have activated biochemical signaling pathways that are consistent with sensitivity to ACR-368. We are planning to file one or more IND application amendments to add one or more of three additional cancer types under the same or a similar trial protocol design at a later time, including head and neck cancer, anal cancer, and cervical cancer.

Patients with additional tumor types, including sarcomas, have been observed to be sensitive to ACR-368

Several investigator-initiated trials, or IITs, have demonstrated clinical activity of ACR-368 in combination with various chemotherapeutic agents in patients with different types of sarcomas. These are of high unmet need for improved treatments, and only 17% of patients with metastatic soft tissue sarcomas survive more than five years. Importantly, these IITs have not only demonstrated clinical activity of ACR-368, but have also demonstrated that combination with chemotherapy is generally well-tolerated in these patients. For example, in a Phase 1/2 trial in patients with relapsed/refractory desmoplastic small round cell tumor and rhabdomyosarcoma conducted at Memorial Sloan Kettering Cancer Center, it was reported that ACR-368 in combination with irinotecan resulted in a 32% ORR and mPFS of over 5.5 months. The combination was generally well-tolerated, leading to primarily hematological adverse events, which were manageable. We intend to initiate certain carefully selected trials in patients with sarcomas that have demonstrated promising preliminary clinical results in past trials at a later date.

Our Proprietary, Internal Preclinical Programs Targeting Critical Nodes in the DDR Pathways

We intend to leverage our AP3 platform and OncoSignature tests to aim for enrichment of patient responders for our internal preclinical programs. We strategically work on drug targets for which early-stage clinical programs from other companies have demonstrated clinical activity or where there is a strong rationale for clinical activity, and where we believe genetics-based approaches are insufficient for patient responder identification. Our programs include ACR-2316, a novel dual WEE1 and PKMYT1 inhibitor development candidate, designed using our AP3 platform to achieve potent single agent activity. The field designing drugs that target the DDR pathway is rapidly expanding to include a number of drug candidates in development against targets such as ATR, ATM, DNA-PK, CHK1/2, and WEE1. Although several of these candidates have demonstrated anti-tumor activity in the clinic, the ORRs to treatment with these candidates have been relatively low. We believe that our AP3 platform provides us with the opportunity to not only develop OncoSignature tests to improve the response rates of existing drug candidates but can also guide the design and optimization of novel drug candidates as described above.

We are using co-crystallography-guided drug design and use of cellular drug target engagement imaging assays that incorporate insights derived from our AP3 platform, aiming to accelerate the advancement, and maximally improve the likelihood of success of, these internal programs. We are not only using our AP3 platform to generate drug-tailored, response-predictive clinical OncoSignature tests, but we also use our AP3 platform to provide unbiased, quantitative analyses of off-target effects on intracellular signaling using phosphoproteomic profiling, potentially enabling us to discover inhibitors that are both highly potent and highly selective.

ACR-2316 has shown potent WEE1 inhibition (IC50 = 1 nM) in intact cells, and with a balanced, yet potent PKMYT1 inhibition (IC50 = 27nM). In addition, ACR-2316 has shown superior in vitro and in vivo anti-cancer activity when compared to benchmark WEE1 and PKMYT1 inhibitors, including complete regression at lower doses than competitors not able to elicit regression. We have shown in cell cycle studies, that this is driven by a profound arrest in S and G2/m of the cell cycle resulting in replicative stress and pro-apoptotic cell death. We are also developing a target and drug tailored OncoSignature test for patient selection.

We anticipate ACR-2316 will be ready for IND submission by the fourth quarter of 2024.

Expansion of Our Pipeline Through Application of AP3 and OncoSignature Tests

We have shown that our AP3 platform is capable of generating OncoSignature tests that can predict preclinical sensitivity to a number of potential cancer therapies. We are applying the power of this technology to expand our pipeline in several ways:

- Selectively pursue carefully selected in-licensing candidates for which we believe a genetics-based patient selection method is challenging and where we believe an OncoSignature predictive test can be developed that will significantly improve response rates, similar to how we identified ACR-368.
- In addition to ACR-368, Acrivon is also leveraging its proprietary AP3 precision medicine platform for developing its co-crystallography-driven, internally-discovered preclinical stage pipeline programs. These include ACR-2316, a potent, selective WEE1/PKMYT1 inhibitor with single-agent activity, and a cell cycle program with an undisclosed target.
- Establish carefully selected co-development partnerships with leading biopharmaceutical organizations that either have approved products or attractive drug candidates under competitive pressure where the availability of an OncoSignature test could significantly increase response rates, leading to new drug approvals, label expansions and the ability to deliver effective therapies to the right patients.

Broad Utility and Applications of Our AP3 Platform

Based on our extensive studies, we have demonstrated that our AP3 platform has many high impact applications, including:

- Predictive biomarkers and patient responder identification. Our AP3 platform enables identification of predictive biomarkers that are assembled into OncoSignature tests used to select patients to be treated that are predicted to be sensitive to a drug or drug candidate, so-called patient responders. This capability has been demonstrated in the studies described above. Using this approach, we have also developed predictive OncoSignature tests for a clinical stage CDK7 inhibitor and a clinical stage CDC7 inhibitor. The goal is to only treat patients most likely to benefit from the drug and avoid overtreatment of patients that do not benefit from it with the potential for side effects.
- Indication finding and expansion. The drug-tailored OncoSignature tests are also used to identify tumor types predicted to be sensitive to a drug or drug candidate. By screening across human patient tumor samples across tumor types, one can estimate the proportion of predicted responders within these samples in a matter of weeks. The goal is to identify and treat patients with attractive, high unmet need tumor types with an appropriate proportion of predicted responders and to avoid treatment of patients with tumor types that are predicted to be unresponsive to the drug or drug candidate. This is applicable

to both clinical stage drug candidates and preclinical lead series. For example, through this approach we were able to identify endometrial and bladder cancer as two predicted highly ACR-368-sensitive tumor types, which are now included in our upcoming Phase 2 clinical trials. Conversely, we also found that sqNSCLC is predicted non-sensitive to the drug candidate, consistent with the clinical trial conducted by Lilly, which showed 0% ORR in their prior clinical trial in sqNSCLC. Likewise, for preclinical stage lead series, our AP3 platform enables us to know and plan for exactly which tumor types to include in any future clinical trials. This enables indication expansion and could potentially increase the response rates in clinical trials.

- Identification of resistance mechanisms. The AP3 approach is also used to identify resistance mechanisms in human cancer, preventing a desirable drug response. Resistance mechanisms can be divided into two main categories: naïve, or intrinsic, resistance and therapy-induced, or acquired, resistance. For example, we have shown that the IRS-2 adaptor protein is a key mediator of ALK-driven tumor cell survival in neuroblastoma and can serve as an intrinsic resistance mechanism to ALK inhibition. As an example of therapy-induced resistance we have shown that protein kinase C-delta, or PKC-δ, is a resistance mechanism to Notch1 inhibition in leukemia. Moreover, in studies deploying advanced MS with so-called spatial phosphoproteomics to quantify phosphopeptides with high accuracy in the nucleus and cytoplasm of cells, a method developed in co-founder Jesper Olsen's lab, we found that upregulated AKT-Foxo3 signaling and p53 loss-of-function are acquired and intrinsic resistance mechanisms to selinexor, a selective inhibitor of the nuclear export protein XPO1, in patients with AML. Understanding of resistance mechanisms is often clinically actionable, as such patients can either effectively be excluded from therapy or, as described in next paragraph, receive rational drug combinations.

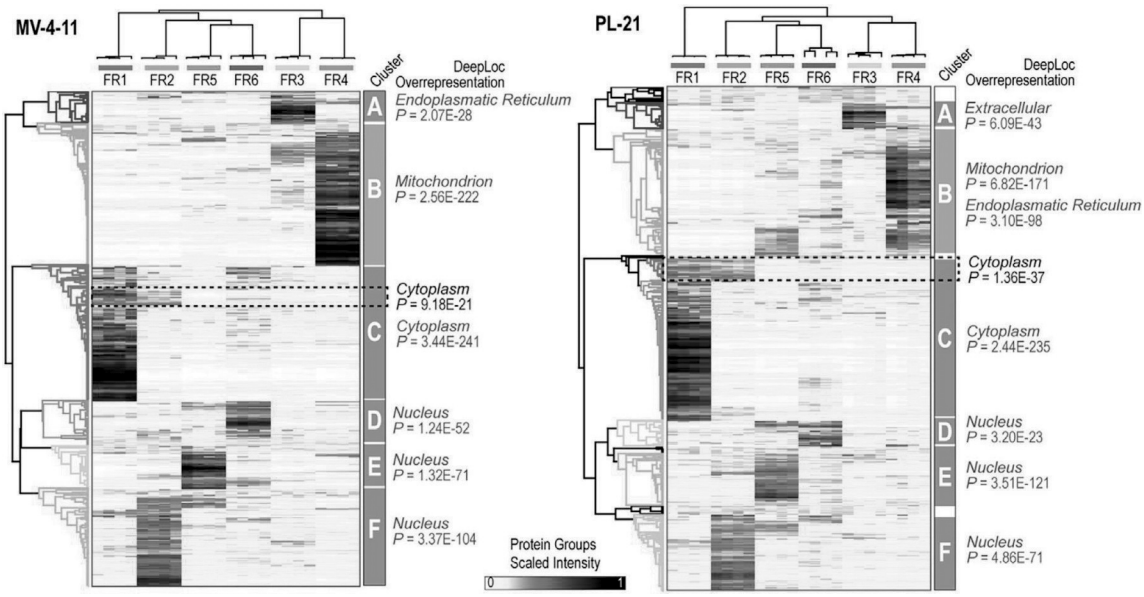


Figure 26. Spatial phosphoproteomics conducted in two human AML cell lines quantifies the nuclear and cytoplasmic levels of more than 35,000 phosphopeptides and identifies upregulated, nuclear signaling of AKT-FOXO3A as a resistance mechanism to Selinexor.

- Identification of rational drug combinations. To the extent that identified resistance mechanisms include druggable targets, these can be the basis for rational drug combinations. For example, in the studies referenced above, the uncovered resistance mechanisms included the druggable targets PKC-δ, AKT, and MDM2. Accordingly, it was demonstrated that (i) combination with the PKC inhibitor sotrastaurin overcame Notch inhibitor resistance in leukemia, (ii) combination with the AKT inhibitor MK-2206 overcame selinexor resistance, and (iii) combination with the MDM2 inhibitor, nutlin, which enhances p53 activity, enhanced selinexor sensitivity in AML. These results demonstrate the wider applicability of our AP3 platform to a number of drug target classes beyond DDR, including targets for which there is currently only limited understanding of their biological mechanisms of action.

- Unbiased drug target engagement and PD biomarker discovery. Through our high resolution phosphoproteomic drug profiling we uncover and quantify typically in the order of approximately 6,000 statistically significantly regulated phosphoproteomic changes that correlate with drug exposure. This provides a rich source of potential clinically useful biomarkers that can be developed to quantify PD drug target exposure. Such biomarkers can be used for dose-optimization through measure of the drug target engagement in patient tumor tissue in dose-finding Phase 1 clinical trials. Moreover, they can inform whether the drug candidate elicits the predicted changes in biological signaling pathways in a patient's tumor. Typically at least one of our three classes of biomarkers in our OncoSignature tests is a key PD biomarker for our drug target.

In summary, the AP3 method is broadly applicable across products and drug candidates and is developed and designed to be a transformative, efficient method to accurately match the right therapy to the right patient. Given the highly structured data resulting from AP3, we have been able to engineer it as a machine learning pipeline, aiming for high throughput and reproducible results. We expect this to be highly beneficial in our pursuit of expanding our proprietary pipeline and portfolio through continued in-licensing and co-development pharmaceutical partnerships.

Business Protection

Our AP3 platform and OncoSignature methodology has been developed and implemented for over a decade by our founding scientific team as an expert system. As such, we have multiple layers of protection. Firstly, we have over the years established a number of tools and trade secrets that we keep as proprietary know-how in-house. Secondly, we file patient stratification and treatment patent applications for our drug-tailored OncoSignature tests. For example, we have filed an ACR-368 OncoSignature patent application claiming treatment of patients with ACR-368 OncoSignature-positive tumors with ACR-368 monotherapy based on predicted sensitivity to the drug. Finally, through an exclusive license arrangement with our CDx partner who will be conducting the clinical development for our test and, pending successful market approval, commercialize it, we believe we have ensured that the test cannot be offered for other DDR inhibitors.

Manufacturing

We acquired sufficient ACR-368 drug substance and drug product from Lilly to treat several hundred patients. Aside from this material, we expect to rely on, for the foreseeable future, third-party contract manufacturing organizations, or CMOs, to produce our drug candidates for preclinical studies and clinical trials, as well as for future commercial manufacture of any drugs, if approved. We require all our CMOs to conduct manufacturing activities in compliance with current good manufacturing practice, or cGMP, requirements. We have assembled a team of experienced employees and consultants who provide the necessary technical, quality and regulatory oversight to ensure the cGMP compliance of our CMOs. Currently, we have manufacturing agreements in place with three CMOs for the manufacture of ACR-368. To date, we have successfully completed three familiarization campaigns, one GMP engineering campaign, and three registrational batches of the drug substance. We have also manufactured two batches of GMP drug product.

We plan to continue to rely on third-party manufacturers for any future trials and commercialization, if approved, of ACR-368, ACR-2316, and any future drug candidates. We anticipate that these CMOs will have the capacity to support commercial scale production, but do not have any formal agreements in place at this time. If needed, we believe we can identify and engage additional CMOs to provide active pharmaceutical ingredient and finished drug product without significant disruption to our business or clinical development timelines.

Licensing and Collaborations

License Agreement with Lilly

In January 2021, we entered into a license agreement and stock issuance agreement, or, collectively, the Lilly Agreement, with Lilly, pursuant to which we have been granted an exclusive, royalty-bearing sublicensable license to certain intellectual property rights owned or controlled by Lilly, to commercially develop, manufacture, use, distribute and sell therapeutic products containing the compound prexasertib.

Under the terms of the agreement, we paid Lilly an initial upfront fee payment of $5.0 million. In connection with entering into the agreement, we also entered into a common stock issuance agreement with Lilly pursuant to which we issued Lilly 336,575 shares of our common stock and 46,058 shares of Series B convertible preferred stock, which converted into 18,677 shares of common stock immediately upon the closing of our initial public offering, or IPO. As additional consideration for the license, we are required to pay Lilly aggregate development and commercial milestone payments of up to $168.0 million, of which $5.0 million is due prior to NDA. We are also obligated to pay a tiered percentage royalty on annual net sales ranging from a low single-digit up to a maximum of 10% subject to certain specified reductions. Royalties are payable by us on a licensed product-by-licensed product and country-by-country basis until the later of the expiration of the last valid claim covering the licensed product in such country, expiration of all applicable regulatory exclusivities in such country for such licensed product and the tenth anniversary of the first commercial sale of such licensed product in such country, provided, that our obligation to pay royalties for a given licensed product in a given country will expire earlier upon achievement of certain sales thresholds by generic products is such country.

We also have provided Lilly with certain, limited rights of first negotiation with us for reacquisition of the ACR-368 program with such right expiring 45 days following the completion of certain clinical milestones. The right to first negotiation expressly does not restrict any potential Change of Control transaction of our company (as each such term is contractually defined in the agreement).

Companion Diagnostic Agreement

In June 2022, we entered into a companion diagnostic agreement with Akoya pursuant to which we agreed to co-develop, validate, and commercialize our proprietary ACR-368 OncoSignature test, the CDx that will be used to identify patients with cancer most likely to respond to ACR-368.

Pursuant to the agreement, Akoya, in partnership with us, will develop, clinically validate, seek regulatory approval for, and, pending ACR-368 approval, commercialize the OncoSignature test required for prescribing ACR-368. Development of the CDx will be overseen by a joint steering committee. Each party is required to use commercially reasonable efforts to carry out its activities under the agreement. The agreement contains certain mutual exclusivity obligations of the parties with respect to the biomarkers and drug target, subject to certain specified limitations, including in the event that Akoya is unable to sufficiently supply commercial needs of such CDx.

Pursuant to the agreement, we paid Akoya a one-time, non-refundable, non-creditable upfront payment in the amount of $0.6 million. The Company is obligated to pay Akoya up to an aggregate of $17.3 million upon the achievement of specified development milestones. As of March 28, 2024, development milestones have been achieved under the agreement, resulting in payments of $8.3 million by the Company to Akoya. Other than certain specified pass-through costs, each party is responsible for its own costs associated with the development of the companion diagnostic. Akoya will procure and manufacture necessary supplies to perform the ACR-368 OncoSignature test to support our clinical development and commercial requirements, in accordance with a supply agreement to be mutually agreed upon by the parties. We may terminate the agreement at our convenience, subject to the payment of a termination fee in the amount of $1.0 million.

The agreement shall, unless terminated early, continue in perpetuity. Either party may terminate the agreement in the event of an uncured, material breach by the other party or insolvency of the other party. Additionally, we may terminate the agreement for any reason subject to a specified notice period.

Patent License Agreement

In April 2018, we entered into a patent license agreement, or the Blume-Jensen License Agreement, with Peter Blume-Jensen, our Chief Executive Officer and President, that granted us an exclusive, worldwide, irrevocable, perpetual, royalty-free license under certain licensed patents relating to broad aspects of the general discovery process for biomarkers in our drug-tailored OncoSignature tests, such as our ACR-368 OncoSignature test, for any and all purposes and uses, including without limitation and rights to sublicense through multiple tiers.

Under the terms of the Blume-Jensen License Agreement, we issued 871,857 shares of our common stock to Dr. Blume-Jensen. In addition, we were obligated to reimburse Dr. Blume-Jensen the sum of $150,000, which represented the parties' agreed upon estimate of unreimbursed past expenses incurred by Dr. Blume-Jensen with respect to the preparation, filing, prosecution, protection and maintenance of the licensed patents, within 30 days following the closing of an equity financing by us with gross proceeds of at least $2,000,000. Following the closing of our Series A-1 Preferred Stock financing, we paid Dr. Blume-Jensen $150,000 in October 2020 to satisfy this obligation.

Unless otherwise terminated pursuant to its termination provisions, the Blume-Jensen License Agreement will expire upon the expiration of all claims under the licensed patents. We have the right to terminate the Blume-Jensen License Agreement at any time upon written notice to Dr. Blume-Jensen. Dr. Blume-Jensen may also terminate the Blume-Jensen License Agreement in the event of our dissolution, liquidation, bankruptcy or if we cease operations for a continuous period of 12 months.

Intellectual Property

We pursue a layered intellectual property strategy, including patents, trademarks, and trade secret rights, to protect our AP3 platform, the OncoSignature tests we develop with it, and the drug candidates we work to commercialize.

Given the early stage of development of our drug candidates, we cannot be certain that any of our intellectual property rights will provide protection for any drug candidate that may ultimately be commercialized. ACR-368 is our only drug candidate that has advanced to clinical testing, and there can be no certainty that its clinical development will be successful, or that significant modification or adjustment will not be required for successful commercialization.

Our future commercial success depends, in part, on our abilities to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; to defend and enforce our patents and other intellectual property; to preserve the confidentiality of our trade secrets; and to operate without infringing, misappropriating or violating the valid and enforceable patents and other intellectual property rights of third parties. Our ability to stop third parties from making,

using, selling, offering to sell or importing our products, or from developing competing diagnostic technologies, may depend on the extent to which we have rights under valid and enforceable patents, trade secrets or other intellectual property rights that cover these activities. We cannot be sure that patents will issue with respect to any of the owned or licensed pending patent applications or, with respect to any patent applications that we may file or license in the future, nor can we be sure that any of our owned or licensed patents or any patents that may be issued now or in the future will be commercially useful in protecting any products that we ultimately attempt to commercialize, or any method of making or using such products. Moreover, we may be unable to obtain patent protection for certain of our drug candidates, or for our OncoSignature tests or AP3 platform. See the section titled "Risk Factors—Risks Related to Intellectual Property" for a more comprehensive description of risks related to our intellectual property.

Patents

An issued patent provides its owner (or its licensee) with a right to exclude others from making, using or selling that which is claimed in the patent, for a specified period of time (the "term" of the patent), in the jurisdiction in which the patent is issued. In the United States, and in many other countries, patents have a presumptive term of 20 years from their effective filing date (which is the earliest non-provisional filing date to which the patent claims priority). However, many jurisdictions, including the United States, require the payment of periodic maintenance fees in order for patents to remain in force for the full 20-year term; some jurisdictions require periodic annuities to be paid even to maintain pendency of an application. The United States also has provisions that may shorten the term of a patent if its claims are too similar to another patent owned by the same party that has a shorter term. The United States and certain other jurisdictions also have provisions that permit extension of patent term for patents that claim a drug or drug product, or its approved use, if the patent was issued before clinical trials were completed and certain other requirements were satisfied. In the United States, such extension is called a Patent Term Extension, or PTE, and it is limited to a period of not more than five years, or a period that would extend the patent so that the total patent term including the PTE does not exceed 14 years after the date of regulatory approval; only one patent can be extended per product approval. The United States also offers a different form of patent term extension, known as Patent Term Adjustment, or PTA, whereby a particular patent's term is automatically extended beyond the 20-year date if the United States Patent and Trademark Office, or the USPTO, caused delay during its examination; however, potentially available PTA is reduced by any amount of any delay caused by the patent applicant.

Our patent portfolio includes both in-licensed and owned patent filings, as discussed in more detail below. Particularly given our pre-commercial state of development, we cannot be certain that any of the patent filings in our portfolio will provide meaningful protection for any drug or OncoSignature test we ultimately attempt to commercialize.

We have in-licensed from Lilly a portfolio including three families of patent filings relating to ACR-368. See the section titled "Business—Licensing and Collaborations." The first family, with a presumptive twenty-year term extending into 2029, includes issued patents in the United States (including US patent 8,314,108, which, due to PTA, will expire in 2030) and including in Europe, China, Hong Kong, Japan, Macao and Taiwan. The second family, with a presumptive twenty-year term extending into 2036, includes issued patents in the United States (including US patent 11,123,326, which, due to PTA, will expire in 2037) and in Europe, Japan and Taiwan and a pending application in the United States, that claim use of ACR-368 to treat certain particular types of cancer. The third family, with a presumptive twenty-year term extending into late 2036, includes issued patents in the United States (including US patent 10,189,818, which, due to PTA, will expire in 2037) and in Europe, China, Hong Kong, Japan and Taiwan. We may be able to pursue patent term extension in one or more jurisdictions for patents in this in-licensed portfolio to provide extended protection to ACR-368.

We have also in-licensed from our founder a patent family with a presumptive twenty-year term extending into 2028 that includes issued EP and pending US filings that claims aspects of our AP3 platform relating to methods of identifying responder populations.

We own an international patent application directed to our OncoSignature test for ACR-368, including claims to methods of treating patients identified by the OncoSignature test with ACR-368; non-provisional filings in the United States that claim the benefit of this filing and filings in other jurisdictions that claim priority to this filing would have a presumptive twenty-year term extending into 2043. We also own a provisional patent application directed to an additional OncoSignature test; non-provisional filings in the United States that claim the benefit of this filing and filings in other jurisdictions that claim priority to this filing would have a presumptive twenty-year term extending into 2045.

We own international patent applications directed to composition of matter for our WEE1 and PKMYT1 programs; non-provisional filings in the United States that claim the benefit of these filings and filings in other jurisdictions that claim priority to these filings would have a presumptive twenty-year term extending into 2043. We also own provisional patent filings in the United States directed to composition of matter for our dual WEE1/PKMYT1 program; non-provisional filings in the United States that claim the benefit of these filings and filings in other jurisdictions that claim priority to these filing would have a presumptive twenty-year term extending into 2044.

We intend to pursue patent protection, whether through in-licensing or our own development, for future drug candidates and OncoSignature tests. We may also pursue additional patent protection for features of our AP3 platform, though we will rely on confidentiality and trade secret protections for certain aspects of that platform.

Trademarks

We have registered our rights in the OncoSignature mark in the United States and various other jurisdictions. We expect to pursue trademark protection for additional marks in the future for products and assays that we commercialize.

Trade Secrets and Confidential Information

For certain of our technologies, including aspects of our AP3 platform and how we use it to develop OncoSignature tests, we rely on unpatented trade secrets and confidential know-how to develop and maintain our competitive position. However, trade secrets are notoriously difficult to protect. Breaches of trade secret or confidentiality provisions can be challenging to detect, and even more challenging to prove. We seek to protect our proprietary information, in part, through confidentiality and non-competition agreements with employees, consultants, partners, and other advisors. These agreements may be breached and we may not be able to successfully defend our rights. Moreover, we may not be able to secure adequate remedies for harm caused by such breach. Furthermore, our trade secrets or confidential information may be independently developed by a third party, and we may not have any ability to restrain or secure any remedy from them. As a result, we may be unable to meaningfully protect our trade secrets and proprietary information. See the section titled "Risk Factors—Risks Related to Intellectual Property" for a more comprehensive description of risks related to our trade secrets and confidential information.

Competition

The biopharmaceutical industry is characterized by the rapid evolution of technologies and understanding of precision medicine in oncology, intense competition and a strong emphasis on intellectual property. As one of the first companies to adopt a phosphoproteomics-based approach with a platform designed to develop predictive protein signature tests for patient responder identification, we believe that our differentiated approach, strategy, as well as our scientific capabilities, know-how and experience provide us with significant competitive advantages. However, in the future, we expect competition from multiple sources, including major pharmaceutical, specialty pharmaceutical, and existing or emerging biotechnology companies, academic research institutions and governmental agencies and public and private research institutions worldwide. Many of our competitors, either alone or with their collaborators, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient enrollment in clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. As a result, our competitors may discover, develop, license or commercialize products before or more successfully than we do.

At present, we do not believe we face competition from segments of the pharmaceutical, biotechnology and other related markets that pursue the development of precision oncology therapies for the smaller subsets of patients with genetically-defined cancers. However, we anticipate several biopharmaceutical companies will aim to develop precision oncology approaches for the larger subsets of cancers where genetics has proven insufficient for patient responder identification. We expect that the broader biopharmaceutical field will eventually recognize proteomics as the next era of precision medicine, but we believe it will take some time before significant competition will truly emerge in this space. There are several competitors with CHK1/2 inhibitors, WEE1 and PKMYT1 inhibitors and PKMYT1 inhibitors, including Sierra Oncology (SRA737), Astrazeneca/Merck (adavosertib), Zentalis (azenosertib), Debiopharm (Debio0123), Impact Therapeutics (IMP7068),Shouya Holdings (SY-4835) and Repare Therapeutics (lunresertib), and Schrödinger (SGR-3515).

We, like other precision oncology medicine companies, face competition more broadly across the oncology market for cost-effective and reimbursable cancer treatments. The most common methods of treating patients with cancer are surgery, radiation and drug therapy, including chemotherapy, hormone therapy, biologic therapy, such as monoclonal and bispecific antibodies, immunotherapy, cell-based therapy and targeted therapy, or a combination of any such methods. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. While our drug candidates, if any are approved, may compete with these existing drugs and other therapies, to the extent they are ultimately used in combination with or as an adjunct to these therapies, our drug candidates may not be competitive with them. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis. Insurers and other third-party payors may also encourage the use of generic products or specific branded products. As a result, obtaining market acceptance of, and gaining significant share of the market for, any of our drug candidates that we successfully introduce to the market may pose challenges. In addition, many companies are developing new oncology therapeutics, and we cannot predict what the standard of care will be as our drug candidates progress through clinical development.

We could see a reduction or elimination in our commercial opportunity if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient to administer, are less expensive or with a more favorable label than our drug candidates. Our competitors also may obtain FDA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. The key competitive factors affecting the success of all of our drug candidates, if approved, are likely to be their efficacy, safety, convenience, price, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Government Regulation

The FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries impose substantial requirements upon the preclinical and clinical development, manufacture and marketing of pharmaceutical and diagnostic products. These agencies and other federal, state and local entities regulate research and development activities and the testing, manufacture, quality control, safety, effectiveness, labeling, storage, packaging, recordkeeping, tracking, approval, import, export, distribution, advertising and promotion of drug and diagnostic products.

U.S. Government Regulation of Drug Products

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve a pending New Drug Application, or NDA, withdrawal of an approval, imposition of a clinical hold, issuance of untitled or warning letters, product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution, injunctions, debarment, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before drug candidates may be marketed in the United States generally involves the following:

- nonclinical laboratory and animal tests that must be conducted in accordance with applicable regulations, including good laboratory practices, or GLPs;
- submission to the FDA of an investigational new drug, or IND, application, which must become effective before clinical trials may begin;
- approval by an independent institutional review board, or IRB, for each clinical site or centrally before each trial may be initiated;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug candidate for its intended use, performed in accordance with good clinical practices, or GCPs;
- submission to the FDA of an NDA and payment of user fees;
- satisfactory completion of an FDA advisory committee review, if applicable;
- pre-approval inspection of manufacturing facilities and selected clinical investigators for their compliance with cGMPs and GCPs;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- FDA review and approval of an NDA to permit commercial marketing for particular indications for use; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

The testing and approval process requires substantial time, effort and financial resources.

Preclinical Studies

Preclinical studies include laboratory evaluation of drug substance chemistry, pharmacology, toxicity and drug product formulation, as well as animal studies to assess potential safety and efficacy. Prior to commencing the first clinical trial with a drug candidate, a sponsor must submit the results of the preclinical tests and preclinical literature, together with manufacturing information,

analytical data and any available clinical data or literature, among other required information, to the FDA as part of an IND. Some preclinical studies may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the conduct of the clinical trial and imposes a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA also may impose a partial clinical hold that would limit a trial, for example, to certain doses or for a certain length of time or to a certain number of subjects. As a result, submission of an IND may not result in FDA authorization to commence a clinical trial.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development, as well as amendments to previously submitted clinical trials. Further, an independent IRB for each institution participating in the clinical trial must review and approve the plan for any clinical trial, its informed consent form and other communications to study subjects before the clinical trial commences at that site. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB must continue to oversee the clinical trial while it is being conducted, including any changes to the study plans.

Regulatory authorities, an IRB or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk, the clinical trial is not being conducted in accordance with the FDA's or the IRB's requirements, or if the drug has been associated with unexpected serious harm to subjects. Some studies also include a data safety monitoring board, which receives special access to unblinded data during the clinical trial and may advise the sponsor to halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy.

In general, for purposes of NDA approval, human clinical trials are typically conducted in three sequential phases that may overlap.

Phase 1. Studies are initially conducted to test the drug candidate for safety, dosage tolerance, structure-activity relationships, mechanism of action, absorption, metabolism, distribution and excretion in healthy volunteers or subjects with the target disease or condition. If possible, Phase 1 clinical trials may also be used to gain early evidence of product effectiveness.

Phase 2. Controlled studies are conducted with groups of subjects with a specified disease or condition to provide enough data to evaluate the preliminary efficacy, optimal dosages and dosing schedule and expanded evidence of safety. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expansive Phase 3 clinical trials.

Phase 3. These clinical trials are generally undertaken in larger subject populations to provide statistically significant evidence of clinical efficacy and to further test for safety in an expanded subject population at multiple clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling. These clinical trials may be done at trial sites outside the United States as long as the global sites are also representative of the U.S. population and the conduct of the study at global sites comports with FDA regulations and guidance, such as compliance with GCPs.

The FDA may require, or companies may pursue, additional clinical trials after a product is approved. These so-called Phase 4 studies may be made a condition to be satisfied after approval. The results of Phase 4 studies can confirm the effectiveness of a drug candidate and can provide important safety information.

We intend to proceed with the design and conduct of certain of our clinical trials under the FDA's master protocol guidance. This guidance is intended to provide recommendations to sponsors of drugs or biologics for the treatment of cancer to expedite the development of such products by simultaneously evaluating more than one investigational drug and/or more than one cancer type within the same overall trial structure (master protocols) in adult and pediatric cancers. In general, the RP2D should have been established for an investigational drug or drugs evaluated in a master protocol.

Clinical trials must be conducted under the supervision of qualified investigators in accordance with GCP requirements, which include the requirements that all research subjects provide their informed consent in writing for their participation in any clinical trial, and the review and approval of the study by an IRB. Investigators must also provide information to the clinical trial sponsors to allow the sponsors to make specified financial disclosures to the FDA. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the trial procedures, the parameters to be used in monitoring safety and the efficacy criteria to be evaluated and a statistical analysis plan. Information about some clinical trials, including a description of the trial and trial results, must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their ClinicalTrials.gov website.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and the IRB and more frequently if serious adverse events occur.

The manufacture of investigational drugs for the conduct of human clinical trials is subject to cGMP requirements. Investigational drugs and active pharmaceutical ingredients imported into the United States are also subject to regulation by the FDA relating to their labeling and distribution. Further, the export of investigational drug products outside of the United States is subject to regulatory requirements of the receiving country as well as U.S. export requirements under the FDCA.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug candidate as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

Special FDA Expedited Review and Approval Programs

The FDA has various programs, including fast track designation, breakthrough therapy designation, accelerated approval, and priority review, which are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

Under the fast track program, the sponsor of a new drug candidate may request that the FDA designate the drug candidate for a specific indication as a fast track drug concurrent with, or after, the filing of the IND for the drug candidate. To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat patients with a serious or life threatening disease or condition and demonstrates the potential to address an unmet medical need. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. Fast track designation provides additional opportunities for interaction with the FDA's review team and may allow for rolling review of NDA components before the completed application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA. However, the FDA's time period goal for reviewing an application does not begin until the last section of the NDA is submitted. The FDA may decide to rescind the fast track designation if it determines that the qualifying criteria no longer apply.

In addition, a sponsor can request breakthrough therapy designation for a drug if it is intended, alone or in combination with one or more other drugs, to treat patients with a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are eligible for intensive guidance from the FDA on an efficient drug development program, organizational commitment to the development and review of the product including involvement of senior managers, and, like fast track products, are also eligible for rolling review of the NDA. Both fast track and breakthrough therapy products may be eligible for accelerated approval and/or priority review, if relevant criteria are met.

Under the FDA's accelerated approval regulations, the FDA may approve a drug for a serious or life threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. A drug candidate approved on this basis is subject to rigorous post marketing compliance requirements, including the completion of Phase 4 or post approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post approval studies, or confirm a clinical benefit during post marketing studies, will allow the FDA to withdraw the drug from the market on an expedited basis. In addition, for products being considered for accelerated approval, the FDA generally requires, unless otherwise informed by the agency, that all advertising and promotional materials intended for dissemination or publication within 120 days of marketing approval be submitted to the agency for review during the pre-approval review period.

Once an NDA is submitted for a product intended to treat patients with a serious condition, the FDA may assign a priority review designation if the FDA determines that the product, if approved, would provide a significant improvement in safety or effectiveness. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under the Prescription Drug User Fee Act, or PDUFA, guidelines. Under the current PDUFA performance goals, these six and ten month review periods are measured from the 60-day filing date rather than the receipt date for NDAs for new molecular entities, which typically

adds approximately two months to the timeline for review from the date of submission. In addition, the FDA may review applications under Real-Time Oncology Review, or RTOR, which, according to the FDA, aims to explore a more efficient review process to ensure that safe and effective treatments are available to patients as early as possible, while maintaining and improving review quality. Drugs considered for review under RTOR must be likely to demonstrate substantial improvements over available therapy, which may include drugs previously granted breakthrough therapy designation for the same or other indications, and must have straightforward study designs and endpoints that can be easily interpreted. RTOR allows the FDA to review much of the data in a NDA earlier, before the applicant formally submits the complete application. This analysis of the pre-submission package gives the FDA and applicants an early opportunity to address data quality and potential review issues and allows the FDA to provide early feedback regarding the most effective way to analyze data to properly address key regulatory questions.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. In addition, the manufacturer of an investigational drug for a serious or life threatening disease is required to make available, such as by posting on its website, its policy on responding to requests for expanded access. Furthermore, fast track designation, breakthrough therapy designation, accelerated approval and priority review do not change the standards for approval and may not ultimately expedite the development or approval process.

NDA Submission and Review by the FDA

Assuming successful completion of the required clinical and preclinical testing, among other items, the results of product development, including chemistry, manufacture and controls, nonclinical studies and clinical trials are submitted to the FDA, along with proposed labeling, as part of an NDA. The submission of an NDA requires payment of a substantial user fee to the FDA. These user fees must be filed at the time of the first submission of the application, even if the application is being submitted on a rolling basis. Fee waivers or reductions are available in some circumstances. One basis for a waiver of the application user fee is if the applicant employs fewer than 500 employees, including employees of affiliates, the applicant does not have an approved marketing application for a product that has been introduced or delivered for introduction into interstate commerce, and the applicant, including its affiliates, is submitting its first marketing application.

In addition, under the Pediatric Research Equity Act, an NDA or supplement to an NDA for a new active ingredient, indication, dosage form, dosage regimen or route of administration must contain data that are adequate to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults or full or partial waivers from the pediatric data requirements.

The FDA must refer applications for drugs that contain active ingredients, including any ester or salt of the active ingredients, that have not previously been approved by the FDA to an advisory committee or provide in an action letter a summary of the reasons for not referring it to an advisory committee. The FDA may also refer drugs which present difficult questions of safety or efficacy to an advisory committee. An advisory committee is typically a panel that includes clinicians and other experts who review, evaluate and make a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

The FDA reviews applications to determine, among other things, whether a product is safe and effective for its intended use and whether the manufacturing controls are adequate to assure and preserve the product's identity, strength, quality and purity. Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities, including contract manufacturers and subcontracts, are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical trial sites to assure compliance with GCPs.

Once the FDA receives an application, it has 60 days to review the NDA to determine if it is substantially complete to permit a substantive review, before it accepts the application for filing. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has set the review goal of 10 months from the 60-day filing date to complete its initial review of a standard NDA for a new molecular entity, or NME, and make a decision on the application. For priority review applications, the FDA has set the review goal of reviewing NME NDAs within six months of the 60-day filing date. Such deadlines are referred to as the PDUFA date. The PDUFA date is only a goal and the FDA does not always meet its PDUFA dates. The review process and the PDUFA date may also be extended if the FDA requests or the NDA sponsor otherwise provides additional information or clarification regarding the submission during the review period that amends the original application.

Once the FDA's review of the application is complete, the FDA will issue either a Complete Response Letter, or CRL, or an approval letter. A CRL indicates that the review cycle of the application is complete and the application is not ready for approval. A CRL generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing, or other information or analyses in order for the FDA to reconsider the application in the future. Even with the submission of additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA may issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

The FDA may delay or refuse approval of an NDA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product, or impose other conditions, including distribution restrictions or other risk management mechanisms. For example, the FDA may require a REMS as a condition of approval or following approval to mitigate any identified or suspected serious risks and ensure safe use of the drug. The FDA may prevent or limit further marketing of a product, or impose additional post-marketing requirements, based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements, FDA notification and FDA review and approval. Further, should new safety information arise, additional testing, product labeling or FDA notification may be required.

If regulatory approval of a product is granted, such approval may entail limitations on the indicated uses for which such product may be marketed or may include contraindications, warnings or precautions in the product labeling, which has resulted in a boxed warning. A boxed warning is the strictest warning put in the labeling of prescription drugs or drug products by the FDA when there is reasonable evidence of an association of a serious hazard with the drug. The FDA also may not approve the inclusion of all labeling claims sought by an applicant. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing regulatory standards is not maintained or if problems occur after the product reaches the marketplace. In addition, the FDA may require Phase 4 post-marketing studies to monitor the effect of approved products, and may limit further marketing of the product based on the results of these post-marketing studies.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat patients with a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or 200,000 or more individuals in the United States for which there is no reasonable expectation that the cost of developing and making available in the United States a drug or biologic for this type of disease or condition will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting an NDA. After the FDA grants Orphan Drug Designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. The Orphan Drug Designation does not convey any advantage in, or shorten the duration of, the regulatory review or approval process.

If a product that has Orphan Drug Designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusive approval (or exclusivity), which means that the FDA may not approve any other applications, including a full NDA, to market the same drug for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the holder of the orphan drug exclusivity cannot assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of Orphan Drug Designation are tax credits for certain research and a waiver of the NDA application fee.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Moreover, the Inflation Reduction Act (IRA), which includes among its provisions the establishment, beginning in 2026, of a "maximum fair price" for a fixed number of pharmaceutical and biological products covered under Medicare Parts B and D following a price negotiation process with the CMS, specifically exempts orphan drugs designated for only one rare disease or condition and for which the only active approved indication is for such disease or condition from the price negotiation process. However, those drugs with multiple orphan designations are not explicitly excluded from the IRA's drug price negotiation provisions. The imposition of a "maximum fair price" under the IRA could limit the amounts that federal and state governments will pay for our products and prevent us from being able to generate revenue sufficient to cover our costs or attain profitability.

U.S. Post-Approval Requirements

Any products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including periodic reporting, product sampling and distribution, advertising, promotion, drug shortage reporting, compliance with any post-approval requirements imposed as a conditional of approval such as Phase 4 clinical trials, REMS and surveillance, recordkeeping and reporting requirements, including adverse experiences.

After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There also are continuing, annual program fee requirements for approved products, as well as new application fees for supplemental applications with clinical data. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies and to list their drug products, and are subject to periodic announced and unannounced inspections by the FDA and these state agencies for compliance with cGMPs and other requirements, which impose procedural and documentation requirements.

Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented, or FDA notification. FDA regulations also require investigation and correction of any deviations from cGMPs and specifications, and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. Manufacturers and other parties involved in the drug supply chain for prescription drug products must also comply with product tracking and tracing requirements and for notifying the FDA of counterfeit, diverted, stolen and intentionally adulterated products or products that are otherwise unfit for distribution in the United States.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in withdrawal of marketing approval, mandatory revisions to the approved labeling to add new safety information or other limitations, imposition of post-market studies or clinical trials to assess new safety risks, or imposition of distribution or other restrictions under a REMS program, among other consequences.

The FDA closely regulates the marketing and promotion of drugs. A company can make only those claims relating to safety and efficacy that are consistent with the FDA approved labeling. Physicians, in their independent professional medical judgment, may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. However, manufacturers and third parties acting on their behalf are prohibited from marketing or promoting drugs in a manner inconsistent with the approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Failure to comply with any of the FDA's requirements could result in significant adverse enforcement actions. These include a variety of administrative or judicial sanctions, such as refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, imposition of a clinical hold or termination of clinical trials, warning letters, untitled letters, modification of promotional materials or labeling, product recalls, product seizures or detentions, refusal to allow imports or exports, total or partial suspension of production or distribution, debarment, injunctions, fines, consent decrees, corporate integrity agreements, refusals of government contracts and new orders under existing contracts, exclusion from participation in federal and state healthcare programs, restitution, disgorgement or civil or criminal penalties, including fines and imprisonment. It is also possible that failure to comply with the FDA's requirements relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state healthcare fraud and abuse and other laws, as well as state consumer protection laws. Any of these sanctions could result in adverse publicity, among other adverse consequences.

U.S. Marketing Exclusivity

The FDA provides periods of non-patent regulatory exclusivity, which provides the holder of an approved NDA limited protection from new competition in the marketplace for the innovation represented by its approved drug for a period of three or five years following the FDA's approval of the NDA. Five years of exclusivity are available to new chemical entities, or NCEs. A drug is an NCE if the FDA has not previously approved any other new drug containing the same active moiety. An active moiety is the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt, including a salt with hydrogen or coordination bonds, or other noncovalent, or not involving the sharing of electron pairs between atoms, derivatives, such as a complex (i.e., formed by the chemical interaction of two compounds), chelate (i.e., a chemical compound), or clathrate (i.e., a polymer framework that traps molecules), of the molecule, responsible for the therapeutic activity of the drug substance. During the exclusivity period, the FDA may not accept for review or approve an Abbreviated New Drug Application, or ANDA, or a 505(b)(2) NDA submitted by another company that contains the previously approved active moiety. An ANDA or 505(b)(2) application, however, may be submitted one year before NCE exclusivity expires if a Paragraph IV certification is filed.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs or 505(b)(2) NDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product; it does, however, block the FDA from approving ANDAs or 505(b)(2) NDAs during the period of exclusivity. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

Regulation of Companion Diagnostics

We believe that the success of ACR-368 and certain of our drug candidates may depend, in part, on the development and commercialization of OncoSignature, a companion diagnostic candidate. Companion diagnostics identify patients who are most likely to benefit from a particular therapeutic product; identify patients likely to be at increased risk for serious side effects as a result of treatment with a particular therapeutic product; or monitor response to treatment with a particular therapeutic product for the purpose of adjusting treatment to achieve improved safety or effectiveness. Companion diagnostics are regulated as medical devices by the FDA. In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption or FDA exercise of enforcement discretion applies, diagnostic tests generally require marketing clearance or approval from the FDA prior to commercialization. The two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510(k) clearance, and approval of a premarket approval application, or PMA approval. We intend to seek PMA approval of our OncoSignature companion diagnostic candidate.

PMA applications must be supported by valid scientific evidence, which typically requires extensive data, including technical, preclinical, clinical and manufacturing data, to demonstrate to the FDA's satisfaction the safety and effectiveness of the device. For diagnostic tests, a PMA application typically includes data regarding analytical and clinical validation studies. As part of its review of the PMA, the FDA will conduct a pre-approval inspection of the manufacturing facility or facilities to ensure compliance with the Quality System Regulation, or QSR, which requires manufacturers to follow design, testing, control, documentation and other quality assurance procedures. The FDA's review of an initial PMA application is required by statute to take between six to ten months, although the process typically takes longer, and may require several years to complete. If the FDA evaluations of both the PMA application and the manufacturing facilities are favorable, the FDA will either issue an approval letter or an approvable letter, which usually contains a number of conditions that must be met in order to secure the final approval of the PMA. If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny the approval of the PMA or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. Once granted, PMA approval may be withdrawn by the FDA if compliance with post-approval requirements, conditions of approval or other regulatory standards is not maintained or problems are identified following initial marketing.

On July 31, 2014, the FDA issued a final guidance document addressing the development and approval process for "In Vitro Companion Diagnostic Devices." According to the guidance document, for novel therapeutic products that depend on the use of a diagnostic test and where the diagnostic device could be essential for the safe and effective use of the corresponding therapeutic product, the premarket application for the companion diagnostic device should be developed and approved or cleared contemporaneously with the therapeutic, although the FDA recognizes that there may be cases when contemporaneous development may not be possible. However, in cases where a drug cannot be used safely or effectively without the companion diagnostic, the FDA's guidance indicates it will generally not approve the drug without the approval or clearance of the diagnostic device. The FDA also issued a draft guidance in

July 2016 setting forth the principles for co-development of an in vitro companion diagnostic device with a therapeutic product. The draft guidance describes principles to guide the development and contemporaneous marketing authorization for the therapeutic product and its corresponding in vitro companion diagnostic.

Once cleared or approved, the companion diagnostic device must adhere to post-marketing requirements including the requirements of FDA's QSR, adverse event reporting, recalls and corrections along with product marketing requirements and limitations. Like drug and biologic makers, companion diagnostic makers are subject to unannounced FDA inspections at any time during which the FDA will conduct an audit of the product(s) and the company's facilities for compliance with its authorities.

Regulation Outside the United States

In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety, and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable foreign regulatory authorities before we can commence clinical trials or marketing of the product in foreign countries and jurisdictions. Although many of the issues discussed above with respect to the United States apply similarly in the context of the European Union, the approval process varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Other Healthcare Laws and Compliance Requirements

Although we do not currently have any products on the market and do not make patient referrals or bill Medicare, Medicaid, or other government or commercial third-party payers, in addition to FDA restrictions on marketing of pharmaceutical and biological products, we may also be subject to healthcare statutory and regulatory requirements and enforcement by the U.S. federal and state governments through our relationships with healthcare providers, physicians, other pharmaceutical and medical device manufacturers, and third-party payors. These laws include anti-kickback statutes, false claims statutes and other healthcare laws and regulations.

The federal Anti-Kickback Statute is a criminal statute that prohibits, among other things, any person or entity from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, the referral of an individual for, or purchasing, leasing, ordering, or arranging for the purchase, lease or order of, any good, facility, item or service that may be reimbursable, in whole or in part, under Medicare, Medicaid, or other federal healthcare programs. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the ACA) amended the intent element of the federal Anti-Kickback Statute to clarify that a person or entity need not have actual knowledge of the statute or specific intent to violate it in order to commit a violation. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other, including, for example, arrangements relating to consulting/speaking arrangements, discount and rebate offers, grants, charitable contributions, and patient support offerings. The term remuneration has been interpreted broadly to include anything of value. A conviction for violation of the federal Anti-Kickback Statute can result in criminal fines and/or imprisonment and requires mandatory exclusion from participation in federal health care programs. Exclusion from the federal healthcare programs may also be imposed if the government determines that an entity has committed acts that are prohibited by the federal Anti-Kickback Statute. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution or other regulatory sanctions under the law, the exceptions and safe harbors are drawn narrowly and practices that involve remuneration intended to induce prescribing, purchasing, or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the elements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the federal Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances.

The federal civil False Claims Act, prohibits, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim. The False Claims Act covers claims made to programs where the federal government reimburses (directly or indirectly) individuals and entities, such as under the Medicare and Medicaid programs, as well as programs where the federal government is a direct purchaser, such as when it purchases off of the Federal Supply Schedule. The law also prohibits avoiding, decreasing or concealing an obligation to pay money to the federal government. The government can bring claims directly or through a civil whistleblower or *qui tam* action, and potential liability includes mandatory treble damages and significant per claim penalties currently set at $13,948 to $27,894 per false claim or statement for penalties assessed after January 14, 2024. Moreover, the ACA amended the federal Anti-Kickback Statute such that a violation of that statute can serve as a basis for liability

under the federal False Claims Act. Most states also have statutes or regulations similar to the federal Anti-Kickback Statute and False Claims Act, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply to commercially reimbursed items or services or regardless of whether reimbursement from a federal or state healthcare program is available for the item or service. There is also the Federal Criminal False Claims Act, which is similar to the Federal Civil False Claims Act and imposes criminal liability on those that make or present a false, fictitious or fraudulent claim to the federal government.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of whether the payor is public or private, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense and knowingly and willfully falsifying, concealing or covering up by any trick, scheme or device a material fact or making any materially false, fictitious or fraudulent statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Additionally, the ACA amended the intent requirement of some of these criminal statutes under HIPAA so that a person or entity no longer needs to have actual knowledge of the statute, or the specific intent to violate it, to have committed a violation.

Further, pursuant to the ACA, the Centers for Medicare & Medicaid Services (CMS) has promulgated regulations to implement what is commonly known as the federal Physician Payment Sunshine Act (or Open Payments Program), which, among other things, requires certain manufacturers of drugs, devices, biologicals, and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, among others, to track and report annually information related to specified payments or other transfers of value provided to U.S.-licensed physicians (defined to include doctors, dentists, optometrists, podiatrists, and licensed chiropractors), physician assistants, nurse practitioners or clinical nurse specialists, certified registered nurse anesthetists, anesthesiologist assistants, and certified nurse-midwives, as well as, U.S. teaching hospitals. The law also requires manufacturers, among others, to report certain investment interests held by physicians or their immediate family members in the manufacturer. Failure to submit timely, accurately and completely the required information for all payments, transfers of value and ownership or investment interests may result in civil monetary penalties.

Moreover, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, impose requirements relating to the privacy, security and transmission of individually identifiable health information held by covered entities and their business associates. Among other things, HITECH makes HIPAA's security standards directly applicable to business associates, defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. Other federal, international, and state laws and obligations relating to privacy and data protection may impose new and relatively burdensome obligations, and with the substantial uncertainty over the interpretation and application of these and other obligations, we may face challenges in addressing their requirements and making necessary changes to our policies and practices and may incur significant costs and expenses in an effort to do so.

In addition, several states require pharmaceutical companies to report certain expenses relating to the marketing and promotion of drug and biological products and to report gifts and payments to individual healthcare practitioners in these states. Other states prohibit various marketing-related activities, such as the provision of certain kinds of gifts or meals. Still other states require the posting of information relating to clinical studies and their outcomes. Some states require the reporting of certain pricing information, including information pertaining to and justifying price increases, or prohibit prescription drug price gouging. In addition, states such as California, Connecticut, Nevada, and Massachusetts require pharmaceutical companies to implement compliance programs and/or marketing codes. Several additional states are considering similar proposals. Certain states and local jurisdictions also require the registration of pharmaceutical sales representatives. Compliance with these laws is difficult and time consuming, and companies that do not comply with these state laws face civil penalties.

Ensuring that our internal operations and business arrangements with third parties comply with applicable healthcare laws and regulations involves substantial costs. If a drug or biological product or the company's operations are found to be in violation of any such requirements, it may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, the curtailment or restructuring of its operations, loss of eligibility to obtain approvals from the FDA, exclusion from participation in government contracting, healthcare reimbursement, or other federal or state government healthcare programs, including Medicare and Medicaid, integrity oversight and reporting obligations, imprisonment, and reputational harm. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks

cannot be entirely eliminated. Any action for an alleged or suspected violation can cause a drug company to incur significant legal expenses and divert management's attention from the operation of the business, even if such action is successfully defended.

Coverage and Reimbursement

Our ability to commercialize any products successfully will also depend in part on the extent to which coverage and adequate reimbursement for the procedures utilizing our drug candidates, performed by health care providers, once approved, will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, determine which procedures, and the products utilized in such procedures, they will cover and establish reimbursement levels. Assuming coverage is obtained for procedures utilizing a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate to cover our costs or may require co-payments that patients find unacceptably high. Patients who undergo procedures for the treatment of their conditions, and their treating physicians, generally rely on third-party payors to reimburse all or part of the costs associated with the procedures which utilize our products. Treating physicians are unlikely to use and order our products unless coverage is provided and the reimbursement is adequate to cover all or a significant portion of the cost of the procedures which utilize our products. Therefore, coverage and adequate reimbursement for procedures which utilize new products is critical to the acceptance of such new products. Coverage decisions may depend upon clinical and economic standards that disfavor new products when more established or lower cost therapeutic alternatives are already available or subsequently become available.

Government authorities and third-party payors are developing increasingly sophisticated methods of cost containment, such as including price controls, restrictions on coverage and reimbursement and requirements for substitution of less expensive products and procedures. Further, no uniform policy requirement for coverage and reimbursement exists among third-party payors in the United States, which causes significant uncertainty related to the insurance coverage and reimbursement of newly approved products, and the procedures which may utilize such newly approved products. Therefore, coverage and reimbursement can differ significantly from payor to payor and health care provider to health care provider. As a result, the coverage determination process is often a time-consuming and costly process that requires the provision of scientific and clinical support for the use of new products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

Additionally, we may develop, either by ourselves or with collaborators, companion diagnostic tests for our lead drug candidate for certain indications. We, or our collaborators, if any, will be required to obtain coverage and reimbursement for these tests separate and apart from the coverage and reimbursement we seek for our drug candidates, if approved. While we have not yet developed any companion diagnostic test for our drug candidates, if we do, there is significant uncertainty regarding our ability to obtain coverage and adequate reimbursement for the same reasons that are applicable to our drug candidates.

There may also be significant delays in obtaining coverage and reimbursement for newly approved products, and coverage may be more limited than the purposes for which the product is approved by the FDA. Moreover, eligibility for coverage and reimbursement does not imply that a product, or the procedures which utilize such product, will be paid for in all cases or at a rate which the health care providers who purchase those products will find cost effective. Additionally, we expect pricing pressures in connection with the sale of any of our drug candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, and additional legislative changes.

We cannot be sure that coverage and reimbursement will be available for any product that we commercialize, or the procedures which utilize such products, and, if reimbursement is available, what the level of reimbursement will be. Coverage and reimbursement may impact the demand for, or the price of, any drug candidate for which we obtain marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not successfully commercialize any drug candidate for which we obtain marketing approval.

Healthcare Reform

The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality or expanding access.

In the United States there have been, and continue to be, proposals by the federal government, state governments, regulators and third-party payors to control or manage the costs of health care and, more generally, to reform the U.S. healthcare system. The pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. For example, in March 2010, the ACA was enacted, which included changes to the coverage and payment for drug products under government health care programs. This law was designed to expand access to health insurance coverage for uninsured and underinsured

individuals while containing overall healthcare costs. The ACA and certain of its provisions have been subject to judicial challenges as well as legislative and regulatory efforts to repeal or replace them or to alter their interpretation or implementation. For example, on June 17, 2021, the U.S. Supreme Court dismissed a lawsuit challenging the constitutionality of certain aspects of the ACA without ruling on the merits of the constitutionality arguments. Additionally, on March 11, 2021, Congress enacted the American Rescue Plan Act of 2021, which included among its provisions a sunset of the ACA's cap on pharmaceutical manufacturers' rebate liability under the Medicaid Drug Rebate Program. Under the ACA, manufacturers' rebate liability was previously capped at 100% of the average manufacturer price for a covered outpatient drug. However, effective January 1, 2024, manufacturers' MDRP rebate liability is no longer capped, potentially resulting in a manufacturer paying more in MDRP rebates than it receives on the sale of certain covered outpatient drugs. The American Rescue Plan Act also temporarily increased premium tax credit assistance for individuals eligible for subsidies under the ACA for 2021 and 2022 and removed the 400% federal poverty level limit that otherwise applies for purposes of eligibility to receive premium tax credits. Most recently, the IRA extended this increased tax credit assistance and removal of the 400% federal poverty limit through 2025. In the future, there may be additional challenges and/or amendments to the ACA. It remains to be seen precisely what any new legislation will provide, when or if it will be enacted, and what impact it will have on the availability and cost of healthcare items and services, including drug and biological products.

Other legislative changes designed to reduce healthcare expenditures have been proposed and adopted in the United States since the ACA was enacted. For example, through the process created by the Budget Control Act of 2011, there are automatic reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect in April 2013 and, following passage of the BBA and the Infrastructure Investment and Jobs Act, will remain in effect through the first six months of the FY 2032 sequestration order unless additional Congressional action is taken (with the exception of a temporary suspension due to the COVID-19 pandemic from May 1, 2020 through March 31, 2022 and a subsequent reduction to 1% from April 1, 2022 until June 30, 2022). In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Additionally, the cost of prescription pharmaceuticals and biological products has recently been the subject of considerable discussion in the United States. For example, on February 2, 2022, the Biden administration signaled its continued commitment to the Cancer Moonshot initiative, which was initially launched in 2016. In its announcement, the administration noted that its new goals under the initiative include addressing inequities in order to ensure broader access to cutting-edge cancer therapeutics and investing in a robust pipeline for new treatments. In alignment with President Biden's Cancer Moonshot initiative, on June 27, 2023, the Center for Medicare Innovation at CMS announced a new model, the Enhancing Oncology Model, that is designed to make high-quality cancer care more affordable to both patients and Medicare. Additionally, on September 12, 2022, President Biden issued an Executive Order to promote biotechnology and biomanufacturing innovation. The Order noted several methods through which the Biden administration would support the advancement of biotechnology and biomanufacturing in healthcare, and instructed the Department of Health and Human Service to submit, within 180 days of the Order, a report assessing how to use biotechnology and biomanufacturing to achieve medical breakthroughs, reduce the overall burden of disease, and improve health outcomes. On October 14, 2022 President Biden issued an Executive Order on Lowering Prescription Drug Costs for Americans, which instructed the Secretary of the Department of Health and Human Services to consider whether to select for testing by the CMS Innovation Center new health care payment and delivery models that would lower drug costs and promote access to innovative drug therapies for beneficiaries enrolled in the Medicare and Medicaid programs. On February 14, 2023, the Department of Health and Human Services issued a report in response to the October 14, 2022 Executive Order, which, among other things, selects three potential drug affordability and accessibility models to be tested by the CMS Innovation Center. Specifically, the report addresses: (1) a model that would allow Part D Sponsors to establish a "high-value drug list" setting the maximum co-payment amount for certain common generic drugs at $2; (2) a Medicaid-focused model that would establish a partnership between CMS, manufacturers, and state Medicaid agencies that would result in multi-state outcomes-based agreements or certain cell and gene therapy drugs; and (3) a model that would adjust Medicare Part B payment amounts for Accelerated Approval Program drugs to advance the developments of novel treatments.

Moreover, there have been several recent U.S. Congressional inquiries and proposed federal legislation designed to, among other things, bring more transparency to drug and biological product pricing, review the relationship between pricing and manufacturer patient support programs, reduce the cost of prescription drugs and biological products under Medicare and reform government program reimbursement methodologies for drug and biological products. While several proposed reform measures will require Congress to pass legislation to become effective, Congress and the Biden administration have each indicated that it will continue to seek new legislative and/or administrative measures to address prescription drug and biological costs. More recently, in August 2022, President Biden signed into law the IRA, which implements substantial changes to the Medicare program, including drug pricing reforms and changes to the Medicare Part D benefit design. Among other reforms, the IRA imposes inflation rebates on drug and biological product manufacturers for products reimbursed under Medicare Parts B and D if the prices of those products increase faster than inflation beginning in 2023; implements changes to the Medicare Part D benefit that, beginning in 2025, will cap benefit annual out-of-pocket spending at $2,000, with new discount obligations for pharmaceutical manufacturers; and, beginning in 2026, establishes a "maximum fair price" for a fixed number of pharmaceutical and biological products covered under Medicare Parts B and D following a price negotiation process with

the Centers for Medicare and Medicaid Services. CMS has recently taken steps to implement the IRA, including: on June 30, 2023, issuing guidance detailing the requirements and parameters of the first round of price negotiations, to take place during 2023 and 2024, for products subject to the "maximum fair price" provision that would become effective in 2026; on August 29, 2023, releasing the initial list of ten drugs subject to price negotiations; on November 17, 2023, releasing guidance outlining the methodology for identifying certain manufacturers eligible to participate in a phase-in period where discounts on applicable products will be lower than those required by the Medicare Part D Manufacturer Discount Program; and on December 14, 2023, releasing a list of 48 Medicare Part B products that had an adjusted coinsurance rate based on the inflationary rebate provisions of the IRA for the time period of January 1, 2024 to March 31, 2024. If federal spending is further reduced, anticipated budgetary shortfalls may also impact the ability of relevant agencies, such as the FDA or the NIH to continue to function at current levels. Amounts allocated to federal grants and contracts may be reduced or eliminated. These reductions may also impact the ability of relevant agencies to timely review and approve research and development, manufacturing, and marketing activities which may delay our ability to develop, market and sell any products we may develop.

At the state level, individual states in the United States have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Some third-party payors also require pre-approval of coverage for new or innovative devices or therapies before they will reimburse healthcare providers that use such therapies. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize any product that is ultimately approved. In addition, several recently passed state laws require disclosures related to state agencies and/or commercial purchasers with respect to certain price increases that exceed a certain level as identified in the relevant statutes. Some of these laws and regulations contain ambiguous requirements that government officials have not yet clarified. Given the lack of clarity in the laws and their implementation, our future reporting actions could be subject to the penalty provisions of the pertinent federal and state laws and regulations.

We expect that these initiatives, as well as other healthcare reform measures that may be adopted in the future, as well as the trend toward managed healthcare and increasing influence of managed care organizations, may result in more rigorous coverage criteria and lower reimbursement, and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors. The implementation of current and future cost containment measures or other healthcare reforms may adversely affect our operations and prevent us from being able to generate revenue, attain profitability or commercialize our drug candidates.

Data Privacy and Security

In the ordinary course of our business, we collect, process and store confidential and sensitive information, including personal information, intellectual property, trade secrets, and proprietary information owned or controlled by ourselves or other third parties. We, and third parties upon whom we rely, use sophisticated information technology, software and services to process, store, use, generate, transfer and disclose information, as well as other sensitive information controlled by ourselves or other third parties.

We may also be subject to federal, state, and foreign data privacy and security laws and regulations. In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws and regulations (e.g., Section 5 of the FTC Act), govern the collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of our partners, vendors, or other third parties on whom we rely. The legislative and regulatory framework related to the collection, use, retention, safeguarding, disclosure, sharing, transfer, security and other processing of personal data worldwide is rapidly evolving. The number and scope of data protection laws and regulations is changing, subject to differing applications and interpretations, and may be inconsistent among jurisdictions, or in conflict with other rules, laws or other data processing obligations. Efforts to ensure that our current and future business arrangements, including our relationship with our CROs or other vendors who process data on our behalf, comply with applicable data privacy and data security laws and regulations will involve substantial costs.

For example, HIPAA, as amended by HITECH, and its implementing regulations, impose requirements relating to the privacy, security and transmission of individually identifiable health information on certain health care providers, health plans and health care clearinghouses, known as covered entities, as well as their business associates and covered subcontractors that perform certain services that involve creating, receiving, maintaining or transmitting individually identifiable health information for or on behalf of such covered entities. Entities that are found to be in violation of HIPAA as the result of a breach of unsecured protected health information, a complaint about privacy practices or an audit by HHS, may be subject to significant civil, criminal and administrative fines and penalties and/or additional reporting and oversight obligations if required to enter into a resolution agreement and corrective action plan with HHS to settle allegations of HIPAA non-compliance. While we typically only receive aggregated and deidentified data for research purposes, we interact with HIPAA covered entities and business associates and operate within a highly regulated industry. Further, entities that knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA covered entity in a

manner that is not authorized or permitted by HIPAA may be subject to civil and criminal penalties. Even when HIPAA does not apply, according to the FTC, violating consumers' privacy rights or failing to take appropriate steps to keep consumers' personal information secure may constitute unfair acts or practices in or affecting commerce in violation of Section 5 of the FTC Act. The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards.

Likewise, we expect that there will continue to be new proposed laws, regulations and industry standards relating to privacy and data protection in the United States, the EU and other jurisdictions, such as the California Consumer Privacy Act of 2018 and the amendments thereto under the California Privacy Rights Act (CPRA) (collectively, the CCPA). Although the CCPA and other similar state laws discussed below exempt certain data processed in the context of clinical trials, the CCPA and other state laws, to the extent applicable to our business and operations, may increase our compliance costs and potential liability with respect to the personal information we maintain about the covered state residents. The CCPA among other effects, creates individual privacy rights for California consumers (as defined in the law), places increased privacy and security obligations on entities handling certain personal data of consumers or households, requires covered companies to provide disclosures to consumers regarding data collection, use and sharing practices, requires covered companies to allow users to opt-out of certain sales or sharing of personal information, and provides consumers with a private right of action for certain data breaches. As currently written, the CCPA may impact our business activities and exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information. The CPRA significantly amended the CCPA, and imposes additional data protection obligations on covered companies doing business in California, including additional consumer rights processes and opt outs for certain uses of sensitive data. It also created the California Privacy Protection Agency that is specifically tasked to implement and enforce the law, which will likely result in increased regulatory scrutiny of California businesses in the areas of data protection and security. Additional states have passed similar comprehensive privacy legislation and impose similar obligations to those in the CCPA.

In addition, we are or may become subject to certain privacy laws in the jurisdictions in which we are established or (where we are not established) in which we sell or market our products or services or run clinical trials. For example, in the EU, we are subject to Regulation (EU) 2016/679, (the EU GDPR), in relation to our collection, use, disclosure, transfer and other processing of personal information (i.e. data relating to an identified or identifiable living individual) of participants in our clinical trials in the European Economic Area (EEA), including the health and medical information of these participants. The EU GDPR is directly applicable in each EU Member State and has extraterritorial effect where organizations outside of the EEA process personal information of individuals in the EEA in relation to the offering of goods or services to those individuals (the targeting test) or the monitoring of their behavior (the monitoring test). As such, the GDPR applies to us to the extent that we are established in an EU Member State, we are processing personal information in the context of an establishment in an EU Member State or we meet the requirements of either the targeting test or the monitoring test. As noted above, the EU GDPR imposes a number of obligations on controllers and processors, including, among others: (i) onerous accountability obligations requiring controllers and processors to maintain a record of their data processing and implement policies as part of its mandated privacy governance framework; (ii) transparency requirements which require controllers to disclose to data subjects (in a concise, intelligible and easily accessible form) details regarding processing of their personal information; (iii) obligations to consider data protection as any new products or services are developed and to limit the amount of personal information processed; (iv) obligations to comply with data protection rights of data subjects including a right of access to and rectification of personal information, a right to obtain restriction of processing or to object to processing of personal information and a right to ask for a copy of personal information to be provided to a third party in a useable format and erasing personal information in certain circumstances; (v) obligations to implement appropriate technical and organizational security measures to safeguard personal information; (vi) limitations on retention of personal information; (vii) obligations to report certain personal data breaches to the relevant supervisory authority without undue delay (and no later than 72 hours where feasible) and/or concerned individuals; and (viii) higher standards for controllers to demonstrate that they have obtained valid consent for certain data processing activities.

In addition, the EU GDPR prohibits the international transfer of personal information from the EEA to countries outside of the EEA unless made to a country deemed to have adequate data privacy laws by the European Commission or a data transfer mechanism in accordance with the EU GDPR has been put in place. On July 16, 2020, the Court of Justice of the European Union (CJEU), invalidated the EU-U.S. Privacy Shield Framework, or the Privacy Shield, under which personal information could be transferred from the EEA to U.S. entities who had self-certified under the Privacy Shield scheme. While the CJEU upheld the validity of the standard contractual clauses (SCCs) (a standard form of contract approved by the European Commission as an adequate personal information transfer mechanism, and alternative to the Privacy Shield), it made clear that companies relying on SCCs will need to carry out a transfer privacy impact assessment, which among other things, assesses laws governing access to personal information in the recipient country and considers whether supplementary measures that provide privacy protections additional to those provided under SCCs will need to be implemented to ensure an 'essentially equivalent' level of data protection to that afforded in the EEA. Similarly, the Swiss-U.S. Privacy Shield framework was declared as inadequate by the Swiss Federal Data Protection and Information Commissioner in light of the Schrems II decision.

Moreover, on June 4, 2021, the European Commission adopted new SCCs under the EU GDPR for the lawful transfer of personal information from the EEA to the recipients in non-EEA countries, which impose onerous obligations on contracting parties. These new EU SCCs must be used in all new contracts going forward (where there are restricted transfers of personal information), with existing contracts entered into before September 27, 2021 required to be updated by December 27, 2022. As such, any transfers by us or our vendors of personal information from the EU may not comply with European data protection law, may increase our exposure to the EU GDPR's heightened sanctions for violations of its cross-border data transfer restrictions, and may reduce demand from companies subject to European data protection laws.

Further, on October 7, 2022, the U.S. President introduced an executive order to facilitate a new Trans-Atlantic Data Privacy Framework, which is the new EU-US adequacy mechanism following Privacy Shield. On December 13, 2022, the European Commission also published its draft adequacy decision which stated that the new executive order and Trans-Atlantic Data Privacy Framework is able to meet the concerns raised in Schrems II. If the draft adequacy decision is approved by the European Commission and implemented, the agreement will facilitate the transatlantic flow of personal information and provide additional safeguards to data transfer mechanisms (including EU SCCs and Binding Corporate Rules) for companies transferring personal information from the EU to the U.S. However, before parties rely on the new Trans-Atlantic Data Privacy Framework there are still legislative and regulatory steps that must be undertaken in both the EU and the U.S. As such, the current legal position may have implications for our cross-border data flows and may result in compliance costs.

Following the UK's withdrawal from the EU (i.e., Brexit), the EU GDPR has been implemented in the UK as the "UK GDPR" (the UK GDPR and the EU GDPR, referred to as GDPR). The UK GDPR sits alongside the UK Data Protection Act 2018, which implements certain derogations in the EU GDPR into English law. The requirements of the UK GDPR are (at this time) largely aligned with those under the EU GDPR. Under the UK GDPR, companies established in the UK and companies not established in the UK but who process personal information in relation to the offering of goods or services to individuals in the UK, or to the monitoring of their behavior will be subject to the UK GDPR. As a result, we are potentially exposed to two parallel data protection regimes, each of which authorizes fines and the potential for divergent enforcement actions (please see below). It should also be noted that the UK Information Commissioner's Office (ICO) has published its own form of EU SCCs known as the UK International Data Transfer Agreement together with an International Data Transfer Addendum to the new EU SCCs. The ICO has also published its version of the transfer impact assessment and information guidance on international transfers, although entities may choose to adopt either the EU or UK style transfer impact assessment. In terms of international data transfers between the UK and the U.S., it is understood that the UK and the U.S. are negotiating an adequacy agreement. Fines for certain serious breaches of the GDPR are significant: up to the greater of €20.0 million (under the EU GDPR) or £17.5 million (under the UK GDPR) or up to 4% of total global annual turnover. The GDPR identifies a list of points to consider when determining the level of fines to impose (including the nature, gravity and duration of the infringement). Data subjects also have a right to compensation for financial or non-financial losses (e.g., distress). Complying with the GDPR may cause us to incur substantial operational and compliance costs or require us to change our business practices. Despite our efforts to bring practices into compliance with the GDPR, we may not be successful either due to internal or external factors such as resource allocation limitations or a lack of vendor cooperation. Non-compliance could result in proceedings against us by governmental entities, regulators, customers, data subjects, suppliers, vendors or other parties. Further, there is a risk that the measures will not be implemented correctly or that individuals within the business will not be fully compliant with the new procedures. If there are breaches of these measures, we could face significant administrative and monetary sanctions as well as reputational damage which may have a material adverse effect on our operations, financial condition and prospects.

For more information on the potential impact of the GDPR, and associated EEA data protection laws, on our business, see the section titled "Risk Factors—Risks Related to Employee Matters and Our Operations—We are subject to a variety of privacy and data security laws, rules, regulations, policies, industry standards and contractual obligations, and our failure to comply with them could harm our business."

Additional Regulation

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservation and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern the use, handling and disposal of various biologic, chemical and radioactive substances used in, and wastes generated by, operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. Equivalent laws have been adopted in other countries that impose similar obligations.

Foreign Corrupt Practices Act

The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of

influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring the companies to maintain books and records that accurately and fairly reflect all transactions of the companies, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Facilities

Our principal executive office is located in Watertown, Massachusetts, where we lease a total of 13,711 square feet of office and laboratory space that we use for our administrative, research and development and other activities under a lease that currently expires in April 2028, with an option to extend the term for an additional five years at then-market rental rates. Additionally, we also lease laboratory and office space in Lund, Sweden, which will expire in December 2026, with an option to extend the term for an additional three years. We believe that our facilities are sufficient to meet our current needs and that suitable additional space will be available as and when needed.

Employees and Human Capital Resources

As of December 31, 2023, we had 58 full-time employees and three part-time employees. Of our 61 full- and part-time employees, approximately 35 have Ph.D. or M.D. degrees and 48 are engaged in research and development activities. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our employees. We believe our success depends on our ability to attract, retain, develop and motivate diverse highly skilled personnel. In particular, we depend upon the personal efforts and abilities of the principal members of our senior management to partner effectively as a team, and to provide strategic direction, develop our business, manage our operations and maintain a cohesive and stable work environment. We also rely on qualified managers and skilled employees, such as scientists, engineers and laboratory technicians, with technical expertise in operations, scientific knowledge, engineering skills and quality management experience in order to operate our business successfully.

Our compensation program is designed to retain, motivate and, as needed, attract highly qualified employees. Accordingly, we use a mix of competitive base salary, cash-based annual incentive compensation, equity compensation awards and other employee benefits.

Legal Proceedings

From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. We are not currently subject to any material legal proceedings.

Item 1A. Risk Factors.

The following information sets forth risk factors that could cause our actual results to differ materially from those contained in forward-looking statements we have made in this Annual Report on Form 10-K and those we may make from time to time. You should carefully consider the risks described below, in addition to the other information contained in this Annual Report and our other public filings. Our business, financial condition or results of operations could be harmed by any of these risks. The risks and uncertainties described below are not the only ones we face. Additional risks not presently known to us or other factors not perceived by us to present significant risks to our business at this time also may impair our business operations.

Risks Related to Our Financial Position and Capital Needs

We have incurred significant losses since our inception. We expect to incur losses over the next several years and may never achieve or maintain profitability.

Since our inception, we have incurred significant losses, and we expect to continue to incur significant expenses and operating losses for the foreseeable future. Our net loss was $60.4 million and $31.2 million for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023, we had an accumulated deficit of $116.4 million. Since our inception, we have financed our operations with aggregate net proceeds of $119.8 million from the issuance of convertible notes and the sale of our Series A-1 convertible preferred stock and Series B convertible preferred stock, and $92.4 million, or $104.5 million following the sale pursuant to the exercise of the underwriters' option to purchase additional shares, in each case after deducting underwriting discounts and commissions and the placement agent fee but before deducting offering expenses payable by the Company, from our IPO and Concurrent Private Placement. We have no products approved for commercialization and have never generated any revenue from product sales.

All of our drug candidates are still in clinical and preclinical testing. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially as we:

- continue to conduct our ongoing clinical trials of ACR-368, as well as initiate and complete additional clinical trials of future drug candidates or current drug candidates in new indications or patient populations;
- continue to advance the preclinical development of our other drug candidates, and our preclinical and discovery programs;
- seek regulatory approval for any drug candidates that successfully complete clinical trials;
- pursue marketing approvals and reimbursement for our drug candidates;
- manufacture material under current good manufacturing practices, or cGMP, for clinical trials and potential commercial sales at our contracted manufacturing facilities;
- develop, establish and validate our commercial-scale cGMP manufacturing process;
- maintain, expand, enforce, defend and protect our intellectual property portfolio;
- comply with regulatory requirements established by the applicable regulatory authorities;
- establish, either alone or with a third party, a sales, marketing and distribution infrastructure and scale up external, or establish internal, manufacturing and distribution capabilities to commercialize any drug candidates for which we may obtain regulatory approval;
- hire and retain additional personnel, including research, clinical, development, manufacturing quality control, quality assurance, regulatory and scientific personnel;
- add operational, financial, corporate development, management information systems and administrative personnel, including personnel to support our product development and planned future commercialization efforts; and
- incur additional legal, accounting and other expenses in operating as a public company.

To date, we have not generated any revenue from the commercialization of any drug candidate. To become and remain profitable, we must succeed in developing and eventually commercializing drug candidates that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our drug candidates, validating manufacturing processes, obtaining regulatory approval, and manufacturing, marketing and selling any drug candidates for which we may obtain regulatory approval, as well as discovering and developing additional drug candidates. All of our drug candidates are in clinical or preclinical development. We may never succeed in these activities and, even if we do, may never generate any revenue or revenue that is significant enough to achieve profitability.

Because of the numerous risks and uncertainties associated with drug candidate development, we are unable to accurately predict the timing or amount of expenses or when, or if, we will be able to achieve profitability. If we are required by regulatory authorities to perform clinical trials or preclinical studies in addition to those currently expected, or if there are any delays in the initiation and completion of our clinical trials or the development of any of our drug candidates, our expenses could increase.

Even if we achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our development efforts, obtain product approvals, diversify our offerings or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We have a limited operating history and no history of commercializing products, which may make it difficult for an investor to evaluate the success of our business to date and to assess our future viability.

We are a clinical-stage biopharmaceutical company with a limited operating history. We commenced operations in March 2018, and our operations to date have been largely focused on organizing and staffing our company, business planning, raising capital, building our AP3 platform, developing our manufacturing capabilities and developing our clinical and preclinical drug candidates, including undertaking preclinical studies and conducting clinical trials. To date, we have not yet demonstrated our ability to successfully complete pivotal clinical trials, obtain regulatory approvals, manufacture a product on a commercial scale, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization, and we may not be successful in doing so. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing products.

In addition, as a business with a limited operating history, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will eventually need to transition from a company with a research and clinical focus to a company, if any of our drug candidates are approved, capable of supporting commercial activities. We may not be successful in such a transition.

We will need additional funding to meet our financial obligations and to pursue our business objectives. If we are unable to raise capital when needed, we could be forced to curtail our planned longer-term operations and the pursuit of our growth strategy.

Our operations have consumed substantial amounts of cash since inception, and we expect to continue to incur significant expenses and operating losses over the next several years as we continue to develop our drug candidate pipeline and, to a lesser extent, build out our manufacturing capabilities for our drug candidates, which, if approved, may not achieve commercial success. Our revenue, if any, will be derived from sales of products that may not be commercially available for a number of years, if at all. If we obtain marketing approval for any drug candidates that we develop or otherwise acquire, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. We also expect an increase in our expenses associated with creating additional infrastructure to support operations as a public company. Accordingly, we will need to obtain substantial additional funding in order to continue our operations.

As of December 31, 2023, we had cash, cash equivalents and investments of $127.5 million. We believe that our existing cash, cash equivalents and investments as of December 31, 2023, will be sufficient to fund our operating expenses and capital expenditure requirements into the fourth quarter of 2025. This estimate is based on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. Changes may occur beyond our control that would cause us to consume our available capital before that time, including changes in and progress of our development activities, acquisitions of additional drug candidates and changes in regulation. The timing and amount of our funding requirements will depend on many factors, including but not limited to:

- the rate of progress in the development of ACR-368, ACR-2316, and our other drug candidates;
- the scope, progress, results and costs of non-clinical studies, preclinical development, laboratory testing and clinical trials for ACR-368 and future drug candidates and associated development programs;
- the extent to which we develop, in-license or acquire other drug candidates and technologies in our pipeline;
- the scope, progress, results and costs as well as timing of process development and manufacturing scale-up and validation activities associated with ACR-368 and our future drug candidates and other programs as we advance them through preclinical and clinical development;
- the ability of our AP3 platform to identify patient responders;
- the number and development requirements of drug candidates that we may pursue;

- the costs, timing and outcome of regulatory review of our drug candidates;
- our headcount growth and associated costs as we expand our research and development capabilities and establish a commercial infrastructure;
- the timing and costs of securing sufficient capacity for commercial supply of our drug candidates, or the raw material components thereof;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our drug candidates for which we receive marketing approval;
- the costs necessary to obtain regulatory approvals, if any, for products in the United States and other jurisdictions, and the costs of post-marketing studies that could be required by regulatory authorities in jurisdictions where approval is obtained;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the continuation of our existing licensing and collaboration arrangements and entry into new collaborations and licensing arrangements, if at all;
- the need and ability to hire additional research, clinical, development, scientific and manufacturing personnel;
- the costs we incur in maintaining business operations;
- the need to implement additional internal systems and infrastructure;
- the effect of competing technological, product and market developments;
- the revenue, if any, received from commercial sales of our drug candidates for which we receive marketing approval;
- the costs of operating as a public company; and
- business disruptions affecting the initiation, patient enrollment, development and operation of our clinical trials, including a public health emergency (PHE) or geopolitical events, including the ongoing Russian invasion of Ukraine, related sanctions against Russia and conflicts in the Middle East.

We will require additional capital to achieve our business objectives. Additional funds may not be available on a timely basis, on favorable terms or at all, and such funds, if raised, may not be sufficient to enable us to continue to implement our long-term business strategy. Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our drug candidates. Further, our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and the recent disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing Russian invasion of Ukraine and related sanctions against Russia and the Israel-Hamas conflicts. If we are unable to raise sufficient additional capital, we could be forced to curtail our planned operations and the pursuit of our growth strategy.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or drug candidates.

Until such time, if ever, as we can generate substantial revenue, we may finance our cash needs through a combination of equity offerings, government or private-party grants, debt financings and license and collaboration agreements. We do not currently have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing stockholders will be diluted, and the terms of such securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, future revenue streams or drug candidates, grant licenses on terms that may not be favorable to us or commit to future payment streams. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market drug candidates that we would otherwise prefer to develop and market ourselves.

Risks Related to the Design and Development of Our Drug Candidates

Our business substantially depends upon the successful clinical development of drug candidates using our AP3 platform and OncoSignature companion diagnostics. If we are unable to obtain regulatory approval for, and successfully commercialize, drugs developed through the application of our AP3 platform and OncoSignature tests, our business may be materially harmed.

Using our AP3 platform, we have developed predictive OncoSignature tests for our clinical drug candidate, ACR-368, as well as for two other clinical stage drug candidates. Negative results in the development of ACR-368 may also impact our ability to successfully develop other drug candidates, either at all or within anticipated timeframes because, although other drug candidates may target different indications, the underlying technology platform, and specifically the use of an OncoSignature test, to identify patient responders is conceptually the same for all of our drug candidates. Accordingly, a failure in any one program may decrease trust in our AP3 platform. In addition, if ACR-368 shows unexpected adverse events or a lack of efficacy in the indications we intend to treat, or if we experience other regulatory or developmental issues, our development plans and business could be significantly harmed. We cannot guarantee the successful clinical development, approval and commercialization of ACR-368.

The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our drug candidates, on a timely basis or at all, our business will be substantially harmed.

Our lead drug candidate is currently in Phase 2 clinical development under a master protocol designed for expedited drug development using our ACR-368 OncoSignature test. Although we are using our OncoSignature test to specifically treat patients predicted to be sensitive to ACR-368, we cannot guarantee that we will achieve sufficient ORR for marketing approval. For our preclinical drug candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our drug candidate in humans before obtaining marketing approval from regulatory authorities. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to the outcome.

The length of time necessary to complete clinical trials and to submit an application for marketing approval for a decision by a regulatory authority may be difficult to predict. The clinical trial requirements of the FDA and other comparable foreign regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a drug candidate vary substantially according to the type, complexity, novelty and intended use and market of the drug candidate. As a result, the regulatory approval process for drug candidates such as ours is uncertain and may be more expensive and take longer than the approval process for drug candidates based on other, better known or more extensively studied technologies. It is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our drug candidates in either the United States or other comparable regions of the world or how long it will take to commercialize our drug candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential drug candidate to market would adversely affect our business, financial condition, results of operations and prospects.

Our drug candidates, including ACR-368 and ACR-2316, could fail to receive regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a drug candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a drug candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our drug candidates may not be sufficient to support the submission of an NDA to the FDA or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies;
- we or third-party collaborators may fail to obtain regulatory approval of companion diagnostic tests, if required, on a timely basis, or at all; and

- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Prior to obtaining approval to commercialize a drug candidate in the United States or elsewhere, we or our collaborators must demonstrate with substantial evidence from one or more well-controlled clinical trials, and to the satisfaction of the FDA or comparable foreign regulatory agencies, that such drug candidates are safe and effective for their intended uses. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our drug candidates are promising, such data may not be sufficient to support approval by the FDA or comparable foreign regulatory authorities. The FDA may also require us to conduct additional preclinical studies or clinical trials for our drug candidates either prior to or post-approval, or it may object to elements of our clinical development program. Depending on the extent of these or any other studies required by the FDA or comparable foreign regulatory authorities, approval of any regulatory approval applications that we submit may be delayed by several years, or may require us to expend significantly more resources than we have available.

Of the large number of potential products in development, only a small percentage successfully complete the FDA or comparable foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our drug candidates, which would significantly harm our business, results of operations and prospects.

Since March 2020 when foreign and domestic inspections of facilities were largely placed on hold, the FDA has been working to resume routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis. Since April 2021, the FDA has conducted limited inspections and employed remote interactive evaluations, using risk management methods, to meet user fee commitments and goal dates. Travel restrictions and other uncertainties may continue to impact oversight operations both domestic and abroad. Should the FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to be adequate, the agency has stated that it generally intends to issue, depending on the circumstances, a complete response letter or defer action on the application until an inspection can be completed. On February 2, 2022, the FDA announced that it would resume domestic surveillance inspections across all product areas on February 7, 2022.

On May 11, 2023, the COVID-19 PHE declared under the Public Health Service (PHS) Act expired. It is unclear how the FDA's policies and guidance will impact any inspections of our facilities, including our clinical trial sites. During the COVID-19 PHE, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to COVID-19 and may experience delays in their regulatory activities.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our drug candidates for fewer or more limited indications than we request, may impose significant limitations in the form of narrow indications, warnings, or a post-marketing risk management strategy such as a Risk Evaluation and Mitigation Strategy, or REMS, or the equivalent in another jurisdiction. Regulatory authorities may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a drug candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that drug candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our drug candidates.

We are highly dependent on the success of our lead drug candidate, ACR-368, as this is our first drug candidate being developed for clinical development and regulatory approval. We may never obtain approval for ACR-368, ACR-2316 or any other drug candidate.

Our future success is highly dependent on our ability to obtain regulatory approval for, and then successfully commercialize or identify a strategic partner to commercialize, our lead drug candidate, ACR-368. ACR-368 has been dosed in more than 400 patients at the RP2D in past single center and multi-center Phase 2 clinical trials. We have received clearance from the FDA for an IND application to advance ACR-368 in Phase 2 single arm clinical trials conducted under the FDA program known as the master protocol. We currently have no products that are approved for sale in any jurisdiction. ACR-368 or any of our other future drug candidates may not achieve success in their clinical trials or obtain regulatory approval. If we do not obtain regulatory approval for ACR-368 and successfully commercialize ACR-368 in one or more indications or if we experience significant delays in doing so, we may never generate any revenue or become profitable.

Our ability to generate product revenues, which we do not expect will occur for several years, if ever, will depend heavily on the successful development and eventual commercialization of ACR-368, ACR-2316 or other future drug candidates identified through the application of our AP3 platform and OncoSignature companion diagnostics. The success of ACR-368, ACR-2316, or any other future drug candidate will depend on several factors, including the following:

- successful completion of preclinical studies and clinical trials;
- timely and successful enrollment of patients in, and completion of, clinical trials with favorable results;
- demonstration of safety, efficacy and acceptable risk-benefit profiles of ACR-368, ACR-2316, and our future drug candidates to the satisfaction of the FDA and other regulatory agencies;
- the ability of our AP3 platform-based OncoSignature tests to identify patient responders;
- the AP3 platform may not work equally well for all therapeutic targets;
- our ability, or that of our collaborators, to develop and obtain clearance or approval of companion diagnostics, on a timely basis, or at all;
- receipt and related terms of marketing approvals from applicable regulatory authorities for ACR-368 and our future drug candidates, including the completion of any required post-marketing studies or trials;
- raising additional funds necessary to complete the clinical development of and commercialization of ACR-368;
- successfully identifying and developing, acquiring or in-licensing additional drug candidates to expand our pipeline;
- acceptance of an IND application by the FDA or other similar clinical trial applications from other regulatory authorities for clinical trials for ACR-2316 and future drug candidates;
- obtaining and maintaining patent, trade secret and other intellectual property protection and regulatory exclusivity for ACR-368, ACR-2316, and our future drug candidates and our OncoSignature companion diagnostics;
- making arrangements with third-party manufacturers, or establishing manufacturing capabilities, for both clinical and commercial supplies of our drug candidates;
- establishing sales, marketing and distribution capabilities and launching commercial sales of our products, if approved, whether alone or in collaboration with third parties;
- acceptance of our products, if approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies available on the market or in development;
- obtaining and maintaining third-party payor coverage and adequate reimbursement; and
- maintaining a continued acceptable safety profile of any products following regulatory approval.

Many of these factors are beyond our control, and it is possible that none of our drug candidates, including ACR-368 and ACR-2316, will ever obtain regulatory approval even if we expend substantial time and resources seeking such approval. If we experience significant delays or are otherwise unable to successfully commercialize our drug candidates, it would materially harm our business.

Depending on our clinical trial results, we may seek NDA approval for ACR-368 in the United States under the FDA's accelerated approval pathway, but this pathway may not lead to faster development, regulatory review, or approval process and does not increase the likelihood that ACR-368 will receiving marketing approval.

Depending on our clinical trial results, we intend to seek approval for ACR-368 for one or more indications, and we may seek approval of our future drug candidates, where applicable, under the FDA's accelerated approval pathway. A product may be eligible for accelerated approval if it is designed to treat a serious or life-threatening disease or condition, generally provides a meaningful advantage over available therapies, and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as IMM. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new product over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct adequate and well-controlled post-marketing clinical trials to confirm the product's clinical benefit. These confirmatory trials must be completed with due diligence. If the sponsor fails to conduct such studies in a timely manner, or if such post-approval studies fail to verify the product's predicted clinical benefit, the FDA may withdraw its approval of the product on an expedited basis. In addition, for products being considered for accelerated approval, the FDA currently requires, unless otherwise informed by the Agency, pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. There can be no assurance that the FDA would allow ACR-368 or any of the drug candidates we may develop to proceed on an accelerated approval pathway, and even if the FDA did allow such pathway, there can be no assurance that expedited development will occur or that the FDA will review and approve such submission or application on a timely basis, or at all. Moreover, even if we received accelerated approval, any post-marketing studies required to confirm clinical benefit may not show such benefit, which could lead to withdrawal of any approvals we have obtained. In addition, receiving accelerated approval does not assure that the product's accelerated approval will eventually be converted to a traditional approval.

Moreover, Congress has recently enacted changes to the Accelerated Approval Program that could impact our ability to obtain Accelerated Approval, or increase the burdens associated with postmarketing requirements in the event we do obtain Accelerated Approval. In particular, the FDA must specify certain conditions for required postapproval studies for products that receive Accelerated Approval, which may include enrollment targets and milestones, including the target date for study completion, by the time the drug is approved. The FDA may also require postapproval studies to be underway at the time of Accelerated Approval or within a specified time period following Accelerated Approval for such drugs, and must explain any instances where it does not require such studies.

Any delay in obtaining, or inability to obtain, approval through the Accelerated Approval Program, or any issues in maintaining approval granted under the Accelerated Approval Program, would delay or prevent commercialization of our products, and would materially adversely affect our business, financial condition, results of operations and prospects.

ACR-2316 is a preclinical drug candidate, and the outcome of preclinical testing and early clinical trials for ACR-2316 may not predict the success of later clinical trials. Furthermore, the results of clinical trials for ACR-2316 may not satisfy the requirements of the FDA or comparable foreign regulatory authorities.

ACR-2316 is in the early stages of development and is not currently approved for sale and there is no guarantee that it will ever be marketable. Clinical failure can occur at any stage of clinical development. We are required to demonstrate with substantial evidence through well-controlled clinical trials that ACR-2316 is safe and effective for use in a diverse population before we can seek marketing approvals for its commercial sale. Success in preclinical studies and early-stage clinical trials does not mean that future larger registration clinical trials will be successful. This is because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety and efficacy to the satisfaction of the FDA and other regulatory authorities despite having progressed through preclinical studies and early-stage clinical trials. In particular, the outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later-stage clinical trials. We do not know whether any clinical trials we may conduct for ACR-2316 will demonstrate consistent or adequate efficacy and safety results sufficient to obtain marketing approval.

In addition, even if ACR-2316 is approved for commercial sale, the success of ACR-2316 will depend on a number of factors beyond our control, including emerging and competing therapies and the market acceptance and adoption of ACR-2316 versus actual or perceived competing therapies.

We may incur additional costs or experience delays in completing, or ultimately be unable to complete the development and/or commercialization of ACR-368,* ACR-2316, *or our other future drug candidates identified through the application of our AP3 platform and OncoSignature companion diagnostics.

Any delays in the commencement or completion of our ongoing, planned or future clinical trials could significantly increase our product development costs. We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to obtain marketing approval or commercialize ACR-368, ACR-2316, or our future drug candidates identified through the application of our AP3 platform and OncoSignature companion diagnostics, including but not limited to:

- regulators, institutional review boards, or IRBs, or ethics committees, or ECs, may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- the FDA may disagree as to the design or implementation of our clinical trials or with our recommended doses with respect to ACR-368, or any of our future drug candidates;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective CROs and prospective trial sites;
- clinical trials for ACR-368 or our future drug candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials, delay or halt clinical trials or abandon product development programs;
- lack of adequate funding to continue clinical trials;
- the number of patients required for clinical trials may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or may be lower than we anticipate due to challenges in recruiting and enrolling suitable patients who meet the trial criteria, participants may drop out of these clinical trials at a higher rate than we anticipate, or the duration of these clinical trials may be longer than we anticipate;
- competition for clinical trial participants from investigational and approved therapies may make it more difficult to enroll patients in our clinical trials;
- we may experience difficulties in maintaining contact with patients after treatment, resulting in incomplete data;
- we or third-party collaborators may fail to obtain regulatory approval of companion diagnostic tests, if required, on a timely basis, or at all;
- our third-party contractors may fail to meet their contractual obligations to us in a timely manner, or at all, or may fail to comply with regulatory requirements;
- we may have to suspend or terminate clinical trials for various reasons, including a finding by us or by a Data Monitoring Committee for a trial that the participants are being exposed to unacceptable health risks;
- ACR-368, ACR-2316, or our future drug candidates may have undesirable or unexpected side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs or ECs to suspend or terminate the trials;
- the cost of clinical trials may be greater than we anticipate;
- changes to clinical trial protocols; and
- the supply or quality of ACR-368, ACR-2316, or our future drug candidates or other materials necessary to conduct clinical trials may be insufficient or inadequate and result in delays or suspension of our clinical trials.

Delays, including delays caused by the above factors, can be costly and could negatively affect our ability to complete a clinical trial or obtain timely marketing approvals. We do not know whether any of our planned preclinical studies or clinical trials will begin on a timely basis or at all, will need to be restructured or will be completed on schedule, or at all. For example, the FDA may place a partial or full clinical hold on any of our current or future clinical trials for a variety of reasons, including safety concerns and noncompliance with regulatory requirements. If we are not able to complete successful clinical trials, we will not be able to obtain regulatory approval and will not be able to commercialize ACR-368, ACR-2316, or our future drug candidates.

Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our drug candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our drug candidates, which would limit our future revenues and harm our commercial prospects.

The successful clinical development of our drug candidates depends on the co-approval of the OncoSignature test as a companion diagnostic test. If we or our companion diagnostic collaborator are unable to obtain regulatory approval for our OncoSignature companion diagnostic tests for our drug candidates, we may not obtain regulatory approval and realize the commercial potential of our drug candidates.

A key part of our development strategy for our drug candidates is to identify subsets of patients with specific types of tumors. The identification of these patients will require the use and development of companion diagnostics. According to the FDA's 2014 guidance document on In Vitro Companion Diagnostic Devices, for novel therapeutic products that depend on the use of a diagnostic test and where the diagnostic device could be essential for the safe and effective use of the corresponding therapeutic product, the premarket application for the companion diagnostic device should be developed and approved or cleared contemporaneously with the therapeutic, although the FDA recognizes that there may be cases when contemporaneous development may not be possible. However, in cases where a drug cannot be used safely or effectively without the companion diagnostic, the FDA's guidance indicates it will generally not approve the drug without the approval or clearance of the diagnostic device. The FDA also issued a draft guidance in July 2016 setting forth the principles for co-development of an in vitro companion diagnostic device with a therapeutic product. The draft guidance describes principles to guide the development and contemporaneous marketing authorization for the therapeutic product and its corresponding in vitro companion diagnostic.

We do not have experience or capabilities in developing or commercializing diagnostics and plan to rely in large part on our collaboration partner Akoya to perform these functions. Akoya has not commercialized or submitted or obtained Premarket Approval Application, or PMA, for any companion diagnostic, and any setbacks they encounter could delay any commercial launch of ACR-368, if approved. It may be necessary to resolve issues such as selectivity/specificity, analytical validation, reproducibility, or clinical validation of companion diagnostics during the development and regulatory approval processes. Moreover, even if data from preclinical studies and early clinical trials appear to support development of a companion diagnostic for a drug candidate, data generated in later clinical trials may fail to support the analytical and clinical validation of the companion diagnostic. We and our future collaborators may encounter difficulties in developing, obtaining regulatory approval for, manufacturing and commercializing companion diagnostics similar to those we face with respect to our drug candidates, including issues with achieving regulatory clearance or approval, production of sufficient quantities at commercial scale and with appropriate quality standards, and in gaining market acceptance. If we are unable to successfully develop companion diagnostics for our drug candidates, or experience delays in doing so, the development of these drug candidates may be adversely affected, these drug candidates may not obtain marketing approval, and we may not realize the full commercial potential of any of these therapeutics that have or may obtain marketing approval. We may not be able to enter into arrangements with another diagnostic company to develop and obtain regulatory approval for an alternative diagnostic test for use in connection with the development and commercialization of our drug candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of our therapeutic candidates or therapeutics.

Companion diagnostics are subject to regulation by the FDA and comparable foreign regulatory authorities as medical devices and will likely require separate regulatory approval prior to commercialization. If we or third parties are unable to successfully develop companion diagnostics for our drug candidates, or experience delays in doing so:

- the development of these drug candidates may be delayed because it may be difficult to identify patients for enrollment in our clinical trials in a timely manner;
- these drug candidates may not receive marketing approval if their safe and effective use depends on a companion diagnostic; and
- we may not realize the full commercial potential of these drug candidates that receive marketing approval if, among other reasons, we are unable to appropriately identify patients or types of tumors targeted by these drug candidates.

Further, requirements for companion diagnostics may evolve. The FDA has been paying particular focus to laboratory developed tests ("LDTs"), which includes some in vitro diagnostic products. In September 2023, the FDA released a proposed rule to regulate LDTs as medical devices, which would limit or end the FDA's enforcement discretion for LDT products. The FDA's actions demonstrate increased scrutiny on diagnostic products and changes to requirements or enforcement discretion may delay or prevent approval of companion diagnostic products, such as the OncoSignature diagnostic product.

Even if our drug candidates and any associated companion diagnostics are approved for marketing, the need for companion diagnostics may slow or limit adoption of our drug candidates. Although we believe companion diagnostic testing is becoming more prevalent in the diagnosis and treatment of cancer, our drug candidates may be perceived negatively compared to alternative treatments that do not require the use of companion diagnostics, either due to the additional cost of the companion diagnostic or the need to complete additional testing prior to administering our drug candidates.

If any of these events were to occur, our business and growth prospects would be harmed materially.

We may not be able to file INDs or IND amendments to commence additional clinical trials on the timelines we expect, and even if we are able to, the FDA may not permit us to proceed.

Although we received clearance from the FDA for an IND to advance ACR-368 in Phase 2 single arm clinical trials conducted under the master protocol, we may not be able to file INDs for ACR-2316 and our other drug candidates on the timelines we expect. For example, we may experience, or our partners may experience, manufacturing delays or other delays with IND-enabling studies. Further, requirements for master protocols may evolve and we may not be able to conduct future trials under a master protocol. In December 2023, the FDA published a draft guidance, Master Protocols for Drug and Biological Product Development, which provides recommendations on the design and analysis of trials conducted under a master protocol as well as guidance on the submission of documentation to support regulatory review. Evolving requirements for master protocols may delay or inhibit future trials relying on a master protocol. Moreover, we cannot be sure that submission of an IND will result in the FDA allowing further clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate clinical trials. Additionally, even if such regulatory authorities agree with the design and implementation of the clinical trials set forth in an IND, we cannot guarantee that such regulatory authorities will not change their requirements in the future. These considerations also apply to new clinical trials we may submit as amendments to existing INDs or to a new IND. Any failure to file INDs on the timelines we expect or to obtain regulatory approvals for our trials may prevent us from completing our clinical trials or commercializing our products on a timely basis, if at all.

If we experience delays or difficulties in enrolling patients in our ongoing or planned clinical trials, our receipt of necessary regulatory approval could be delayed or prevented.

We may not be able to initiate or continue our ongoing or planned clinical trials if we are unable to identify and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or comparable foreign regulatory authorities. In addition, some of our competitors currently have ongoing clinical trials for drug candidates that would treat the same patients as our lead clinical drug candidate, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' drug candidates. We rely on our external companion diagnostic partner, Akoya, to perform ACR-368 OncoSignature testing in our clinical trial. If Akoya encounters delays or technical challenges, enrollment in our clinical trials may be substantially delayed. Patient enrollment is also affected by other factors, including but not limited to:

- the severity of the disease under investigation;
- our ability to recruit clinical trial investigators of appropriate competencies and experience;
- the incidence and prevalence of our target indications;
- competing studies or trials with similar eligibility criteria;
- invasive procedures required to enroll patients and to obtain evidence of the drug candidates' performance during clinical trials;
- availability and efficacy of approved medications for the disease under investigation;
- eligibility criteria defined in the protocol for the trial in question;
- the size and nature of the patient population required for analysis of the trial's primary endpoints;
- efforts to facilitate timely enrollment in clinical trials;
- whether we are subject to a partial or full clinical hold on any of our clinical trials;
- reluctance of physicians to encourage patient participation in clinical trials;
- the ability to monitor patients adequately during and after treatment;
- our ability to obtain and maintain patient consents; and
- proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll and maintain a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs, which would cause the value of our company to decline, limit our ability to obtain additional financing and delay or limit our ability to obtain regulatory approval for our drug candidates.

Additionally, the FDA may modify or enhance trial requirements which may affect enrollment. In August 2023, the FDA published a guidance document, Informed Consent, Guidance for IRBs, Clinical Investigators, and Sponsors, which supersedes past guidance and finalizes draft guidance on informed consent. The FDA's new guidance presents evolving requirements for informed consent which may affect recruitment and retention of patients in clinical trials. Effects on recruitment and retention of patients may hinder or delay a clinical trial and could cause a significant setback to an applicable program.

Unexpected adverse side effects or other safety risks associated with ACR-368, ACR-2316, or our other future drug candidates could delay or preclude approval, cause us to suspend or discontinue clinical trials or abandon further development, limit the commercial profile of an approved product or result in significant negative consequences following marketing approval, if any.

As is the case with small molecule therapeutics generally, side effects and adverse events associated with ACR-368 have been observed. Although ACR-368 has been evaluated in approximately 1,000 patients in clinical trials to date with a generally favorable tolerability profile, unexpected side effects may still arise in our ongoing or any future clinical trial.

Our trials will be primarily based on the established RP2D dosing regimen used in over 400 patients in past trials. In these trials, the most frequent treatment related adverse events greater than or equal to Grade 3, which are considered serious adverse events, were primarily reversible, manageable hematological toxicities, including neutropenia and thrombocytopenia and there was only limited non-hematological toxicities. In one of the clinical trials (a cohort of 58 platinum-sensitive patients), there were three deaths deemed possibly related to study treatment. In addition, our trials will also, in part, include testing of ACR-368 at RP2D in combination with low dose gemcitabine, which could result in greater severity and prevalence of side effects or unexpected characteristics. Undesirable side effects could result in the delay, suspension or termination of clinical trials by us or regulatory authorities for a number of reasons. Furthermore, clinical trials by their nature utilize a sample of the potential patient population. With a limited number of subjects and limited duration of exposure, rare and severe side effects of our drug candidates or those of our competitors may only be uncovered with a significantly larger number of patients exposed to the drug.

Additionally, due to the high mortality rates of the cancers for which we are initially pursuing development and the pretreated and advanced nature of disease in many patients in our ongoing clinical trials of ACR-368, a material percentage of patients in these clinical trials ultimately will die during a trial for reasons unrelated to the drug. For example, in the Phase 1b/2 combination arm of our Phase 2 trial for ACR-368 we dosed a patient who had previously failed three lines of prior therapy. The patient died prior to receiving a second dose of ACR-368 and the death was determined by the trial investigator not to be drug related, but instead related to the subject's disease progression. If we elect to, or are required to, delay, suspend or terminate any clinical trial, whether due to a patient death or otherwise, the commercial prospects of ACR-368 or our future drug candidates could be harmed and our ability to generate product revenues could potentially be delayed or eliminated. Serious adverse events observed in clinical trials could hinder or prevent market acceptance of our drug candidates, which would harm our commercial prospects, our financial condition and our reputation.

Moreover, if ACR-368, ACR-2316, or any of our future drug candidates are associated with undesirable or unexpected side effects in clinical trials, we may elect to abandon or limit their development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, which may limit the commercial expectations for the drug candidate, even if it is approved. We may also be required to modify our trial plans based on findings in our clinical trials. Side effects could also affect patient recruitment or the ability of enrolled patients to complete a trial. Many drugs that initially showed promise in early stage testing have later been found to cause side effects that prevented further development. In addition, regulatory authorities may draw different conclusions, require additional testing to confirm these determinations, require more restrictive labeling or deny regulatory approval of the drug candidate.

It is possible that, as we test our drug candidates in larger, longer and more extensive clinical trials, including with different dosing regimens, or as the use of our drug candidates becomes more widespread following any regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by patients. If such side effects become known later in development or upon approval, if any, such findings may harm our business, financial condition, results of operations and prospects significantly.

In addition, if ACR-368 receives marketing approval, and we or others later identify undesirable side effects caused by treatment with such drug, a number of potentially significant negative consequences could result, including but not limited to:

- regulatory authorities may withdraw approval of or seize the drug;
- we may be required to recall a product, or change the way the drug is administered to patients, or conduct additional clinical trials;
- regulatory authorities may require additional warnings in the labeling, such as a contraindication or a boxed warning, or issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- we may be required to implement a REMS, or create a medication guide outlining the risks of such side effects for distribution to patients;
- additional restrictions may be imposed on the marketing or promotion of the particular product or the manufacturing processes for the product or any component thereof;

- we could be sued and held liable for harm caused to patients;
- we may be subject to regulatory investigations and government enforcement actions;
- the drug could become less competitive; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of our drug candidates, if approved, and could significantly harm our business, financial condition, results of operations and prospects.

Preliminary, interim and topline data from our clinical trials that we announce or publish from time to time may change as more patient data becomes available and is subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary, interim or topline data from our clinical trials, such as futility analyses, ORR, or various primary and secondary clinical endpoints. These updates will be based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. Additionally, interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data becomes available. Therefore, positive interim results in any ongoing clinical trial may not be predictive of such results in the completed study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data has been received and fully evaluated. Topline data also remains subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data is available. In addition, we may report interim analyses of only certain endpoints rather than all endpoints. Adverse changes between preliminary or interim data and final data could significantly harm our business and prospects. Further, additional disclosure of interim data by us or by our competitors in the future could result in volatility in the price of our common stock. See the description of risks under the heading "Risks Related to Ownership of our Common Stock and our Status as a Public Company" for more disclosure related to the risk of volatility in our stock price.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular drug candidate or product and our company in general. Additionally, requirements regarding clinical trial data may evolve. In June 2023, the FDA published a draft guidance, E6(R3) Good Clinical Practice (GCP), which seeks to unify standards for clinical trial data for ICH member countries and regions. Changes to data requirements may cause the FDA or comparable foreign regulatory authorities to disagree with data from preclinical studies or clinical trials, and may require further studies.

In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is typically selected from a more extensive amount of available information. You or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product, drug candidate or our business.

Additionally, other future clinical trials we conduct may be open-label trials in which both the patient and investigator know whether the patient is receiving the investigational drug candidate or either an existing approved product or placebo. Open-label clinical trials typically test only the investigational drug candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a "patient bias" where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge.

If the preliminary or topline data that we report differs from late, final or actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, ACR-368, ACR-2316, or any other future drug candidates may be harmed.

We may in the future seek to engage in business co-development pharma partnerships leveraging our AP3 platform for patient responder identification or uncovering of resistance mechanisms to drug candidates or in strategic transactions to acquire or in-license additional products, drug candidates or technologies. If we are unable to realize the benefits from such transactions, it may adversely affect our ability to develop and commercialize an expanded pipeline of drug candidates, negatively impact our cash position, increase our expenses and present significant distractions to our management.

From time to time, we may consider strategic transactions, such as additional collaborations, acquisitions of companies, asset purchases, joint ventures and in-licensing of new products, drug candidates or technologies that we believe will complement or augment our existing business. For example, in 2021, we acquired our lead drug candidate, ACR-368, pursuant to worldwide license agreement with Lilly. If we acquire assets with promising markets or technologies, we may not be able to realize the benefit of acquiring such assets if we are not able to successfully integrate them with our existing technologies. We may encounter numerous difficulties in developing, testing, manufacturing and marketing any new products resulting from a strategic acquisition that delay or prevent us from realizing their expected benefits or enhancing our business.

Following any such strategic transaction, we may not achieve any expected synergies to justify the transaction. For example, such transactions may require us to incur non-recurring or other charges, increase our near-term and long-term expenditures and pose significant integration or implementation challenges or disrupt our management or business. These transactions would entail numerous operational and financial risks, including, but not limited to, exposure to unknown liabilities, disruption of our business and diversion of our management's time and attention in order to manage a collaboration or develop acquired products, drug candidates or technologies, incurrence of substantial debt or dilutive issuances of equity securities to pay transaction consideration or costs, higher than expected acquisition or integration costs, write-downs of assets or goodwill or impairment charges, increased amortization expenses, difficulty and cost in facilitating the transaction or combining the operations and personnel of any acquired business, impairment of relationships with key suppliers, manufacturers or customers of any acquired business due to changes in management and ownership and the inability to retain key employees of any acquired business.

Accordingly, although there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete may be subject to the foregoing or other risks and could have a material and adverse effect on our business, financial condition, results of operations and prospects. Conversely, any failure to enter any strategic transaction that would be beneficial to us could delay the development and potential commercialization of our drug candidates and could have a negative impact on the competitiveness of any drug candidate that reaches market.

We may expend our limited resources to pursue a particular drug candidate or indication and fail to capitalize on drug candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and drug candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other future drug candidates or for other indications that later prove to have greater commercial potential.

Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and drug candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular drug candidate, we may relinquish valuable rights to that drug candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to that drug candidate.

Our clinical development is focused on the development of precision oncology medicines utilizing our proprietary precision medicine platform, which is based on a novel scientific approach and may never lead to marketable products.

The development of precision oncology medicines for patients whose tumors are sensitive to a specific product or drug candidate based on direct protein measurement is a rapidly emerging field, and the scientific discoveries that form the basis for our efforts to develop drug candidates are relatively new. Furthermore, our OncoSignature companion diagnostic is based on new technology, which makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval, if at all.

The scientific evidence to support the feasibility of developing drug candidates based on these discoveries is both preliminary and limited. Although we believe, based on our extensive preclinical evaluation, that our approach is applicable across stages of drug development and therapeutic modalities, clinical results may not confirm this hypothesis or may only confirm it for certain tumor types. Therefore, we do not know if our approach will be successful, but if our approach is unsuccessful, our business will suffer.

Efforts to identify, acquire or in-license, and then develop drug candidates require substantial technical, financial and human resources, whether or not any drug candidates are ultimately identified. We apply our AP3 platform and OncoSignature companion diagnostic in our efforts to discover potential precision targets for which drug candidates may be developed. Our efforts may initially show promise in identifying potential drug candidates, yet fail to yield drug candidates for clinical development, approved products or commercial revenues for many reasons, including the following:

- the methodology used may not be successful in identifying potential drug candidates;
- competitors may develop alternatives that render any drug candidates we develop obsolete;
- any drug candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- a drug candidate may be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- a drug candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and
- a drug candidate may not be accepted as safe and effective by physicians, patients, the medical community or third-party payors.

Increasing demand for compassionate use of our drug candidates could negatively affect our reputation and harm our business.

We are developing drug candidates for the treatment of indications for which there are currently limited or no available therapeutic options. It is possible for individuals or groups to target companies with disruptive social media campaigns related to a request for access to unapproved drugs for patients with significant unmet medical need. If we experience a similar social media campaign regarding our decision to provide or not provide access to any of our current or future drug candidates under an expanded access policy, our reputation may be negatively affected and our business may be harmed.

Media attention to individual patients' expanded access requests has resulted in the introduction and enactment of legislation at the local and national level referred to as "Right to Try" laws, such as the federal Right to Try Act of 2017 signed into law on May 30, 2018, which are intended to allow patients access to unapproved therapies earlier than traditional expanded access programs. A possible consequence of both activism and legislation in this area may be the need for us to initiate an unanticipated expanded access program or to make our drug candidates more widely available sooner than anticipated.

In addition, some patients who receive access to drugs prior to their commercial approval through compassionate use, expanded access programs or right to try access have life-threatening illnesses and have exhausted all other available therapies. The risk for serious adverse events in this patient population is high, which could have a negative impact on the safety profile of our drug candidates if we were to provide them to these patients, which could cause significant delays or an inability to successfully commercialize our drug candidates, which could materially harm our business. If we were to provide patients with any of our drug candidates under an expanded access program, we may in the future need to restructure or pause any compassionate use and/or expanded access programs for a variety of reasons, which could prompt adverse publicity or other disruptions related to current or potential participants in such programs.

Our business and operations may be adversely affected by COVID-19 or other similar outbreaks.

Our business and operations may be adversely affected by the effects of the COVID-19 virus or other similar outbreaks. On May 11, 2023, the COVID-19 PHE declared under the PHS Act expired. While the PHE has ended, COVID-19 has resulted in travel and other restrictions in order to reduce the spread of the disease, including public health directives and orders in the United States and globally. Future remote work policies and similar government orders or other restrictions on the conduct of business operations related to COVID-19 or other PHEs may negatively impact productivity; disrupt our ongoing research and development activities and our clinical programs and timelines; and cause disruptions to our supply chain, to the administrative functions of clinical trial sites and to the operations of our other partners, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course. In the event that government authorities were to require or enhance restrictions, such orders also may impact the availability or cost of materials, which would disrupt our supply chain and manufacturing efforts and could affect our ability to conduct ongoing and planned clinical trials and preparatory activities. We may also face difficulties in obtaining access to manufacturing slots for our drug candidates.

The spread of COVID-19, including new variants of the virus, such as the Omicron or JN.1 variants and related subvariants, which have caused a broad impact globally, may materially affect us economically. While the potential economic impact brought by, and the duration of, COVID-19 may be difficult to assess or predict, a widespread pandemic could result in significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common stock.

Since the beginning of the COVID-19 pandemic, several vaccines for COVID-19 have received Emergency Use Authorization by the FDA and a number of those later received marketing approval. Additional vaccines may be authorized or approved in the future. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult and/or more costly to obtain materials or manufacturing slots for the products needed for our clinical trials, which could lead to delays in these trials.

The extent to which COVID-19 impacts our business and operations, including our clinical development and regulatory efforts, will depend on future developments that are highly uncertain and cannot be predicted with confidence, such as the duration and effect of business disruptions. Accordingly, we do not yet know the full extent of impacts on our business, our clinical and regulatory activities, healthcare systems or the global economy as a whole. However, these impacts could adversely affect our business, financial condition, results of operations and growth prospects. In addition, to the extent COVID-19 adversely affects our business and results of operations, it may also have the effect of heightening many of the other risks and uncertainties described in this "Risk Factors" section.

Risks Related to Government Regulation

Our relationships with customers, healthcare providers, including physicians, and third-party payors are subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

Healthcare providers, including physicians, and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any drug candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers and third-party payors subject us to various federal and state fraud and abuse laws and other healthcare laws, including, without limitation, the federal Anti-Kickback Statute, the federal civil and criminal false claims laws and the law commonly referred to as the Physician Payments Sunshine Act, as well as regulations promulgated under such laws. These laws will impact, among other things, our clinical research, proposed sales, marketing and educational programs, and other interactions with healthcare professionals. In addition, we may be subject to patient privacy laws by both the federal government and the states in which we conduct or may conduct our business. See "Part I, Item 1, Business—Government Regulation—Other Healthcare Laws and Compliance Requirements and Healthcare Reform" of our Annual Report on Form 10-K for the year ended December 31, 2023, for more information on the healthcare laws and regulations that may affect our ability to operate.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant penalties, including, without limitation, civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from participating in federal and state funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, diminished profits and future earnings, reputational harm and the curtailment or restructuring of our operations, any of which could harm our business.

The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance and/or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

Even if we obtain FDA approval of any of our drug candidates in the United States, we may never obtain approval for or commercialize any of them in any other jurisdiction, which would limit our ability to realize their full market potential.

In order to market any products in any particular jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a country-by-country basis regarding safety and efficacy.

Approval by the FDA in the United States does not ensure approval by regulatory authorities in other countries or jurisdictions. However, the failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval elsewhere. In addition,

clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country.

Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and increased costs for us and require additional preclinical studies or clinical trials which could be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. We do not have any drug candidates approved for sale in any jurisdiction, including in international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of any product we develop will be unrealized.

Even if we receive regulatory approval of our current or future drug candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our drug candidates.

Any drug candidate for which we obtain marketing approval will be subject to ongoing regulatory requirements for, among other things, manufacturing processes, submission of post-approval clinical data and safety information, labeling, packaging, distribution, adverse event reporting, storage, recordkeeping, export, import, advertising, promotional activities and product tracking and tracing. These requirements include submissions of safety and other post-marketing information and reports, establishment registration and drug listing requirements, continued compliance with cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping and GCP requirements for any clinical trials that we conduct post-approval.

The FDA and other federal and state agencies, including the Department of Justice, closely regulate compliance with all requirements governing prescription drug and biologic products, including requirements pertaining to their marketing and promotion in accordance with the provisions of the approved labeling and manufacturing of products in accordance with cGMP requirements. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we market our products for uses beyond their approved diseases, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug, and Cosmetic Act, relating to the promotion of prescription drugs for unapproved uses may lead to enforcement actions and investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including but not limited to:

- restrictions on manufacturing such products;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning or untitled letters, or holds on clinical trials;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure or detention;
- injunctions or the imposition of civil or criminal penalties; or
- litigation involving patients using our products.

The FDA's policies, and the policies of foreign regulatory agencies, may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, executive orders or other actions could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. If such executive actions were to impose restrictions on the FDA's ability to engage in oversight and implementation activities in the normal course, our business could be negatively impacted. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained which would adversely affect our business, prospects and ability to achieve or sustain profitability.

Enacted and future healthcare legislation may increase the difficulty and cost for us to progress our clinical programs and obtain marketing approval of and commercialize our drug candidates and may affect the prices we may set.

In the United States, the European Union and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could prevent or delay marketing approval or licensure of our product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval or licensure. In the United States, the biopharmaceutical industry has been a particular focus of these efforts and has been significantly affected by legislative initiatives. Current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any FDA-approved product. For example, the Inflation Reduction Act (IRA), which was signed into law on August 16, 2022, allows Medicare to: beginning in 2026, establish a "maximum fair price" for a fixed number of pharmaceutical and biological products covered under Medicare Parts B and D following a price negotiation process with the Centers for Medicare and Medicaid Services (CMS); and, beginning in 2023, penalize drug companies that raise prices for products covered under Medicare Parts B and D faster than inflation, among other reforms. CMS has recently taken steps to implement the IRA, including: on June 30, 2023, issuing guidance detailing the requirements and parameters of the first round of price negotiations, to take place during 2023 and 2024, for products subject to the "maximum fair price" provision that would become effective in 2026; on August 29, 2023, releasing the initial list of ten drugs subject to price negotiations; on November 17, 2023, releasing guidance outlining the methodology for identifying certain manufacturers eligible to participate in a phase-in period where discounts on applicable products will be lower than those required by the Medicare Part D Manufacturer Discount Program; and on December 14, 2023, releasing a list of 48 Medicare Part B products that had an adjusted coinsurance rate based on the inflationary rebate provisions of the IRA for the time period of January 1, 2024 to March 31, 2024. It is unclear how future regulatory actions to implement the IRA, as well as the outcome of pending litigation against the IRA brought against the Department of Health and Human Services (HHS), the Secretary of HHS, CMS, and the CMS Administrator challenging the constitutionality and administrative implementation of the IRA's drug price negotiation provisions, may affect our products and future profitability. Reductions in reimbursement levels may also negatively impact the prices we receive or the frequency with which our products are prescribed or administered, with any reduction in reimbursement from Medicare or other government programs potentially resulting in a similar reduction in payments from private payors. See "Part I, Item 1, Business—Government Regulation—Healthcare Reform" of our Annual Report on Form 10-K for the year ended December 31, 2023, for more information on specific healthcare reform measures that may affect our business.

In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our drug candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than European Union, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing European Union and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our drug candidates, restrict or regulate post-approval activities and affect our ability to commercialize our drug candidates, if approved.

In markets outside of the United States and the European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States, the European Union or any other jurisdiction. If we or any third parties we may engage are slow or unable

to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our drug candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

If we or our third-party manufacturers and suppliers fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Although we do not currently manufacture our drug products or drug candidates on site, our research and development activities do involve the use of biological and hazardous materials and produce hazardous waste products at small quantities. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development, or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties, or other sanctions.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific biological waste or hazardous waste insurance coverage, workers compensation or property and casualty and general liability insurance policies that include coverage for damages and fines arising from biological or hazardous waste exposure or contamination.

Changes in funding for the FDA and other government agencies could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new products and services from being developed or commercialized in a timely manner, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel, accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also lengthen the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. Our business depends upon the ability of the FDA to accept and review our potential regulatory filings. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business and our ability to advance clinical development of our drug candidates.

Further, future shutdowns of other government agencies, such as the U.S. Securities and Exchange Commission, or SEC, may also impact our business through review of our public filings and our ability to access the public markets.

If we obtain approval to commercialize any products outside of the United States, a variety of risks associated with international operations could adversely affect our business.

If ACR-368 or any of our other drug candidates are approved for commercialization, we may seek to enter into agreements with third parties to market them in certain jurisdictions outside the United States. We expect that we would be subject to additional risks related to international pharmaceutical operations, including but not limited to:

- different regulatory requirements for drug and companion diagnostic trials and approvals and rules governing drug and companion diagnostic commercialization in foreign countries;

- reduced protection for intellectual property rights;
- foreign reimbursement, pricing and insurance regimes;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- business interruptions resulting from geopolitical actions, including war, global conflicts and terrorism or natural disasters including earthquakes, typhoons, floods and fires, or from economic or political instability;
- greater difficulty with enforcing our contracts;
- potential noncompliance with the U.S. Foreign Corrupt Practices Act, or FCPA, the U.K. Bribery Act 2010 and similar anti-bribery and anticorruption laws in other jurisdictions; and
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad.

We have no prior experience in these areas. In addition, there are complex regulatory, tax, labor and other legal requirements imposed by individual countries in Europe with which we will need to comply. If we are unable to successfully manage the challenges of international expansion and operations, our business and operating results could be harmed.

We may develop our current and future drug candidates in combination with other therapies, and safety or supply issues with combination-use products may delay or prevent development and approval of our drug candidates.

We may develop our current or future drug candidates in combination with one or more cancer therapies, both approved and unapproved. Even if any drug candidate we develop were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA or similar regulatory authorities outside of the United States could revoke approval of the therapy used in combination with our drug candidates or that safety, efficacy, manufacturing or supply issues could arise with these existing therapies. Combination therapies are commonly used for the treatment of cancer, and we would be subject to similar risks if we develop any of our drug candidates for use in combination with other drugs or for indications other than cancer. Similarly, if the therapies we use in combination with our drug candidates are replaced as the standard of care for the indications we choose for any of our drug candidates, the FDA or similar regulatory authorities outside of the United States may require us to conduct additional clinical trials. The occurrence of any of these risks could result in our own products, if approved, being removed from the market or being less successful commercially.

We may also evaluate our drug candidates in combination with one or more cancer therapies that have not yet been approved for marketing by the FDA or a similar regulatory authority outside of the United States. We may be unable to effectively identify and collaborate with third parties for the evaluation of our drug candidates in combination with their therapies. We will not be able to market and sell any drug candidate we develop in combination with any such unapproved cancer therapies that do not ultimately obtain marketing approval. The regulations prohibiting the promotion of products for unapproved uses are complex and subject to substantial interpretation by the FDA and other government agencies. In addition, there are additional risks similar to the ones described for our products currently in development and clinical trials that result from the fact that such cancer therapies are unapproved, such as the potential for serious adverse effects, delay in their clinical trials and lack of FDA approval.

If the FDA or a similar regulatory authority outside of the United States does not approve these other drugs or revokes approval of, or if safety, efficacy, manufacturing, or supply issues arise with, the drugs we choose to evaluate in combination with any drug candidate we develop, we may be unable to obtain approval of or market such product.

We may not be able to obtain or maintain orphan drug designation or exclusivity for our drug candidates.

Regulatory authorities in some jurisdictions, including the United States, may designate drugs for relatively small patient populations as "orphan drugs." Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is intended to treat patients with a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States, or if the disease or condition affects more than 200,000 individuals in the United States and there is no reasonable expectation that the cost of developing the drug for the type of disease or condition will be recovered from sales of the product in the United States.

Orphan drug designation entitles a party to financial incentives, such as opportunities for grant funding towards clinical trial costs, tax advantages and user fee waivers. Additionally, if a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years, except in certain circumstances, such as a showing of clinical superiority (i.e., another product is safer, more effective or makes a major contribution to patient care) over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity. Competitors, however, may receive approval of different products for the same indication for which the orphan product has exclusivity, or obtain approval for the same product but for a different indication than that for which the orphan product has exclusivity.

ACR-368 has been granted orphan drug designation, or ODD, for the treatment of anal cancer. We may apply for an ODD in the United States or other geographies for ACR-368 for the treatment of other diseases or conditions or for our future drug candidates. However, obtaining an orphan drug designation can be difficult, and we may not be successful in doing so. Even if we obtain orphan drug designation for a drug candidate in specific indications, we may not be the first to obtain regulatory approval of the drug candidate for the orphan-designated indication due to the uncertainties associated with developing drug products. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for orphan designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Orphan drug designation does not ensure that we will receive marketing exclusivity in a particular market, and we cannot assure you that any future application for orphan drug designation in any other geography or with respect to any other future drug candidate will be granted. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process.

In addition, Congress is considering updates to the orphan drug provisions of the FDCA in response to a recent decision by the U.S. Court of Appeals for the Eleventh Circuit. Any changes to the orphan drug provisions could change our opportunities for, or likelihood of success in obtaining, orphan drug designation and/or exclusivity and would materially adversely affect our business, results of operations, financial condition and prospects.

A Fast Track designation by the FDA, even if granted for our lead drug candidate, or any of our future drug candidates, may not lead to a faster development or regulatory review or approval process and does not increase the likelihood that our drug candidates will receive marketing approval.

At various times, we may seek Fast Track designation for one or more of our drug candidates. If a drug candidate is intended for the treatment of a serious or life-threatening condition and the drug candidate demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA Fast Track designation for a particular indication.

On May 8, 2023, ACR-368 was granted two Fast Track designations from the U.S. Food and Drug Administration for the investigation of ACR-368 monotherapy for patients with OncoSignature-positive platinum-resistant ovarian cancer and endometrial cancer. We may seek Fast Track designation for certain of our future drug candidates, but there is no assurance that the FDA will grant this status to any of our proposed drug candidates and we might only be successful in receiving a Fast Track designation from the FDA for a drug candidate after applying on more than one occasion. Sponsors may have greater interactions with the FDA and marketing applications filed by sponsors of products in Fast Track development may qualify for priority review and rolling review under the policies and procedures offered by the FDA, but the receipt of a Fast Track designation does not assure any such qualification or ultimate marketing approval by the FDA. The FDA has broad discretion whether or not to grant a Fast Track designation, so even if we believe a particular drug candidate is eligible for this designation, there can be no assurance that the FDA would decide to grant it. Even if we do receive a Fast Track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures, and receiving a Fast Track designation does not provide assurance of ultimate FDA approval. In addition, the FDA may withdraw a Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program. In addition, the FDA may withdraw any Fast Track designation at any time.

A Breakthrough Therapy or Breakthrough Device designation by the FDA, even if granted for any of our current or future drug candidates or companion diagnostics, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our drug candidates will receive marketing approval.

At various times, we may seek Breakthrough Therapy designation for our lead drug candidate and some or all of our future drug candidates and Breakthrough Device designation for our OncoSignature companion diagnostic and future companion diagnostic candidates. Breakthrough Therapy designation is a process designed to expedite the development and review of drugs that are intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drug candidates that have been designated as Breakthrough Therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA may also be eligible for other expedited approval programs, including accelerated approval.

The FDA has also implemented a Breakthrough Device program that is intended to help patients receive more timely access to breakthrough medical technologies that have the potential to provide more effective treatment or diagnosis for life-threatening or irreversibly debilitating diseases or conditions. A device also must meet one of the following criteria: (i) it represents breakthrough technology; (ii) there is no approved or cleared alternative; (iii) it offers significant advantages over existing cleared or approved devices; or (iv) availability of the device is in the best interest of patients. Under the program, device candidates are eligible to receive priority review and interactive communications from the FDA regarding device development and clinical trial protocols, all the way through to commercialization decisions. On November 16, 2023, the FDA granted Breakthrough Device Designation to the ACR-368 OncoSignature assay for the identification of ovarian cancer patients who may benefit from ACR-368 treatment.

Designation as a Breakthrough Therapy or Breakthrough Device is within the discretion of the FDA. Accordingly, even if we believe a product candidate meets the criteria for designation as a Breakthrough Therapy or Breakthrough Device, the FDA may disagree and instead determine not to make such a designation. In any event, the receipt of a Breakthrough Therapy or Breakthrough Device designation for a product candidate may not result in a faster development process, review or approval compared to candidate products considered for approval under non-expedited FDA review procedures and does not assure ultimate approval by the FDA of a product candidate. In addition, even if a product candidate qualifies as a Breakthrough Therapy or Breakthrough Device, the FDA may later decide that the product candidate no longer meets the conditions for qualification. Thus, even though we intend to seek Breakthrough Therapy designation for our lead drug candidate and some or all of our future drug candidates and Breakthrough Device designation for our OncoSignature companion diagnostic and any future companion diagnostic candidates for the treatment of various cancers, there can be no assurance that we will receive Breakthrough Therapy or Breakthrough Device designations.

Risks Related to Our Reliance on Third Parties

We rely, and expect to continue to rely, on third parties, including independent clinical investigators, contracted laboratories and CROs, to conduct our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our drug candidates and our business could be substantially harmed.

We have relied upon and plan to continue to rely upon third parties, including independent clinical investigators, contracted laboratories and third-party CROs, to conduct our preclinical studies and clinical trials in accordance with applicable regulatory requirements and to monitor and manage data for our ongoing preclinical and clinical programs. We rely on these parties for execution of our preclinical studies and clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies and trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and our third party contractors and CROs are required to comply with good laboratory practices, or GLPs, as applicable, and GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for all of our products in clinical development. Regulatory authorities enforce these GLPs and GCPs through periodic inspections of laboratories conducting GLP studies, trial sponsors, principal investigators and trial sites. If we, our investigators or any of our CROs or contracted laboratories fail to comply with applicable GLPs and GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional preclinical studies or clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our preclinical studies or clinical trials comply with applicable GLP or GCP regulations. In addition, our clinical trials must be conducted with drug products produced in compliance with applicable cGMP regulations. Our failure to comply with these regulations may require us to repeat preclinical studies or clinical trials, which would delay the regulatory approval process.

Further, these laboratories, investigators and CROs are not our employees and we will not be able to control, other than by contract, the amount of resources, including time, which they devote to our drug candidates and clinical trials. If independent laboratories, investigators or CROs fail to devote sufficient resources to the development of our drug candidates, or if their performance is

substandard, it may delay or compromise the prospects for approval and commercialization of any drug candidates that we develop. In addition, the use of third-party service providers requires us to disclose our proprietary information to these parties, which could increase the risk that this information will be misappropriated.

Our CROs have the right to terminate their agreements with us in the event of an uncured material breach. In addition, some of our CROs have an ability to terminate their respective agreements with us if we make a general assignment for the benefit of our creditors or if we are liquidated.

If any of our relationships with these third-party laboratories, CROs or clinical investigators terminate, we may not be able to enter into arrangements with alternative laboratories, CROs or investigators or to do so in a timely manner or on commercially reasonable terms. If laboratories, CROs or clinical investigators do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our preclinical or clinical protocols, regulatory requirements or for other reasons, our preclinical or clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our drug candidates. As a result, our results of operations and the commercial prospects for our drug candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Switching or adding additional laboratories or CROs or investigators involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new laboratory or CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our contracted laboratories and CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and results of operations.

In addition, clinical investigators may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected the interpretation of the preclinical study or clinical trial, the integrity of the data generated at the applicable preclinical study or clinical trial site may be questioned and the utility of the preclinical study or clinical trial itself may be jeopardized, which could result in the delay or rejection by the FDA. Any such delay or rejection could prevent us from commercializing our clinical-stage drug candidate or any future drug candidates.

We rely on third parties to supply and manufacture our drug candidates, and we expect to continue to rely on third parties to manufacture our products, if approved. The development of such drug candidates and the commercialization of any products, if approved, could be stopped, delayed or made less profitable if any such third party fails to provide us with sufficient quantities of drug candidates or products or fails to do so at acceptable quality levels or prices or fails to maintain or achieve satisfactory regulatory compliance.

We do not currently have the infrastructure or capability internally to manufacture all our drug candidates for use in the conduct of our preclinical studies and clinical trials or for commercial supply, if our products are approved. We rely on, and expect to continue to rely on CMOs. Any replacement of our CMOs could require significant effort and expertise because there may be a limited number of qualified CMOs. This could be particularly problematic if we rely on a single-source supplier. Reliance on third-party providers may expose us to more risk than if we were to manufacture our drug candidates ourselves. We are dependent on our CMOs for the production of our drug candidates in accordance with relevant regulations, such as cGMP, which includes, among other things, quality control, quality assurance and the maintenance of records and documentation. Moreover, many of the third parties with whom we contract may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting product development activities that could harm our competitive position.

Our third-party manufacturers may be subject to damage or interruption from, among other things, fire, natural or man-made disaster, war, global conflicts, disease outbreaks or public health pandemics, power loss, telecommunications failure, unauthorized entry, computer viruses, denial-of-service attacks, acts of terrorism, human error, vandalism or sabotage, financial insolvency, bankruptcy and similar events.

If we were to experience an unexpected loss of supply of or if any supplier were unable to meet our demand for any of our drug candidates, we could experience delays in our research or ongoing and planned clinical trials or commercialization. We could be unable to find alternative suppliers of acceptable quality, in the appropriate volumes who could meet our timelines at an acceptable cost. Moreover, our suppliers are often subject to strict manufacturing requirements and rigorous testing requirements, which could limit or delay production. The long transition periods necessary to switch manufacturers and suppliers, if necessary, could significantly delay our preclinical studies, our clinical trials and the commercialization of our products, if approved, which could materially adversely affect our business, financial condition and results of operation.

In complying with the applicable manufacturing regulations of the FDA and comparable foreign regulatory authorities, we and our third-party suppliers must spend significant time, money and effort in the areas of design and development, testing, production, record-keeping and quality control to assure that the products meet applicable specifications and other regulatory requirements. The failure to comply with these requirements could result in an enforcement action against us, including the seizure of products and shutting down of production. We and any of these third-party suppliers may also be subject to audits by the FDA and comparable foreign regulatory authorities. If any of our third-party suppliers fails to comply with cGMP or other applicable manufacturing regulations, our ability to develop and commercialize the products could suffer significant interruptions. We face risks inherent in relying on CMOs, as any disruption, such as a fire, natural hazards, global conflicts, vandalism or an outbreak of contagious disease affecting the CMO or any supplier of the CMO could significantly interrupt our manufacturing capability. In case of a disruption, we will have to establish alternative manufacturing sources. This would require substantial capital on our part, which we may not be able to obtain on commercially acceptable terms or at all. Additionally, we would likely experience months of manufacturing delays as the CMO builds or locates replacement facilities and seeks and obtains necessary regulatory approvals. If this occurs, we will be unable to satisfy manufacturing needs on a timely basis, if at all.

Our current and future partnerships will be important to our business. If we are unable to enter into new partnerships, or if these partnerships are not successful, our business could be adversely affected.

We have existing partnerships and license agreements, including with Lilly for ACR-368 and with Akoya to co-develop, validate and commercialize our ACR-368 OncoSignature test. Moreover, a part of our business strategy is to carefully evaluate and, as deemed appropriate, potentially enter into partnerships in the future, including with major biotechnology or pharmaceutical companies. We have limited capabilities for product development and do not yet have any capability for commercialization. Accordingly, we may enter into partnerships with other companies to provide us with additional drug candidates and funding for our programs and AP3 platform. If we fail to enter into or maintain partnerships on reasonable terms or at all, our ability to develop our existing or future research programs and drug candidates or to identify future drug candidates through the application of our AP3 platform and OncoSignature companion diagnostics could be delayed, the commercial potential of our product could change and our costs of development and commercialization could increase. Furthermore, we may find that our programs require the use of intellectual property rights held by third parties, and the growth of our business may depend in part on our ability to acquire or in-license these intellectual property rights.

Our current partnerships, and any partnerships we may enter into in the future, may pose a number of risks, including, but not limited to, the following:

- partners have significant discretion in determining the efforts and resources that they will apply;
- partners may not perform their obligations as expected;
- partners could independently develop, or develop with third parties, products that compete directly or indirectly with our products and drug candidates if the partners believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- partners may fail to comply with applicable regulatory requirements regarding the development, manufacture, distribution or marketing of a drug candidate or product;
- disagreements with partners, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or commercialization of drug candidates, might lead to additional responsibilities for us with respect to drug candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- partners may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- partners may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- if a partners of ours is involved in a business combination, the partner might deemphasize or terminate the development or commercialization of any drug candidate licensed to it by us; and
- partnerships may be terminated by the partner, and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable drug candidates.

If our partnerships do not result in the successful discovery, development and commercialization of drug candidates or if one of our partners terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under such partnership.

All of the risks relating to product development, regulatory approval and commercialization also apply to the activities of our partners. Additionally, if one of our partners terminates its agreement with us, we may find it more difficult to attract new partners and our perception in the business and financial communities could be adversely affected.

We may not be able to negotiate partnerships on a timely basis, on acceptable terms, or at all. Our ability to reach a definitive agreement for a partnership will depend, among other things, upon an assessment of the partner's resources and expertise, the terms and conditions of the proposed partnership and the proposed partner's evaluation of a number of factors. These factors may include the design or results of preclinical studies or clinical trials, the likelihood of regulatory approval, the potential market for the subject drug candidate, the costs and complexities of manufacturing and delivering such drug candidate to patients, the potential of competing products, the existence of any uncertainty with respect to our ownership of technology (which can exist if there is a challenge to such ownership regardless of the merits of the challenge) and industry and market conditions generally. The partner may also consider alternative drug candidates or technologies for similar indications that may be available to collaborate on and whether such a partnership could be more attractive than the one with us.

Risks Related to Commercialization of Our Drug Candidates

Even if any of our current or drug candidates receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If ACR-368, ACR-2316, or our future drug candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, current cancer treatments, such as existing targeted therapies, chemotherapy, and radiation therapy, are well established in the medical community, and doctors may continue to rely on these treatments. If our drug candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of our drug candidates, if approved for commercial sale, will depend on a number of factors, including but not limited to:

- the efficacy, safety and potential advantages compared to alternative treatments;
- the acceptance of our drug candidates as front-line treatments for various indications;
- the prevalence and severity of any side effects, in particular compared to alternative treatments;
- limitations or warnings contained in the labeling approved by the FDA or other regulatory authorities;
- the size of the target patient population;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- our ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the strength of marketing and distribution support;
- publicity for our drug candidates and competing products and treatments;
- the existence of distribution and/or use restrictions, such as through a REMS;
- the availability of third-party payor coverage and adequate reimbursement;
- the timing of any marketing approval in relation to other product approvals;
- support from patient advocacy groups; and
- any restrictions on the use of our products together with other medications.

If the market opportunities for our drug candidates are smaller than we estimate or if any approval that we obtain is based on a narrower definition of the patient population, then our revenue potential and ability to achieve profitability will be adversely affected.

The total addressable market opportunity for ACR-368, ACR-2316, and any other future drug candidates we may develop will ultimately depend upon, among other things, the proportion of patients identified as sensitive to our treatments based on our OncoSignature tests in our target indications, acceptance by the medical community, patient access, drug and any related companion diagnostic pricing and their reimbursement.

We may initially seek regulatory approval of ACR-368, ACR-2316, or our future drug candidates as therapies for patients with platinum-resistant ovarian, bladder, endometrial cancer, and other types of cancer that are found, or predicted using AP3 to be, sensitive

to our current and future drug candidates. The number of patients in our targeted commercial markets and elsewhere may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our drugs or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business.

We currently have no marketing and sales organization and may have to invest significant resources to develop these capabilities. If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our products, we may not be able to generate revenue.

We currently have no sales or marketing infrastructure or experience in the sale, marketing or distribution of drug products. Our operations to date have been focused on developing and extensively evaluating in preclinical studies our AP3 platform and our proprietary predictive OncoSignature tests, acquiring the rights to ACR-368, advancing our preclinical drug candidate programs, including ACR-2316, organizing and staffing our company, business planning and raising capital. To achieve commercial success for any product for which we obtain marketing approval, we will need to establish sales, marketing and distribution capabilities, either ourselves or through collaboration or other arrangements with third parties.

There are risks involved with establishing our own sales and marketing capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a drug candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. These efforts are expected to be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- our inability to raise financing necessary to build our commercialization infrastructure;
- the inability of sales personnel to obtain access to physicians or educate an adequate number of physicians as to the benefits of our products;
- unfavorable third-party payor coverage and reimbursement in any geography;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

Furthermore, developing a sales and marketing organization requires significant investment, is time-consuming and could delay the launch of our drug candidate. We may not be able to build an effective sales and marketing organization in the United States, the European Union or other key global markets. If we are unable to build our own distribution and marketing capabilities or to find suitable partners for the commercialization of our drug candidate, we may have difficulties generating revenue from them.

If we enter into arrangements with third parties to perform sales and marketing services, our product revenues and our profitability, if any, are likely to be lower than if we were to market and sell any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to market and sell our drug candidates or may be unable to do so on terms that are acceptable to us. We will also have less oversight and control of a third party sales force than we would with an employed sales force. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing any drug candidate for which we receive marketing approval.

The precision oncology space is competitive, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of drug products is highly competitive. We face competition with respect to our current drug candidates and will face competition with respect to any drug candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and existing or emerging biotechnology companies, academic research institutions and governmental agencies and public and private research institutions worldwide.

We anticipate several biopharmaceutical companies will aim to develop precision oncology approaches for the larger subsets of cancers where genetics has proven insufficient for patient responder identification over the next decade. We expect that the broader biopharmaceutical field will eventually recognize proteomics as the next era of precision medicine. We are aware of several competitors with CHK1/2 inhibitors and WEE1 inhibitors, including Sierra Oncology (SRA737), Zentalis (azenosertib), Debiopharm (Debio0123),

Impact Therapeutics (IMP7068) and Shouya Holdings (SY-4835), one company with a PKMYT1 inhibitor, Repare Therapeutics (lunresertib), and one company with a dual WEE1/PKMYT1 inhibitor, Schrödinger (SGR-3515).

Many of the companies against which we are competing or against which we may compete in the future, either alone or through collaborations, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific, management and sales and marketing personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Furthermore, we also face competition more broadly across the oncology market for cost-effective and reimbursable cancer treatments. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. While ACR-368 or our future drug candidates, if approved, may compete with these existing drugs and other therapies, to the extent they are ultimately used in combination with or as an adjunct to these therapies, our drug candidates may not be competitive with them. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis. Insurers and other third-party payors may also encourage the use of generic products or specific branded products. As a result, obtaining market acceptance of, and gaining significant share of the market for, our drug candidates may pose challenges. In addition, many companies are developing new oncology therapeutics, and we cannot predict what the standard of care will be as drug candidates progress through clinical development.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient to administer, are less expensive or with a more favorable labeling than ACR-368 or our future drug candidates. Our competitors also may obtain FDA, foreign regulatory authority, or other marketing or regulatory approval for their products more rapidly than any approval we may obtain for ours, which could result in our competitors establishing a strong market position before we are able to enter the market, thereby limiting our potential for commercial success.

Even if we are able to commercialize any drug candidates, the products may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our drug candidate to other available therapies. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a drug candidate in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues, if any, we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more drug candidates, even if such drug candidates obtain marketing approval.

Our ability to commercialize any drug candidates successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third-party payors, including government healthcare programs, private health insurers and other organizations. Third-party payors decide which medications they will pay for and establish reimbursement levels. In the United States, the principal decisions about reimbursement for new medicines are typically made by the CMS, which decides whether and to what extent a new medicine will be covered and reimbursed under Medicare. Private payors often, but not always, follow CMS's decisions regarding coverage and reimbursement.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, government authorities and third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Coverage and reimbursement may not be available for any product that we commercialize and, even if these are available, the level of reimbursement may not be sufficient to cover our costs. Reimbursement may affect the demand for, or the price of, any drug candidate for which we obtain marketing approval or licensure. Obtaining and maintaining coverage and adequate reimbursement for our products may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies.

If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any drug candidate for which we obtain marketing approval or licensure.

Additionally, companion diagnostic tests will be required to obtain coverage and reimbursement separate and apart from the coverage and reimbursement we seek for our drug candidates, if approved.

There may also be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside of the United States. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, intellectual property, manufacture, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies, but also have their own methods and approval process apart from Medicare determinations. Our inability to promptly obtain coverage and adequate reimbursement rates from third-party payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, our drug candidates may lose any marketing approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business.

The market opportunities for any current or future drug candidate we develop, if and when approved, may be limited to those patients who are ineligible for established therapies or for whom prior therapies have failed, and may be small.

Cancer therapies are sometimes characterized as first-line, second-line, or third-line, and the FDA often approves new therapies initially only for third-line use. When cancer is detected early enough, first-line therapy, usually chemotherapy, hormone therapy, surgery, radiation therapy or a combination of these, is sometimes adequate to cure the cancer or prolong life without a cure. Second- and third-line therapies are administered to patients when prior therapy is not effective. We expect to initially seek approval of our drug candidates we develop as a therapy for patients who have received one or more prior treatments. Subsequently, for those products that prove to be sufficiently beneficial, if any, we would expect to seek approval potentially as a first-line therapy, but there is no guarantee that drug candidates we develop, even if approved, would be approved for first-line therapy, and, prior to any such approvals, we may have to conduct additional clinical trials.

The number of patients who have the cancers we are targeting may turn out to be lower than expected. Additionally, the potentially addressable patient population for our current programs or future drug candidates in both oncology and non-oncology indications may be limited, if and when approved. Even if we obtain significant market share for any drug candidate, if and when approved, if the potential target populations are small, we may never achieve profitability without obtaining marketing approval for additional indications, including to be used as first- or second-line therapy.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our drug candidates in human clinical trials and will face an even greater risk if we commercialize any products that we may develop. If we cannot successfully defend ourselves against any claims that our drug candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in, but are not limited to:

- decreased demand for any drug candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- initiation of investigations by regulators;
- withdrawal of clinical trial participants;
- significant time and costs to defend the related litigation;
- diversion of management and scientific resources from our business operations;

- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

Our current product liability insurance coverage for the United States and certain other jurisdictions may not be adequate to cover all liabilities that we may incur. We likely will need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of ACR-368 or our future drug candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. A successful product liability claim or series of claims brought against us could decrease our cash and adversely affect our business and financial condition.

Risks Related to Employee Matters and Our Operations

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the management, development, clinical, financial and business development expertise of our executive officers, particularly Peter Blume-Jensen, M.D., Ph.D., our co-founder, President and CEO, the inventor of our AP3 platform and OncoSignature patient selection method and a member of our board of directors and Kristina Masson, Ph.D., M.B.A., our co-founder, EVP of Business Operations, a member of our board of directors, and President and CEO of our phosphoproteomics subsidiary in Lund, Sweden. Each of our executive officers may currently terminate their employment with us at any time. We do not currently maintain "key person" insurance for any of our executives or employees.

Recruiting and retaining qualified scientific and clinical personnel and, if we progress the development of our product pipeline toward scaling up for commercialization, manufacturing and sales and marketing personnel, will also be critical to our success. The loss of the services of our executive officers or other key personnel, including any of our scientific founders, could impede the achievement of our development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We expect to expand our clinical development, manufacturing and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As of December 31, 2023, we had 58 full-time employees and three part-time employees. As our development progresses, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of clinical product development, regulatory affairs and, if any of our drug candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. Our choice to focus on multiple therapeutic areas may negatively affect our ability to develop adequately the specialized capability and expertise necessary for operations. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Our employees, independent contractors, consultants, collaborators, principal investigators, CROs, suppliers and vendors may be improperly classified and may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements.

We endeavor to properly classify our employees as exempt or non-exempt with respect to wage and hour laws, including, but not limited to, for purposes of minimum wage, overtime and applicable meal and rest periods, and we monitor and evaluate such classifications. Although there are no current, pending, or threatened claims or investigations against us asserting that any employees have been incorrectly classified as exempt, the possibility nevertheless exists that certain job roles could be deemed to have been incorrectly classified as exempt. In addition, we endeavor to classify independent contractors properly, and we monitor and evaluate such classifications. Although there are no current, pending, or threatened claims or investigations against us asserting that any independent contractors have been incorrectly classified, the possibility nevertheless exists that certain contractors could be deemed to be employees.

We are exposed to the risk that our employees, independent contractors, consultants, collaborators, principal investigators, CROs, suppliers and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include:

- intentional, reckless and/or negligent conduct or disclosure to us of unauthorized activities that violate the requirements of the FDCA, regulations of the FDA or similar foreign regulatory authorities;
- healthcare fraud and abuse in violation of U.S. and foreign laws and regulations;
- violations of U.S. federal securities laws relating to trading in our common stock; and
- failures to report financial information or data accurately.

In particular, sales, marketing, and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing, and other abusive practices. These laws and regulations regulate a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Misconduct by these parties could also involve the improper use of individually identifiable information, including, without limitation, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. While we have adopted a code of business conduct and ethics, it is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, including, without limitation, damages, fines, disgorgement, imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations.

Our business and operations would suffer in the event of system failures, cyberattacks or a deficiency in our or our CROs', manufacturers', contractors', consultants' or collaborators' cybersecurity.

Despite the implementation of security measures, our internal computer systems, as well as those of third parties on which we rely, are vulnerable to damage from, among other things, computer viruses, malware, unauthorized access, natural disasters, terrorism, war, global conflicts, telecommunication and electrical failures, system malfunctions, cyberattacks or cyber-intrusions over the Internet, attachments to emails, phishing attacks, persons inside our organization, or persons with access to systems inside our organization. The risk of a security breach or disruption, particularly through cyberattacks or cyber intrusion, including by computer hackers, foreign governments and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. We and our third party vendors frequently detect, contain and respond to data security incidents. If such an event were to occur and cause interruptions in our operations, it could lead to the loss, destruction, alteration, prevention of access to, disclosure, dissemination of, or damage or unauthorized access to, our data (including trade secrets or other confidential information, intellectual property, proprietary business information and personal data) or data that is processed or maintained on our behalf, and cause interruptions in our operations, which could result in a material disruption of our drug candidate development programs. For example, the loss of preclinical study or clinical trial data from completed, ongoing or planned trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of personal, confidential or proprietary information, we could incur liability and the further development of our drug candidates could be delayed.

In the ordinary course of our business, we collect or may unintentionally receive and store sensitive data, including intellectual property, clinical trial data, proprietary business information, personal data and personally identifiable information of our clinical trial

subjects and employees, in our data centers and on our networks. The secure processing, maintenance and transmission of this information is critical to our operations. Despite our security measures, we cannot ensure that our information technology and infrastructure will prevent breakdowns or breaches in our or their systems or other cybersecurity incidents that cause loss, destruction, unavailability, alteration, dissemination of, or damage or unauthorized access to, our data, including personal data, assets and other data processed or maintained on our behalf, that could have a material adverse effect upon our reputation, business, operations or financial condition. Although, to our knowledge, we have not experienced any such material security breach to date, any such breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, significant regulatory penalties, and such an event could disrupt our operations, damage our reputation, and cause a loss of confidence in us and our ability to conduct clinical trials, which could adversely affect our reputation and delay clinical development of our drug candidates.

To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information or personal data, we could incur material legal claims and liability and damage to our reputation, and the further development of our drug candidates could be delayed. Any such event could also compel us to comply with federal and state breach notification laws, and foreign law equivalents, subject us to mandatory corrective action and otherwise subject us to substantial liability under laws, rules, regulations and standards that protect the privacy and security of personal data, which could result in significant legal and financial exposure and reputational damages that could potentially have an adverse effect on our business.

Notifications and follow-up actions related to a data breach or other security incident could impact our reputation and cause us to incur significant costs, including significant legal expenses and remediation costs. We expect to incur significant costs in an effort to detect and prevent security incidents, and we may face increased costs and requirements to expend substantial resources in the event of an actual or perceived security incident. However, we cannot guarantee that we will be able to detect or prevent any such incidents, or that we can remediate any such incidents in an effective or timely manner. Our efforts to improve security and protect data from compromise may also identify previously undiscovered instances of data breaches or other cybersecurity incidents. To the extent that any data breach, disruption or security incident were to result in any loss, destruction, or alteration of, damage, unauthorized access to or inappropriate or unauthorized disclosure or dissemination of, our data, including personal data, or other information that is processed or maintained on our behalf, we could be exposed to litigation and governmental investigations and inquiries, the further development and commercialization of our drug candidates could be delayed and we could be subject to significant fines or penalties for any noncompliance with applicable state, federal and foreign privacy and security laws, rules, regulations and standards.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations, and those of our CROs, CMOs and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or man-made disasters or business interruptions, for which we are predominantly self-insured. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce our drug candidates. Our ability to obtain clinical supplies of our drug candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption.

We are subject to a variety of privacy and data security laws, rules, regulations, policies, industry standards and contractual obligations, and our failure to comply with them could harm our business.

We maintain a large quantity of sensitive information, including confidential business and personal information in connection with the conduct of our clinical trials and related to our employees, and we are subject to laws and regulations governing the privacy and security of such information. In the United States, there are numerous federal and state privacy and data security laws and regulations governing the collection, use, disclosure and protection of personal information, including federal and state health information privacy laws, federal and state security breach notification laws and federal and state consumer protection laws. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues, which may affect our business and is expected to increase our compliance costs and exposure to liability. In the United States, numerous federal and state laws and regulations could apply to our operations or the operations of our partners, including state data breach notification laws, state health information privacy laws and federal and state consumer protection laws and regulations, including Section 5 of the Federal Trade Commission Act, that govern the collection, use, disclosure and protection of health-related and other personal information. State privacy laws in particular are evolving, with more than a dozen new state privacy laws passed in recent years, along with additional health privacy specific laws. These laws may further increase our compliance obligations, and potential legal privacy risks. For example, Washington recently passed the My Health My Data Act, which has a broader scope than HIPAA and includes a private right of action. In addition, we may obtain health information from third parties, including research institutions from

which we obtain clinical trial data, that are subject to privacy and security requirements under HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and the regulations promulgated thereunder. Depending on the facts and circumstances, we could be subject to significant penalties if we obtain, use or disclose individually identifiable health information in a manner that is not authorized or permitted by HIPAA.

We may encounter vendors that engage in information blocking practices that may inhibit our ability to access the relevant data on behalf of patients or researchers or impose new or additional costs. In 2020, the U.S. Department of Health and Human Services' Office of the National Coordinator for Health Information Technology (ONC) and the Centers for Medicare and Medicaid Services promulgated final rules to support access, exchange, and use of electronic health information (EHI). Specifically, the information blocking rules were implemented as part of the 21st Century Cures Act, and are primarily designed to facilitate technology interoperability and enable the free flow of healthcare information for healthcare treatment, payment or operation purposes. On June 27, 2023, the Department of Health and Human Services Office of the Inspector General ("HHS-OIG") published its final rule implementing information blocking penalties for "actors," which is supplemented by ONC's January 9, 2024 final rule enhancing certain information blocking requirements. HHS-OIG may impose penalties for information blocking that has occurred after September 1, 2023, and ONC and HHS proposed a rule on November 1, 2023 listing certain disincentives for actors that conduct information blocking. The impact on the information blocking rules to our business is currently unclear.

In the EU, the EU General Data Protection Regulation, or EU GDPR, took effect in all EU Member States on and from May 25, 2018. The UK has implemented the EU GDPR as the "UK GDPR," which sits alongside the UK Data Protection Act 2018, (the UK GDPR, together with the EU GDPR, the "GDPR"). The GDPR governs the collection, use, disclosure, transfer, and other processing of personal data, which may include clinical trial data. The GDPR has direct effect where an entity is established in the EEA or the UK (as applicable) and has extraterritorial effect, including where an entity established outside of the EEA or the UK processes personal data in relation to offering goods or services to individuals in the EEA and/or the UK or monitoring their behavior.

The GDPR imposes obligations on controllers, including, among others accountability and transparency requirements, requiring controllers to demonstrate and record compliance with the GDPR and to provide more detailed information to data subjects regarding processing of their personal data; requirements to process personal data lawfully including specific requirements for obtaining valid consent where consent is the lawful basis for processing; obligations to consider data protection when any new products or services are developed and designed (including e.g., to limit the amount of personal data processed); obligations to comply with data protection rights of data subjects including a right: (i) of access to, erasure of, or rectification of personal data, (ii) to restriction of processing or to withdraw consent to processing, and (iii) to object to processing or to ask for a copy of personal data to be provided to a third party; and an obligation to report personal data breaches to: (i) the data supervisory authority without undue delay (and no later than 72 hours after discovering the personal data breach, where feasible), unless the personal data breach is unlikely to result in a risk to the data subjects' rights and freedoms; and (ii) to affected data subjects, where the personal data breach is likely to result in a high risk to their rights and freedoms.

In addition, the EU GDPR prohibits the international transfer of personal data from the EEA to jurisdictions that the European Commission does not recognize as having 'adequate' data protection laws unless a data transfer mechanism has been put in place or a derogation under the EU GDPR can be relied on. In July 2020, the Court of Justice of the EU ("CJEU") in its Schrems II judgement limited how organizations could lawfully transfer personal data from the EEA to the US by invalidating the EU-US Privacy Shield for purposes of international transfers and imposing further restrictions on the use of standard contractual clauses ("EU SCCs"), including a requirement for companies to carry out a transfer privacy impact assessment ("TIAs"). A TIA, among other things, assesses laws governing access to personal data in the recipient country and considers whether supplementary measures that provide privacy protections additional to those provided under EU SCCs will need to be implemented to ensure an 'essentially equivalent' level of data protection to that afforded in the EEA.

On October 7, 2022, US President Biden introduced an Executive Order to facilitate a new Trans-Atlantic Data Privacy Framework ("DPF") and on 10 July 2023, the European Commission adopted its Final Implementing Decision granting the U.S. adequacy ("Adequacy Decision") for EU-US transfers of personal data for entities self-certified to the DPF. Entities relying on EU SCCs for transfers to the U.S. are also able to rely on the analysis in the Adequacy Decision as support for their TIA regarding the equivalence of U.S. national security safeguards and redress. This may have implications for our cross-border data flows and has and may in the future result in increased compliance costs.

The UK GDPR also imposes similar restrictions on transfers of personal data from the UK to jurisdictions that the UK Government does not consider adequate, including the United States. The UK Government has published its own form of the EU SCCs, known as the International Data Transfer Agreement and an International Data Transfer Addendum to the new EU SCCs. The UK Information Commissioner's Office has also published its version of the TIA and guidance on international transfers, although entities may choose to adopt either the EU or UK style TIA. Further, on September 21, 2023, the UK Secretary of State for Science, Innovation and Technology established a UK-U.S. data bridge (i.e., a UK adequacy decision) and adopted UK regulations to implement the UK-U.S.

data bridge ("UK Adequacy Regulations"). The UK Adequacy Regulations have now been passed in the UK Parliament, and personal data may be transferred from the UK under the UK-U.S. data bridge through the UK extension to the DPF, from October 12, 2023 to organizations self-certified under the DPF.

The GDPR imposes fines for serious breaches of up to the higher of 4% of the organization's annual worldwide turnover or €20m (under the EU GDPR) or £17.5m (under the UK GDPR). The GDPR identifies a list of points to consider when determining the level of fines for data supervisory authorities to impose (including the nature, gravity and duration of the infringement). Data subjects also have a right to compensation, as a result of an organization's breach of the GDPR which has affected them, for financial or non-financial losses (e.g., distress).

Compliance with these and any other applicable privacy and data security laws and regulations is a rigorous and time-intensive process, and we may be required to substantially amend existing procedures and policies or put in place additional procedures and policies to ensure compliance with privacy and data protection rules and requirements. These changes could adversely impact our business by increasing operational and compliance costs or impact business practices. Further, there is a risk that the amended policies and procedures will not be implemented correctly or that individuals within the business will not be fully compliant with the new procedures. If we fail to comply with any such laws or regulations, we may face significant litigation, government investigations, fines and penalties as well as reputational damage which could adversely affect our business, operations, financial condition and prospects. Furthermore, the laws are not consistent, and compliance in the event of a widespread data breach is costly. In addition, states are constantly adopting new laws or amending existing laws, requiring attention to frequently changing regulatory requirements. For example, the CCPA took effect on January 1, 2020, and the amendments thereto under the CPRA took effect on January 1, 2023. The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing and receive detailed information about how their personal information is used by requiring covered companies to provide new disclosures to California consumers (as that term is broadly defined) and provide such consumers new ways to opt out of certain sales and sharing of personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Further, the CPRA imposed additional data protection obligations on companies doing business in California, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data and opt outs for certain uses of sensitive data. It also created the California Privacy Protection Agency to implement and enforce the law, which could result in increased privacy and information security enforcement. As a result of the CPRA going into effect earlier this year, additional compliance investment and potential business process changes may be required. Although the CCPA currently exempts certain health-related information, including clinical trial data, the CCPA and the amendments under the CPRA may increase our compliance costs and potential liability.

Multiple states have followed California to legislate comprehensive privacy laws with data privacy rights. For example, Virginia passed the Virginia Consumer Data Protection Act ("VCDPA"), which went into effect on January 1, 2023 and affords consumers similar rights to the CCPA, along with additional rights, such as the right to opt-out of processing for profiling and targeted advertising purposes. Additionally, the Colorado Privacy Act ("CPA") and Connecticut Personal Data Privacy and Online Monitoring Act ("CTDPA") went into effect on July 1, 2023 and the Utah Privacy Rights Act will go into effect later this year, and each impose similar obligations to those in the CCPA and VCDPA. While these new laws generally include exemptions for HIPAA-covered and clinical trial data, they impact the overall privacy landscape. Several other states have followed suit and passed similar legislation which will go into effect in the coming years. Further, additional privacy laws that are similar in nature have been proposed in other states and at the federal level and, if passed, such laws may have potentially conflicting requirements that would make compliance challenging.

With the GDPR, CCPA, and other US state privacy laws, as well as other laws, regulations and other obligations relating to privacy and data protection imposing new and relatively burdensome obligations, and with the substantial uncertainty over the interpretation and application of these and other obligations, we may face challenges in addressing their requirements and making necessary changes to our policies and practices and may incur significant costs and expenses in an effort to do so. We are currently in the process of developing and updating our policies and procedures in accordance with requirements under applicable data privacy and protection laws and regulations. We do not currently have any formal data privacy policies and procedures in place and have not completed formal assessments of whether we are in compliance with all applicable data privacy laws and regulations. Additionally, if third parties with which we work, such as vendors or service providers, violate applicable laws, rules or regulations or our policies, such violations may also put our or our clinical trial and employee data, including personal data, at risk, which could in turn have an adverse effect on our business.

Risks Related to Intellectual Property

Our success depends in part on our ability to obtain intellectual property rights for our proprietary technologies and drug candidates, as well as our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.

Our commercial success will depend in large part on obtaining and maintaining patent, trademark and trade secret protection of our proprietary technologies and our drug candidates, their respective components, formulations, combination therapies, methods used to manufacture them and methods of treatment, as well as successfully defending these patents, trademarks and trade secrets against third-party challenges or violations. Our ability to stop unauthorized third parties from making, using, selling, offering to sell or importing our technologies and drug candidates is dependent upon the extent to which we have rights under valid and enforceable patents that cover these activities. If we are unable to secure and maintain patent protection for any product or technology we develop, or if the scope of the patent protection secured is not sufficiently broad, our competitors could develop and commercialize products and technologies similar or identical to ours, and our ability to commercialize any drug candidates and technologies we may develop may be adversely affected.

The patenting process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, we may not pursue or obtain patent protection in all relevant markets. It is also possible that we will fail to identify, or to file on, patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering drug candidates and technologies that we license from or license to third parties and are reliant on our licensors or licensees.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our drug candidates, technologies or uses thereof in the United States or in other countries. Some of our technologies relate to identifying and treating subjects, which have been deemed to be patentable and outside the bar on patenting laws of nature affirmed in the *Athena Diagnostics v. Mayo Collaborative Services,* 915 F.3d 743 (Fed. Cir. 2019), *cert. denied,* 140 S. Ct. 855 (2020) case.

Even if we do successfully issue patents that cover our products or technologies, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around or otherwise avoiding our claims. If the breadth or strength of protection provided by the patent applications we hold with respect to our drug candidates is insufficient or is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our drug candidates and our technologies.

Further, patents have limited terms. We may not be able to issue patents whose terms provide sufficient protection during the commercial lifetime of our drug candidates or of our technologies. For example, if we encounter delays in our clinical trials, the period of time during which we could market our drug candidates under patent protection could be reduced.

Some or all of our patents may have claims whose infringement is difficult to detect or prove. Courts place the legal burden of proving infringement on patent holders. If we cannot convince a court that we have met this burden of proof, then our patent may not provide useful protection even if valid and enforceable against infringers.

Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to our drug candidates or technologies. Furthermore, for United States applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third-party or instituted by the United States Patent and Trademark Office, or USPTO, to determine who was the first to invent any of the subject matter covered by the patent claims of our applications.

We cannot be certain that we are the first to invent the inventions covered by pending patent applications or issued patents (collectively, our "patent filings") and, if we are not, we may be subject to priority disputes or derivation challenges. We may be required to disclaim part or all of the term of certain patent filings. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. No assurance can be given that if challenged, our patents would be declared by a court or patent office to be valid or enforceable or that even if found valid and enforceable, a competitor's technology or product would be found by a court to infringe our patents. We may analyze patents or patent applications of our competitors that we believe are relevant to our activities, and consider that we are free to operate in relation to our drug candidates and technologies, but our competitors may achieve issued claims, including in patents we consider to be unrelated, which block our efforts or may potentially result in our drug candidates, our technologies or our activities infringing such claims. The possibility exists that others will develop products which have the same effect as our products on an independent basis which do not infringe our patents or other intellectual property rights, or will design around or otherwise avoid the claims of patents that we have had issued that cover our products and technologies.

It is possible that we may not perfect ownership of all of the patents, patent applications or other intellectual property upon which we rely. This possibility includes the risk that we do not identify all inventors, or identify incorrect inventors, which may lead to claims disputing inventorship or ownership of our patents, patent applications or other intellectual property by former employees or other third parties. There is also a risk that we do not establish an unbroken chain of title from inventors to us. Errors in inventorship or ownership can sometimes also impact priority claims. If we were to lose ability to claim priority for certain patent filings, intervening art or other events may preclude us from issuing patents.

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. Under the enacted Leahy-Smith America Invents Act, or America Invents Act, enacted in 2013, the United States moved from a "first to invent" to a "first-to-file" system. Under a "first-to-file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. The America Invents Act includes a number of other significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted, redefine prior art and establish a set of new patent office procedures for reviewing patents after issuance.

The degree of future protection for our intellectual property rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to make or use compounds or formulations similar or equivalent to our drug candidates, or to develop technologies similar or comparable to ours, but that are not covered by the claims of any patents, should they issue, that we own or control;
- the active ingredients in our current drug candidates will eventually become commercially available in generic drug products, and is it possible that patent protection may not be available with regard to formulation or method of use;
- we or our licensors or collaborators, as the case may be, may fail to meet our obligations to the U.S. government in regards to any patents and patent applications funded by U.S. government grants, leading to the loss of patent rights;
- we or our licensors or collaborators, as the case may be, might not have been the first to invent, or the first to file patent applications for our inventions, or may be found to have derived these inventions from others;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights in a way that we can detect and prove;
- it is possible that our pending patent applications will not result in issued patents in jurisdictions where we or our competitors operate commercially, in time to provide useful commercial protection, or at all;
- our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights, and then use the information learned from such activities to develop competitive products or technologies for sale in our major commercial markets;
- it is possible that there are prior public disclosures that could invalidate our patents or our licensors' patents, as the case may be, or parts of our or their patents;
- it is possible that others may circumvent our owned or in-licensed patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our products or technologies;
- the laws of foreign countries may not protect our or our licensors', as the case may be, proprietary rights to the extent required for us to benefit commercially, or at all;
- the claims of our owned or in-licensed issued patents or patent applications, if and when issued, may not cover our drug candidates or technologies;
- our owned or in-licensed issued patents may not provide us with any competitive advantages, may be narrowed in scope, or be held invalid or unenforceable as a result of legal challenges;
- we may not be able to detect or to prove infringement of our owned or in-licensed patents;
- the inventors of our owned or in-licensed patents or patent applications may become involved with competitors, develop products or processes which design around our patents, or become hostile to us or the patents or patent applications on which they are named as inventors;

- it is possible that our owned or in-licensed patents or patent applications omit individual(s) that should be listed as inventor(s) or include individual(s) that should not be listed as inventor(s), which may cause these patents or patents issuing from these patent applications to be held invalid or unenforceable;
- we have engaged in scientific collaborations in the past, and will continue to do so in the future. Such collaborators may develop adjacent or competing products or technologies to ours that are outside the scope of our patents;
- we may not develop additional proprietary technologies for which we can obtain patent protection;
- we may choose not to file for patent protection in order to maintain certain trade secrets, and a third party may subsequently obtain a patent covering such intellectual property;
- it is possible that drug candidates or technologies we develop may be covered by third parties' patents or other exclusive rights;
- the patents of others may have an adverse effect on our business;
- we may be unable to protect the confidentiality of key information, including trade secrets, that are required for us to achieve or maintain our business goals;
- we may not be able to detect breaches of confidentiality obligations to us before significant damage is done to our business; or
- we may not be able to build brand identity in the marks we use to label our products or technologies, or third parties may misuse them or create brand confusion, and our business may be negatively impacted.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects.

We rely in part on trade secrets to protect our technology, and our failure to obtain or maintain trade secret protection could harm our business.

We rely on trade secrets to protect some of our technology and proprietary information, especially where we believe patent protection is not appropriate or obtainable, or may not provide effective protection. However, trade secrets are difficult to protect. It can be difficult or impossible to detect trade secret breaches. Furthermore, litigating a claim that a third party had illegally obtained and was using our trade secrets would be expensive and time consuming, and the outcome would be unpredictable. Moreover, if our competitors independently develop similar knowledge, methods and know-how, our business could be harmed.

Patent terms may be inadequate to protect our competitive position on our drug candidates for an adequate amount of time.

We have issued patents covering the composition-of-matter and the salt form of ACR-368 through 2030 and 2037, respectively, without extension, and also seek protection through our OncoSignature patent filings. We expect to seek extensions of patent terms in the United States and, if available, in other countries where we are prosecuting patents. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years beyond the normal expiration of the patent, which is limited to the approved indication (or any additional indications approved during the period of extension). However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their drug earlier than might otherwise be the case.

Patent term extensions in other countries may also be subject to certain procedural or administrative requirements including adherence to certain strict timelines. A failure to meet such requirements may result in a loss of the extension in those countries.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by government patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In addition, periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and/or applications will have to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our owned patents and/or applications and any patent rights we may

own or license in the future. We employ reputable law firms and other professionals to help us comply with such requirements and fee payments. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our products or technologies, we may not be able to stop a competitor from marketing products or technologies that are the same as or similar to our drug candidates or technologies, which would have a material adverse effect on our business. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market and this circumstance could harm our business.

We may be subject to claims challenging the inventorship or ownership of our future patents and other intellectual property.

We may also be subject to claims that former employees, collaborators, or other third parties have an ownership interest in our patent applications, our future patents, or other intellectual property. We may be subject to ownership disputes in the future arising, for example, from conflicting obligations of consultants or others who are involved in developing our drug candidates and platform discovery. Although it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own, and we cannot be certain that our agreements with such parties will be upheld in the face of a potential challenge, or that they will not be breached, for which we may not have an adequate remedy. The assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property rights, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our present or future issued patents, trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us, including claims alleging that we infringe their patents, trademarks, copyrights or other intellectual property. In addition, in a patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, or that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from making, using, selling, offering to sell or importing the invention at issue on the grounds that our patents do not cover the invention. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making, using, selling, offering to sell or importing similar or competitive products. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that another party has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

In any infringement litigation, any award of monetary damages we receive may not be commercially valuable. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing, misappropriating or successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a negative impact on our ability to compete in the marketplace.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a negative impact on the success of our business.

Our commercial success depends, in part, upon our ability and the ability of future collaborators, if any, to develop, use, manufacture, market and sell our drug candidates and our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights. We may in the future become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our drug candidates and technology, including interference proceedings, derivation proceedings, ex parte reexamination, post grant review and inter partes review before the USPTO or equivalent foreign regulatory authority. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could have a negative impact on our ability to commercialize our current and any future drug candidates. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. Foreign courts will have similar burdens to overcome in order to successfully challenge a third party claim of patent infringement. If we are found to infringe a third party's valid and enforceable intellectual property rights, we could be required to obtain a license from such third party to continue developing, manufacturing and marketing our drug candidate(s) and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or drug candidate. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us from manufacturing and commercializing our drug candidates or force us to cease some or all of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects.

We may need to license intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property rights, including patent rights, that are important or necessary to the development of our drug candidates and technologies. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our drug candidates or our technologies, in which case we would be required to obtain a license from these third parties. Such a license may not be available on commercially reasonable terms, or at all, and we could be forced to accept unfavorable contractual terms. If we are unable to obtain such licenses on commercially reasonable terms, our business could be harmed.

We depend on intellectual property licensed from a third party and termination of this license could result in the loss of significant rights, which would harm our business.

We are dependent on patents, know-how and proprietary technology, both our own and licensed from others. In particular, we are dependent on our license agreement with Lilly. Any termination of this license could result in the loss of significant rights and could harm our ability to commercialize our drug candidates. For a more detailed description of this agreement, see Note 12 to our consolidated financial statements included elsewhere in this Annual Report.

Disputes may also arise between us and our current licensor or future licensors regarding intellectual property subject to a license agreement, including but not limited to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our drug candidates and technologies infringe intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our drug candidates, and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and

- our payment obligations with respect to licensed technology.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current or future licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected drug candidates and technologies.

We are generally also subject to all of the same risks with respect to protection of intellectual property that we license, as we are for intellectual property that we own, which are described below. If we, Lilly, or any future licensors fail to adequately protect any licensed intellectual property, our ability to commercialize products could suffer.

We may be subject to claims asserting that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Many of our employees, consultants or advisors are currently, or were previously, employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, we may in the future be subject to claims by our former employees or consultants asserting an ownership right in our patents or patent applications, as a result of the work they performed on our behalf. Although it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own, and we cannot be certain that our agreements with such parties will be upheld in the face of a potential challenge or that they will not be breached, for which we may not have an adequate remedy. The assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property.

Changes in U.S. patent law or the patent law of other countries or jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our future drug candidates.

The United States Congress periodically enacts legislation that significantly impacts the patent system. The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. Various decisions by the U.S. Supreme Court and other U.S. federal courts are widely considered to have reduced patent protections available to developers of diagnostic technologies. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce patents that we own or have licensed, or that we might obtain in the future. Similarly, changes in patent law and regulations in other countries or jurisdictions, changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we own or have licensed or that we may obtain in the future.

We may not be able to protect our intellectual property rights throughout the world, which could negatively impact our business.

Filing, prosecuting and defending patents on drug candidates and technologies in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. In some cases, we may not be able to obtain patent protection for certain technologies outside the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States, even in jurisdictions where we do pursue patent protection. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, even in jurisdictions where we do pursue patent protection or from selling or importing products made using our inventions in and into the United States or other jurisdictions.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents, if pursued and obtained, or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights

in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Reliance on third parties requires us to share our proprietary information, which increases the possibility that such information will be misappropriated or disclosed.

Because we rely on third parties for aspects of development, manufacture, or commercialization of our drug candidates and technologies, or if we collaborate with third parties for the development or commercialization of our future drug candidates and technologies, we must, at times, share proprietary information with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information. Despite the contractual provisions employed when working with third parties, the need to share confidential information increases the risk that such information become known by our competitors, is inadvertently incorporated into the technology of others, or is disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how, a competitor's discovery of our know-how or other unauthorized use or disclosure could have an adverse effect on our business and results of operations.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our know-how. Despite our efforts to protect our know-how, we may not be able to prevent the unauthorized disclosure or use of our technical know-how by the parties to these agreements. Moreover, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our confidential information or proprietary technology and processes. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the collaborators, scientific advisors, employees, contractors and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation. Moreover, if confidential information that is licensed or disclosed to us by our partners, collaborators, or others is inadvertently disclosed or subject to a breach or violation, we may be exposed to liability to the owner of that confidential information. Enforcing a claim that a third-party illegally obtained and is using our proprietary information, like patent litigation, is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect proprietary information.

Trademarks we own, license or may obtain may be infringed or successfully challenged, resulting in harm to our business.

We rely on trademarks and expect to rely on future trademarks as one means to distinguish our drug candidates that are approved for marketing and technologies from the products of our competitors. OncoSignature is trademarked. Once we select trademarks and apply to register them, our trademark applications may not be approved. Third parties may oppose our trademark applications or otherwise challenge our use of the trademarks. In the event that our trademarks are successfully challenged, we could be forced to rebrand our products, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe our trademarks, and we may not have adequate resources to enforce our trademarks.

In addition, any proprietary name we propose to use with ACR-368 or any future drug candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of the potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable proprietary product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. Comparable foreign regulators may have similar requirements, and it is possible that different proprietary or non-proprietary names may be required in different jurisdictions.

If we are unable to protect the confidentiality of our proprietary information, our business and competitive position would be harmed.

In addition to seeking patent and trademark protection for our drug candidates and technologies, we also rely on unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect our proprietary information, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information. Monitoring unauthorized uses and disclosures of

our intellectual property is difficult, and we do not know whether the steps we have taken to protect our intellectual property will be effective. In addition, we may not be able to obtain adequate remedies for any such breaches. Enforcing a claim that a party illegally disclosed or misappropriated proprietary information is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets.

Moreover, our competitors may independently develop knowledge, methods and know-how equivalent to our proprietary information. Competitors may be able to obtain or reverse engineer information about our products or technologies that would permit them to replicate some or all of the competitive advantages we derive from our development efforts for technologies on which we do not have patent protection. If any of our proprietary information were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our proprietary information were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

We also seek to preserve the integrity and confidentiality of our data and other confidential information by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached and detecting the disclosure or misappropriation of confidential information and enforcing a claim that a party illegally disclosed or misappropriated confidential information is difficult, expensive and time-consuming, and the outcome is unpredictable. Further, we may not be able to obtain adequate remedies for any breach. In addition, our confidential information may otherwise become known or be independently discovered by competitors, in which case we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us.

If we do not obtain patent term extension for patents covering our drug candidates, our business may be materially harmed, and in any case, the terms of our patents may not be sufficient to effectively protect our drug candidates and business.

Patents have a limited term. In most countries, including the United States, the expiration of a patent is generally 20 years after its first effective non-provisional filing date. However, depending upon the timing, duration and specifics of FDA marketing approval of ACR-368, our other drug candidates or any future drug candidates, one or more of any U.S. patents we may be issued or have licensed may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Amendments.

The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. The Hatch-Waxman Act allows a maximum of one patent to be extended per FDA-approved product as compensation for the patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Patent term extension may also be available in certain foreign countries upon regulatory approval of our drug candidates. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our competitive position, business, financial condition, results of operations, and prospects could be harmed, possibly materially.

If there are delays in obtaining regulatory approvals or other additional delays, the period of time during which we can market our drug candidates under patent protection could be further reduced. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such drug candidates might expire before or shortly after such drug candidates are commercialized. Once the patent term has expired, we may be open to competition from similar or generic products. The launch of a generic version of one of our products in particular would be likely to result in an immediate and substantial reduction in the demand for that product, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Ownership of our Common Stock and our Status as a Public Company

An active trading market for our common stock may not continue to be developed or sustained.

Prior to our IPO, there was no public market for our common stock. Although our common stock is listed on the Nasdaq Global Market, an active trading market for our shares may not continue to develop or be sustained. If an active market for our common stock does not continue to develop or be sustained, it may be difficult for you to sell shares of our common stock at an attractive price or at all.

In addition, concentration of ownership by our existing stockholders may result in fewer shares being actively traded in the public market because these stockholders may be restricted from selling such shares under applicable securities laws, which could reduce the liquidity of the market and the available public float for our shares of common stock.

The trading price of the shares of our common stock may be volatile, and purchasers of our common stock could incur substantial losses.

Our stock price may be volatile. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their common stock at or above the price paid for the shares. The market price for our common stock may be influenced by many factors, including but not limited to:

- the reporting of unfavorable preclinical results;
- the commencement, enrollment or results of our clinical trials of ACR-368 or any future clinical trials we may conduct, or changes in the development status of our drug candidates;
- any delay in our regulatory filings for ACR-368 or any other drug candidate we may develop, and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings, including without limitation the FDA's issuance of a "refusal to file" letter or a request for additional information;
- adverse results from, delays in or termination of clinical trials;
- adverse regulatory decisions, including failure to receive regulatory approval of our drug candidates;
- unanticipated serious safety concerns related to the use of ACR-368 or any other drug candidate;
- changes in financial estimates by us or by any equity research analysts who might cover our stock;
- conditions or trends in our industry;
- changes in the market valuations of similar companies;
- stock market price and volume fluctuations of comparable companies and, in particular, those that operate in the biopharmaceutical industry;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- announcements by us or our competitors of significant acquisitions, strategic partnerships or divestitures;
- our relationships with our collaborators;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- investors' general perception of our company and our business;
- recruitment or departure of key personnel;
- overall performance of the equity markets;
- trading volume of our common stock;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation or employee or independent contractor litigation;
- changes in the structure of healthcare payment systems;
- general political and economic conditions; and
- other events or factors, many of which are beyond our control.

The stock market in general, and the market for biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies, including in connection with the Russian invasion of Ukraine, Israel-Hamas conflicts, inflation and increasing interest rates, which have resulted in decreased stock prices for many companies notwithstanding the lack of a fundamental change in their underlying business models or prospects. Broad market and industry factors, including potentially worsening economic conditions, may negatively affect the market

price of our common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in this section, could have a significant and material adverse impact on the market price of our common stock.

In addition, in the past, stockholders have initiated class action lawsuits against pharmaceutical and biotechnology companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources from our business.

A significant portion of our total outstanding shares are restricted from immediate resale but may be sold into the market in the near future. This could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. As of March 25, 2024, we had 22,636,951 shares of common stock outstanding. This includes 7,550,000 shares sold in our IPO, which may be resold in the public market. As of March 25, 2024, approximately 10.3 million shares were held by our affiliates, who are generally restricted from selling pursuant to securities laws. Our shares may be resold and the market price of our stock could decline if the holders of currently-restricted shares sell them or are perceived by the market as intending to sell them.

We have filed a registration statement on Form S-8 under the Securities Act registering shares subject to outstanding stock options issued under the 2019 Stock Incentive Plan, or the 2019 Plan, and shares of common stock reserved for issuance under the 2022 Stock Option and Incentive Plan, or the 2022 Plan, and the 2022 Employee Stock Purchase Plan, or the 2022 ESPP. Both the 2022 Plan and the 2022 ESPP provide for annual automatic increases in the shares reserved for issuance under the plans which could result in additional dilution to our stockholders. Shares registered under these registration statements on Form S-8 can be freely sold in the public market upon issuance, subject to the vesting of the equity awards, other restrictions provided under the terms of the applicable plan or equity award, and the restrictions of Rule 144 in the case of our affiliates.

If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that equity research analysts publish about us and our business. Equity research analysts may elect not to provide research coverage of our common stock, and such lack of research coverage may adversely affect the market price of our common stock. In the event we do have equity research analyst coverage, we will not have any control over the analysts or the content and opinions included in their reports. The price of our stock could decline if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which in turn could cause our stock price or trading volume to decline.

Concentration of ownership of our common stock among our existing executive officers, directors and principal stockholders may prevent new investors from influencing significant corporate decisions.

Our executive officers, directors and current beneficial owners of 5% or more of our common stock and their respective affiliates beneficially own a majority of our outstanding common stock. As a result, these persons, acting together, would be able to significantly influence all matters requiring stockholder approval, including the election and removal of directors, any merger, consolidation, sale of all or substantially all of our assets, or other significant corporate transactions.

Some of these persons or entities may have interests different than yours. For example, because many of these stockholders purchased their shares at prices substantially different than the current market price of our common stock and have held their shares for a longer period, they may be more interested in selling our company to an acquirer than other investors, or they may want us to pursue strategies that deviate from the interests of other stockholders.

We are an "emerging growth company" and a "smaller reporting company" and, as a result of the reduced disclosure and governance requirements applicable to emerging growth companies and smaller reporting companies, our common stock may be less attractive to investors.

We are an "emerging growth company" as defined in the JOBS Act and we intend to take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- an exemption from compliance with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, in the assessment of our internal control over financial reporting;
- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements;
- exemptions from the requirements of holding non-binding advisory votes on executive compensation or golden parachute arrangements; and
- an exemption from compliance with the requirements of the Public Company Accounting Oversight Board regarding the communication of critical audit matters in the auditor's report on financial statements.

We cannot predict if investors will find our common stock less attractive because we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an emerging growth company.

We will remain an emerging growth company until the last day of our fiscal year following the fifth anniversary of the completion of our IPO or, if earlier, (i) the last day of the fiscal year in which we have total annual gross revenue of at least $1.235 billion, (ii) the date on which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th, or (iii) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

In addition, we have elected to take advantage of the extended transition period to comply with new or revised accounting standards and to adopt certain of the reduced disclosure requirements available to emerging growth companies. As a result of the accounting standards election, we will not be subject to the same implementation timing for new or revised accounting standards as other public companies that are not emerging growth companies, which may make comparison of our financials to those of other public companies more difficult. As a result of these elections, the information that we provide in this Annual Report may be different than the information investors may receive from other public companies in which they hold equity interests. In addition, it is possible that some investors will find our common stock less attractive as a result of these elections, which may result in a less active trading market for our common stock and higher volatility in our share price.

Even after we no longer qualify as an emerging growth company, we may, under certain circumstances, still qualify as a "smaller reporting company," which would allow us to take advantage of many of the same exemptions from disclosure requirements, including reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements.

We have broad discretion in the use of our cash, cash equivalents and investments and may invest or spend the cash, cash equivalents and investments in ways with which you do not agree and in ways that may not yield a return.

We have broad discretion over the use of our cash, cash equivalents and investments. You may not agree with our decisions, and our use of the cash, cash equivalents and investments may not yield any return. Our failure to apply our cash, cash equivalents and investments effectively could compromise our ability to pursue our growth strategy and we might not be able to yield a significant return, if any, on our investment. Stockholders will not have the opportunity to influence our decisions on how to use our cash, cash equivalents and investments.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware and the federal district courts of the United States of America will be the exclusive forums for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law:

- any derivative action or proceeding brought on our behalf;
- any action asserting a breach of fiduciary duty;
- any action asserting a claim against us arising under the Delaware General Corporation Law, our amended and restated certificate of incorporation, or our amended and restated bylaws;

- any claim or cause of action seeking to interpret, apply, enforce or determine the validity of our restated certificate or our amended and restated bylaws;
- any claim or cause of action as to which the Delaware General Corporation Law confers jurisdiction on the Court of Chancery of the state of Delaware; and
- any action asserting a claim against us that is governed by the internal-affairs doctrine.

This provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, Section 22 of the Securities Act of 1933, as amended, or the Securities Act, creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our amended and restated certificate of incorporation further provides that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated certificate of incorporation. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions.

These exclusive forum provisions may result in increased costs for investors to bring a claim. Further, these exclusive forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers and other employees. If a court were to find either exclusive-forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving the dispute in other jurisdictions, all of which could seriously harm our business.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our certificate of incorporation and our bylaws may discourage, delay, or prevent a merger, acquisition, or other change in control of our company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that directors are elected at the annual stockholder meeting;
- allow the authorized number of our directors to be changed from time to time by our stockholders or our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- establish requirements for stockholder proposals that can be acted on at stockholder meetings;
- require that stockholder actions must be effected at a duly called stockholder meeting and allow actions by our stockholders by written consent, with certain requirements;
- limit who may call stockholder meetings; and
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biopharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

General Risks

We are subject to U.S. and certain foreign anti-corruption laws and regulations, export and import controls, sanctions and embargoes. We could face liability and other serious consequences for violations.

We are subject to anti-corruption laws and regulations, including the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act and other state and national anti-bribery laws in the countries in which we may conduct activities in the future. Anti-corruption laws are interpreted broadly and generally prohibit companies and their employees, agents, contractors and other third-party collaborators from offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly through third parties, to any person in the public or private sector to obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls.

Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-United States governments. Additionally, in many other countries, the healthcare providers who prescribe pharmaceuticals are employed by their government, and therefore will be considered foreign officials for purposes of the FCPA. We also expect to rely on third parties for research, preclinical studies and clinical trials and/or to obtain necessary permits, licenses, patent registrations and other marketing approvals. We can be held liable for the corrupt or other illegal activities of our employees, agents, CROs, contractors and other collaborators and partners, even if we do not explicitly authorize or have actual knowledge of such activities.

We are also subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations and various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls. Compliance with applicable regulatory requirements regarding the export of our products may create delays in the introduction of our products in international markets or, in some cases, prevent the export of our products to some countries altogether. Furthermore, U.S. export control laws and economic sanctions prohibit the shipment of certain products and services to countries, governments and persons targeted by U.S. sanctions.

There is no certainty that all of our employees, agents, suppliers, manufacturers, contractors or collaborators, or those of our affiliates, will comply with all applicable anti-corruption, export and import control, and sanctions laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers, or our employees, the closing down of facilities, including those of our suppliers and manufacturers, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries as well as difficulties in manufacturing or continuing to develop our products, and could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees, and our business, prospects, operating results and financial condition.

If we are unable to design and maintain effective internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports and the market price of our common stock may decline.

Ensuring that we have adequate internal control over financial reporting in place to produce accurate financial statements on a timely basis needs to be periodically re-evaluated and is costly and time-consuming. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles. In connection with our IPO, we began the process of documenting, reviewing and improving our internal control over financial reporting for compliance with Section 404, which requires an annual management assessment of the effectiveness of our internal control over financial reporting. Prior to our IPO, we were not required to test our internal controls within a specified period and, as a result, we may experience difficulty in meeting these reporting requirements. For example, in connection with the audit of our financial statements for the years ended December 31, 2022, we and our independent registered public accounting firm identified four material weaknesses in our internal control over financial reporting. For the year ended December 31, 2023, these material weaknesses have been remediated, but we could experience further difficulty with internal control over financing reporting in the future.

Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements

due to error or fraud will not occur or that all control issues and instances of fraud will be detected. If we identify material weaknesses in our internal control over financial reporting in the future; if we are unable to comply with the requirements of Section 404 in a timely manner; or if we are unable to assert that our internal control over financial reporting is effective, investors may lose confidence in the accuracy and completeness of our financial reports and the market price of our common stock could decline, and we could also become subject to investigations by the stock exchange on which our common stock is listed, the SEC or other regulatory authorities, which could require additional financial and management resources.

We may not be able to utilize a significant portion of our net operating loss carryforwards and other tax attributes.

As of December 31, 2023, we had approximately $33.0 million in federal net operating loss carryforwards and $35.3 million in state net operating loss carryforwards. The federal net operating loss carryforward can be carried forward indefinitely while the state net operating loss carryforward will begin to expire in varying amounts in 2038. The net operating loss carryforwards subject to expiration could expire unused and be unavailable to offset future income tax liabilities. Under the 2017 Tax Cuts and Jobs Act, or the Tax Act, as modified by the Coronavirus Aid, Relief and Economic Security Act, or CARES Act, federal net operating losses generated in taxable years beginning after December 31, 2017 and in future taxable years, if any, will not expire and may be carried forward indefinitely, but the deductibility of such federal net operating losses in taxable years beginning after December 31, 2020 are limited to the lesser of the net operating loss carryover or 80% of the corporation's adjusted taxable income (subject to Section 382 of the Internal Revenue Code of 1986, as amended, or the Code). There is variation in how states are responding to the Tax Act and CARES Act. In addition, for state income tax purposes, there may be periods during which the use of net operating losses, or NOLs, is suspended or otherwise limited.

Separately, under Section 382 of the Code, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50 percentage point change, by value, in its equity ownership by certain stockholders over a rolling three-year period, the corporation's ability to use its pre-change NOL carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. The completion of our IPO, together with private placements and other transactions that have occurred since our inception, may have triggered such an ownership change pursuant to Section 382 of the Code. We have not completed a Section 382 analysis, and therefore, there can be no assurances that the NOL carryforwards are not already limited.

In addition, we may experience ownership changes as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. If an ownership change occurs and our ability to use our NOL carryforwards is materially limited, it could harm our future operating results by effectively increasing our future tax obligations.

New or future changes to tax laws could materially adversely affect our company.

The tax regimes we are subject to or operate under, including with respect to income and non-income taxes, are unsettled and may be subject to significant change. Changes in tax laws, regulations, or rulings, or changes in interpretations of existing laws and regulations, could materially adversely affect our company. For example, the Tax Act, together with the CARES Act, made broad and complex changes to the U.S. tax code, including changes to U.S. federal tax rates, additional limitations on the deductibility of interest, both positive and negative changes to the utilization of future NOL carryforwards, allowing for the expensing of certain capital expenditures, and putting into effect the migration from a "worldwide" system of taxation to a territorial system. More recently, the Inflation Reduction Act of 2022 enacted further changes to federal income tax law. In addition, many countries in Europe, as well as a number of other countries and organizations (including the Organization for Economic Cooperation and Development and the European Commission), have recently proposed, recommended, or (in the case of countries) enacted or otherwise become subject to changes to existing tax laws or new tax laws that could significantly increase our tax obligations in the countries where we do business or require us to change the manner in which we operate our business. These proposals, recommendations and enactments include changes to the existing framework in respect of income taxes that could apply to our business.

Unfavorable global political or economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The global credit and financial markets have experienced severe volatility and disruptions in the past several years, including as a result of recent events in the U.S. banking sector. A severe or prolonged economic downturn, such as the global financial crisis, could result in a variety of risks to our business, including our ability to raise additional capital when needed on acceptable terms, if at all. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment, higher inflation, bank failures or continued unpredictable and unstable market conditions. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. In addition, the current military conflict between Russia and Ukraine and / or conflicts in the Middle East could disrupt or otherwise adversely impact our operations and those of third parties upon which we rely. Related sanctions, export controls or other actions have been or may in the

future be initiated by nations including the United States, the European Union or Russia (e.g., potential cyberattacks, disruption of energy flows, etc.), which could adversely affect our business and/or our supply chain, our CROs, CMOs and other third parties with whom we conduct business. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

We have incurred and will continue to incur increased costs and demands upon management as a result of being a public company.

As a public company listed in the United States, we have incurred and will continue to incur significant additional legal, accounting and other expenses that we did not incur as a private company, including the cost of director and officer liability insurance. These additional costs could negatively affect our financial results. In addition, changing laws, regulations and standards relating to corporate governance and public disclosure, including regulations implemented by the SEC and Nasdaq, may increase legal and financial compliance costs and make some activities more time-consuming. These laws, regulations and standards are subject to varying interpretations and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue-generating activities to compliance activities. If notwithstanding our efforts to comply with new laws, regulations and standards, we fail to comply, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

Failure to comply with these rules might also make it more difficult for us to obtain some types of insurance, including director and officer liability insurance, and we might be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, on committees of our board of directors or as members of senior management.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to certain reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized, and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people, or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected.

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity.

Cybersecurity Risk Management and Strategy

We recognize the importance of assessing, identifying, and managing material risks associated with cybersecurity threats, as such term is defined in Item 106(a) of Regulation S-K. These risks include, among other things, operational risks; intellectual property theft; fraud; extortion; harm to employees; violation of privacy or security laws and other litigation and legal risk; and reputational risks. We have implemented several cybersecurity technologies, and controls and processes to aid in our efforts to assess, identify, and manage such risks.

We are subject to cybersecurity threat risks associated with our use of third-party service providers, including independent clinical investigators, contracted laboratories and contract research organizations. Cybersecurity considerations affect the selection and oversight of these third-party service providers.

We engage certain external parties, including cybersecurity and privacy firms and consultants, to provide IT support and cybersecurity oversight, and enhance our risk reduction abilities, including the engagement of a third-party to review our cybersecurity program to help identify areas for continued focus and improvement. We also use automated tools designed to monitor, identify, and address cybersecurity risks.

As of the date of this report, we have not identified cybersecurity threats, including as a result of any previous cybersecurity incidents, that have materially affected us, our business strategy, results of operation or financial condition. We are in the process of formalizing an incident response plan. For additional information regarding risks from cybersecurity threats, please refer to Item 1A, "Risk Factors," of this Annual Report on Form 10-K.

Cybersecurity Governance

Our Head of Information Technology, who reports directly to the Chief Operating Officer, has day-to-day responsibility for preventing, mitigating and remediating cybersecurity threats and incidents. The individual currently serving in this role has two decades of experience in information technology and cybersecurity. Our Disclosure Committee evaluates the materiality of any threats and/or incidents to determine if there is any required disclosure. Our external SEC counsel is also apprised of certain threats and/or incidents that may occur and is available to advise management on any disclosure obligations.

Our Board of Directors addresses our cybersecurity risk management as part of its general oversight function. The Audit Committee is responsible for overseeing our cybersecurity risk management processes, including oversight and mitigation of risks from cybersecurity threats. Periodically, the Audit Committee receives an overview from our Head of Information Technology of our cybersecurity threat risk management and strategy processes covering topics such as data security posture, results from third-party assessments, progress towards pre-determined risk-mitigation-related goals, and material cybersecurity threat risks or incidents and developments, as well as the steps management has taken to respond to such risks.

Item 2. Properties.

Our principal office is located in Watertown, Massachusetts, where we lease 13,711 square feet of office and laboratory space under a lease that expires in 2028. We also occupy 529 square meters of office space located in Lund, Sweden under a lease that expires in December 2026 and will automatically renew for an additional term of three years unless we provide written notice of termination nine months prior to the termination date. We believe that our current facilities are sufficient to meet our current and near-term needs and that, should it be needed, suitable additional space will be available.

Item 3. Legal Proceedings.

From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. We are not currently subject to any material legal proceedings.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

Our common stock began trading on the Nasdaq Global Market on November 15, 2022, under the symbol "ACRV." Prior to that time, there was no public market for our common stock.

Holders of Record

As of March 25, 2024, there were 7 holders of record of our common stock. This number was derived from our stockholder records and does not include beneficial owners of our common stock whose shares are held in "street" name with various dealers, clearing agencies, banks, brokers and other fiduciaries.

Dividend Policy

We have never declared or paid, and do not anticipate declaring or paying in the foreseeable future, any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business. Any future determination related to our dividend policy will be made at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, contractual restrictions, business prospects and other factors our board of directors may deem relevant.

Securities Authorized for Issuance Under Equity Compensation Plans

Information about our equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report on Form 10-K.

Recent Sales of Unregistered Equity Securities

Private Placement

In November 2022, we completed a private placement which closed concurrently with the IPO, in which we issued and sold 400,000 shares of our common stock at $12.50 per share to Chione Limited, an existing investor. We received aggregate net proceeds of $4.7 million, after deducting the placement agent fee. We believe the offers, sales, and issuances of the above securities were exempt from the registration requirements of the Securities Act as a transaction not involving a public offering pursuant to Section 4(a)(2) of the Securities Act of 1933, as amended (or Regulation D or Regulation S promulgated thereunder).

Issuances Pursuant to our Equity Plans

We deemed the equity grants and exercises of stock options issued under our equity compensation plans prior to the completion of our initial public offering in November 2022 to be exempt from registration in reliance on Rule 701 of the Securities Act as offers and sales of securities under compensatory benefit plans and contracts relating to compensation. Each of the recipients of securities in any transaction exempt from registration either received or had adequate access, through employment, business or other relationships, to information about us.

Use of Proceeds from our Public Offering of Common Stock and Concurrent Private Placement

The offer and sale of shares in our IPO was registered under the Securities Act pursuant to a Registration Statement on Form S-1 (File No. 333-267911), which was declared effective by the SEC on November 9, 2022. As of December 31, 2023, we had used $42.2 million of the net proceeds from the IPO. We have invested the net proceeds from the offering in money market funds, short-term investments, and long-term investments. There has been no material change in the planned use of proceeds from our IPO as described in our final prospectus filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act on November 16, 2022.

Issuer Purchases of Equity Securities

None.

Item 6. Reserved

Not applicable.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes and other financial information included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Special Note Regarding Forward-Looking Statements" and "Risk Factors" sections of this Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. . Unless the context requires otherwise, references in this Annual Report on Form 10-K to "Acrivon" the "Company," "we," "us," and "our" refer to Acrivon Therapeutics, Inc. and its subsidiaries.

Overview

We are a clinical stage biopharmaceutical company developing precision oncology medicines that we match to patients whose tumors are predicted to be sensitive to each specific medicine by utilizing our proprietary proteomics-based patient responder identification platform. Recently approved precision oncology treatments, such as kinase inhibitors, have transformed the cancer treatment landscape, and while the therapeutic benefit of these agents has provided significant benefit to patients, these precision oncology treatments unfortunately only address the less than 10% of patients with cancers that harbor certain easily-identifiable genetic mutations. Our approach is designed to overcome the limitations of genomics-based patient selection methods. We do this by using our proprietary precision medicine platform, AP3, to develop our pipeline of oncology drug candidates. Our AP3 platform enables the creation of drug-specific proprietary OncoSignature companion diagnostics that are used to identify the patients most likely to benefit from our drug candidates, which we refer to as patient responders. We are currently advancing our lead candidate, ACR-368, a selective small molecule inhibitor targeting CHK1 and CHK2 with sub single-digit nM and single-digit nM potency, respectively, in a potentially registrational Phase 2 trial across multiple solid tumor types. We are continuing enrollment and dosing of patients in this multi-center trial based on OncoSignature-predicted sensitivity to ACR-368 in patients with locally advanced or metastatic, recurrent platinum-resistant ovarian cancer, as well as endometrial adenocarcinoma or urothelial cancer, two tumor types predicted to be sensitive to ACR-368 through OncoSignature screening and not previously evaluated in past clinical trials.

In November 2023, we announced initial clinical observations from the ongoing Phase 2 trial. Consistent with the overall favorable tolerability profile previously observed in multiple past single-arm trials conducted at recommended Phase 2 dose (RP2D), drug-related adverse events were primarily reversible, manageable hematological toxicities, including neutropenia and thrombocytopenia. In the limited number of patients evaluated by imaging to date, preliminary evidence of clinical activity was observed in OncoSignature-positive patients across all three tumor types treated with single agent ACR-368 at RP2D. Consistent with AP3-predicted tumor sensitivity to the combination of ACR-368 and low dose gemcitabine (LDG) in OncoSignature-negative patients, early imaging-based evidence of clinical activity across all three tumor types was also observed in patients treated with ACR-368 at RP2D and LDG during the dose escalation phase.

Our ACR-368 OncoSignature test, which has not yet obtained regulatory approval, has been extensively evaluated in preclinical studies, including in two separate, blinded, prospectively-designed studies on pretreatment tumor biopsies collected from patients with ovarian cancer treated with ACR-368 in past Phase 2 clinical trials conducted by Lilly and at NCI providing evidence of robust enrichment of responders through our method. On May 8, 2023, ACR-368 was granted two Fast Track designations from the U.S. Food and Drug Administration for the investigation of ACR-368 monotherapy for patients with OncoSignature-positive platinum-resistant ovarian cancer and endometrial cancer. On November 16, 2023, the ACR-368 OncoSignature test was granted Breakthrough Device Designation for the identification of ovarian cancer patients who may benefit from treatment with ACR-368. In addition to ACR-368, Acrivon is also leveraging its proprietary AP3 precision medicine platform for developing its internally-discovered preclinical stage pipeline programs, consisting of its development candidate, ACR-2316, a potentially first-in-class, selective, dual WEE1/PKMYT1 inhibitor, and additional programs targeting these two critical nodes in the DDR pathways.

Since our inception in 2018, we have devoted substantially all of our resources toward conducting discovery and research activities, organizing and staffing our company, business planning, acquiring and internally discovering drug candidates, establishing and protecting our intellectual property portfolio, developing and progressing ACR-368 and the ACR-368 OncoSignature, preparing for and conducting preclinical studies and clinical trials, establishing arrangements with third parties for the manufacture of ACR-368, the ACR-368 OncoSignature and component materials, advancing our internal co-crystallography-driven, AP3-enabled preclinical programs, conducting preclinical studies for ACR-2316, and initiating IND-enabling studies for ACR-2316, as well as raising capital. We do not have any drug candidates approved for sale and have not generated any revenue from drug sales.

In November 2022, we completed our initial public offering, or IPO, pursuant to which we issued and sold 7,550,000 shares of our common stock for net proceeds. Additionally, we completed our concurrent private placement, or the Concurrent Private Placement,

pursuant to which we issued and sold 400,000 shares of our common stock. In connection with the IPO, in December 2022, the underwriters partially exercised their option to purchase 1,035,540 additional shares. The sale pursuant to the exercise of the underwriters' option to purchase additional shares closed on December 16, 2022, upon which we issued 1,035,540 additional shares of common stock. We received aggregate net proceeds from our IPO, including the partial exercise by the underwriters of their option to purchase additional shares, and the Concurrent Private Placement, of $104.5 million, after deducting underwriting discounts and commissions and the placement agent fee, but before deducting offering expenses payable by us of $3.6 million.

Since inception, we have funded our operations primarily through equity and convertible debt financings and have received aggregate net proceeds of $119.8 million from the issuance of convertible notes and the sale of our Series A-1 convertible preferred stock, or Series A-1 Preferred Stock, and Series B convertible preferred stock, or Series B Preferred Stock, which we refer to collectively as our Preferred Stock, all of which fully converted into common stock upon the closing of the IPO, and most recently, with aggregate net proceeds from our IPO, including the partial exercise by the underwriters of their option to purchase additional shares, and Concurrent Private Placement of $104.5 million, after deducting underwriting discounts and commissions and the placement agent fee, but before deducting offering expenses payable by the Company.

We have incurred operating losses since inception. Our net losses for the years ended December 31, 2023 and 2022 were $60.4 million and $31.2 million, respectively. As of December 31, 2023, we had an accumulated deficit of $116.4 million. These losses have resulted primarily from costs incurred in connection with research and development activities and general and administrative costs associated with our operations. We expect to continue to incur significant and increasing expenses and operating losses for the foreseeable future, particularly if and as we:

- continue to conduct preclinical studies and clinical trials for ACR-368;
- initiate and conduct additional preclinical studies and clinical trials for ACR-368;
- continue to discover and develop additional drug candidates, including ACR-2316, and drug-tailored OncoSignature tests;
- acquire or in-license other drug candidates and technologies;
- maintain, expand, and protect our intellectual property portfolio;
- hire additional clinical and scientific personnel;
- further develop and refine the manufacturing processes for ACR-368, the ACR-368 OncoSignature, ACR-2316, or any future drug candidates;
- seek regulatory approvals and pursue commercialization for any drug candidates that successfully complete clinical trials; and
- add operational, financial, and management information systems and personnel, including personnel to support our drug development and planned future commercialization efforts, as well as to support our obligations as a public reporting company.

We are incurring and expect to continue to incur additional costs associated with operating as a public company, including significant legal, accounting, insurance, investor relations and other expenses that we did not incur as a private company. Furthermore, we will not generate revenue from drug sales until we successfully complete clinical development and obtain regulatory approval for a drug candidate. In addition, if we obtain regulatory approval for a drug candidate and do not enter into a third-party commercialization partnership, we expect to incur significant expenses related to developing our commercialization capability to support drug sales, marketing, manufacturing and distribution activities. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our planned clinical studies and our expenditures on other research and development activities.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time that we can generate significant revenue from drug sales, if ever, we expect to finance our operations through the sale of equity, debt financings or other capital sources, including potential collaborations with other companies or other strategic transactions. If we are unable to raise capital as needed, this could have a negative impact on our financial condition and ability to pursue our business strategies including requiring us to delay, reduce or eliminate drug development or future commercialization efforts. The amount and timing of our future funding requirements will depend on many factors including the successful advancement of ACR-368, the ACR-368 OncoSignature, or any future drug candidates. Our ability to raise additional funds may also be adversely impacted by potential worsening global economic conditions, and disruptions to, and volatility in the credit and financial markets in the United States and worldwide, such as those resulting from conflicts in the Middle East and the war in Ukraine. There can be no assurances that the current operating plan will be achieved or that additional funding will be available on terms acceptable to us, or at all.

As of December 31, 2023, we had cash, cash equivalents and investments of $127.5 million. We believe that our existing cash, cash equivalents and investments as of December 31, 2023, will enable us to fund our operating expenses and capital expenditure requirements into the fourth quarter of 2025. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. See the section titled "—Liquidity and Capital Resources."

Companion Diagnostic Agreement

In June 2022, we entered into a companion diagnostic agreement with Akoya Biosciences, Inc., or Akoya, pursuant to which we agreed to co-develop, validate, and commercialize our proprietary ACR-368 OncoSignature test, the companion diagnostic that will be used to identify patients with cancer most likely to respond to ACR-368.

Pursuant to the agreement, we paid Akoya a one-time, non-refundable, non-creditable upfront payment in the amount of $0.6 million. We are obligated to pay Akoya up to an aggregate of $17.3 million upon the achievement of specified development milestones. As of March 28, 2024, development milestones have been achieved under the agreement, resulting in payments of $8.3 million by us to Akoya. Other than certain specified pass-through costs, each party is responsible for its own costs associated with the development of the companion diagnostic. Akoya will procure and manufacture necessary supplies to perform the ACR-368 OncoSignature test to support our clinical development and commercial requirements, in accordance with a supply agreement to be mutually agreed upon by the parties. We may terminate the agreement at our convenience, subject to the payment of a termination fee in the amount of $1.0 million.

For a more detailed description of this agreement, see the sections titled "Business—Licensing and Collaborations" and "—Contractual Obligations."

Components of Results of Operations

Revenue

To date, we have not generated any revenue, and we do not expect to generate any revenue in the foreseeable future from drug sales. We may in the future generate revenue from payments received under collaboration agreements, which could potentially include (but not be limited to) payments of upfront fees, license fees, milestone-based payments and reimbursements for research and development efforts.

Operating Expenses

Research and Development

The majority of our expenses have been research and development expenses, which consist primarily of costs incurred in connection with our research and development activities, including our drug discovery efforts and the development of ACR-368 and the ACR-368 OncoSignature. We expense research and development costs as incurred, which include:

- direct cost for conducting internal research and development to generate preclinical validation data for ACR-368 including the ACR-368 OncoSignature, and for our internal preclinical drug discovery programs, including ACR-2316;
- the cost to obtain and maintain licenses to intellectual property, such as those with Lilly and related future payments should certain milestones be achieved;
- external research and development expenses incurred under agreements with CROs, as well as investigative sites and consultants that conduct our clinical trials and other scientific development services;
- costs related to manufacturing material for our clinical trials, including fees paid to CMOs;
- manufacturing scale-up expenses and the cost of acquiring and manufacturing clinical trial materials;
- employee-related expenses, including salaries, bonuses, benefits, stock-based compensation, and other related costs for those employees involved in research and development efforts;
- costs of outside consultants, including their fees, stock-based compensation, and related travel expenses;
- expenses to acquire technologies, such as intellectual property, to be used in research and development;
- upfront and maintenance fees incurred under license, acquisition, and other third-party agreements;

- costs related to regulatory activities, including filing fees paid to regulatory agencies and compliance with regulatory requirements; and
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent, maintenance of facilities, and equipment and software.

Research and development costs are expensed as incurred. We recognize external development costs as related goods are delivered or services are performed. Significant judgments and estimates are made in determining the accrued expense balances at the end of any reporting period.

We characterize research costs incurred prior to the identification of a drug candidate as discovery costs. Once a drug candidate has been identified, research costs incurred are allocated as drug candidate costs.

Our external research and development expenses consist primarily of fees paid to outside consultants, CROs, CMOs and research laboratories in connection with our process development, manufacturing, and clinical development activities. Our direct external research and development expenses also include fees incurred under license and intellectual property purchase agreements. We track these external research and development costs on a program-by-program basis once we have identified a drug candidate.

Our indirect research and development costs are primarily personnel-related costs, facilities, which is offset by a portion of our allocable sublease rent income, and other costs. Employees and infrastructure are not directly tied to any one program and are deployed across our programs. As such, we do not track these costs on a specific program basis.

The successful development of our ACR-368 and ACR-368 OncoSignature test or any other future drug candidates, including ACR-2316, is highly uncertain. We plan to substantially increase our research and development expenses for the foreseeable future as we continue the development of ACR-368 and manufacturing processes and conduct discovery and research activities for our clinical programs and continue preclinical development of ACR-2316 through IND-enabling studies.

We cannot determine with certainty the timing of initiation, the duration, or the completion costs of current or future clinical trials of our drug candidates due to the inherently unpredictable nature of preclinical and clinical development. Clinical development timelines, the probability of success and development costs can differ materially from expectations. We anticipate that we will make determinations as to which drug candidates to pursue and how much funding to direct to each drug candidate on an ongoing basis in response to the results of ongoing and future clinical trials, regulatory developments and our ongoing assessments as to each drug candidate's commercial potential. We will need to raise substantial additional capital in the future. Our clinical development costs are expected to increase significantly with our ongoing clinical trials. We anticipate that our expenses will increase substantially, particularly due to the numerous risks and uncertainties associated with developing drug candidates, including the uncertainty of:

- the scope, rate of progress and expenses of our ongoing research activities and clinical trials and other research and development activities;
- confirming the appropriate safety profile established in past clinical trials;
- successful enrollment in and completion of clinical trials;
- whether our drug candidates show efficacy with an increased objective response rate through patient responder identification in our clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our drug candidates;
- the extent to which we establish additional collaboration or license agreements;
- commercializing drug candidates, if and when approved, whether alone or in collaboration with others; and
- continued acceptable safety profile of the products following any regulatory approval.

Any changes in the outcome of any of these variables with respect to the development of our drug candidates in clinical development could mean a significant change in the costs and timing associated with the development of these drug candidates. We may never succeed in achieving regulatory approval for any of our drug candidates. We may obtain unexpected results from our clinical trials. We may elect to discontinue, delay or modify clinical trials of some drug candidates or focus on others. For example, if the U.S. Food and Drug Administration, European Medicines Agency or another regulatory authority were to delay our planned start of clinical

trials or require us to conduct clinical trials or other testing beyond those that we currently expect or if we experience significant delays in enrollment in any of our planned clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development of that drug candidate.

General and Administrative

General and administrative expenses consist primarily of employee-related costs, including salaries, bonuses, benefits, and stock-based compensation expenses for personnel in executive, finance, accounting, human resources and other administrative functions. Other significant general and administrative expenses include legal fees relating to patent, intellectual property and corporate matters, fees paid for accounting, audit, consulting and other professional services, and expenses for rent, insurance and other operating costs. An allocated portion of sublease rent income is recorded as an offset to general and administrative expenses.

We anticipate that our general and administrative expenses will continue to increase in the future as we increase our headcount to support our continued research activities and development of our drug candidates. We also anticipate that we will continue to incur increased accounting, audit, legal, regulatory, compliance and director and officer insurance costs, as well as investor and public relations expenses associated with operating as a public company.

Other Income, Net

Other income, net primarily consists of interest income, which is earned on cash equivalents and investments, amortization of premiums and accretion of discounts to maturity for available-for-sale debt securities, offset by investment management fees, unrealized gains and losses on foreign currency transactions, and state taxes.

Income Taxes

Since our inception, we have not recorded any income tax benefits for the net losses we have incurred or for the research and development tax credits earned in each year and interim period, as we believe, based upon the weight of available evidence, that it is more likely than not that all of our net operating loss carryforwards and tax credit carryforwards will not be realized.

As of December 31, 2023, we had $33.0 million and $35.3 million of federal and state net operating loss carryforwards, respectively. The federal net operating losses are not subject to expiration and the state net operating losses begin to expire in 2038. These loss carryforwards are available to reduce future federal taxable income, if any.

Results of Operations

Comparison of the Years Ended December 31, 2023 and 2022

The following table summarizes our results of operations (in thousands):

	Year Ended December 31,		
	2023	2022	Change
Operating expenses:			
Research and development	$ 46,024	$ 23,949	$ 22,075
General and administrative	21,079	8,708	12,371
Total operating expenses	67,103	32,657	34,446
Loss from operations	(67,103)	(32,657)	(34,446)
Other income, net	6,715	1,490	5,225
Net loss	$ (60,388)	$ (31,167)	$ (29,221)

Research and Development Expenses

The following table summarizes our research and development expenses (in thousands):

	Year Ended December 31,		
	2023	2022	Change
Direct research and development expenses by program:			
ACR-368	$ 21,764	$ 9,733	$ 12,031
Unallocated research and development expenses:			
Personnel related (including stock-based compensation)	13,987	7,398	6,589
Other drug discovery programs, including ACR-2316	6,982	5,468	1,514
Facilities, supplies and other	3,291	1,350	1,941
Total research and development expenses	$ 46,024	$ 23,949	$ 22,075

Research and development expenses were $46.0 million for the year ended December 31, 2023, compared to $23.9 million for the year ended December 31, 2022. The increase of $22.1 million was primarily due to:

- a $12.0 million increase in costs related to the continued progression of the ACR-368 clinical trial and related activities, inclusive of $3.7 million related to Akoya milestones;
- a $6.6 million increase in personnel-related costs, including $1.7 million of stock-based compensation expense, primarily due to an increase in headcount in support of research activities and progression of our clinical stage ACR-368 program;
- a $1.5 million increase in costs related to the progression of preclinical drug discovery activities, inclusive of the novel, internally-discovered development candidate ACR-2316; and
- a $1.9 million increase in facilities, supplies and other expenses, primarily due to an increase in headcount and related research activities, as well as the cessation of sublease rent income, which had been recorded as an offset to research and development expenses.

General and Administrative Expenses

The following table summarizes our general and administrative expenses for each of the periods presented (in thousands):

	Year Ended December 31,		
	2023	2022	Change
Personnel related (including stock-based compensation)	$ 14,619	$ 5,068	$ 9,551
Legal and professional fees	4,800	2,747	2,053
Facilities, supplies and other	1,660	893	767
Total general and administrative expenses	$ 21,079	$ 8,708	$ 12,371

General and administrative expenses were $21.1 million for the year ended December 31, 2023, compared to $8.7 million for the year ended December 31, 2022. The increase of $12.4 million was primarily due to:

- a $9.6 million increase in payroll and employee-related expenses, including $7.7 million of stock-based compensation expense;
- a $2.1 million increase in legal, accounting and professional fees due to additional costs associated with operating as a public company; and
- a $0.8 million increase in facilities, supplies, and other expenses, primarily due to an increase in headcount.

Other Income, Net

Other income, net was $6.7 million for the year ended December 31, 2023, compared to other income, net of $1.5 million for the year ended December 31, 2022. The change of $5.2 million is primarily attributable to an increase in interest income and accretion earned on our investments.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, we have not recognized any revenue and have incurred significant losses in each period and on an aggregate basis. We have not yet commercialized any drug candidates, and we do not expect to generate revenue from sales of any drug candidates or from other sources for several years, if at all. As of December 31, 2023, we had $127.5 million in cash, cash equivalents and investments, and we had an accumulated deficit of $116.4 million. We have funded our operations primarily with net proceeds of $119.8 million from the issuance of convertible notes and sales of our Preferred Stock, all of which fully converted into common stock upon the closing of the IPO, and $104.5 million in net proceeds from the IPO and the Concurrent Private Placement. On December 1, 2023, we filed the Registration Statement with the SEC and simultaneously entered into a sales agreement with TD Cowen, as sales agent, for the ATM Program. We believe that our existing cash, cash equivalents and investments will enable us to fund our operating expenses and capital expenditure requirements into the fourth quarter of 2025.

Other Liquidity Matters

We have a banking relationship with SVB. On March 10, 2023, SVB was closed by the California Department of Financial Protection and Innovation, which appointed the FDIC as receiver. On March 12, 2023, the Treasury Department announced that the FDIC would complete its resolution of SVB in a manner that fully protects all depositors. We had access to all of our money starting March 13, 2023. As a result, we did not incur any losses nor do we anticipate any future losses with respect to such cash balances. As of March 28, 2024, we have maintained full access to our holdings and have diversified our banking relationships.

Cash Flows

The following table summarizes our cash flows for each of the periods presented (in thousands):

	Year Ended December 31,	
	2023	2022
Net cash used in operating activities	$ (42,641)	$ (30,117)
Net cash provided by (used in) investing activities	50,717	(141,676)
Net cash (used in) provided by financing activities	(1,554)	101,709
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 6,522	$ (70,084)

Net Cash Used in Operating Activities

Net cash used in operating activities was $42.6 million for the year ended December 31, 2023, compared to net cash used in operating activities of $30.1 million for the year ended December 31, 2022. The increase in net cash used in operating activities of $12.5 million was primarily driven by an increase in net loss of $29.2 million, partially offset by a $9.4 million increase in non-cash stock-based compensation expense.

Net Cash Provided by (Used in) Investing Activities

Net cash provided by investing activities was $50.7 million for the year ended December 31, 2023, resulting from $108.5 million in proceeds from maturities of short-term investments, offset by our purchases of short-term and long-term investments of $56.5 million and purchases of property and equipment of $1.3 million.

Net cash used in investing activities was $141.7 million for the year ended December 31, 2022, resulting from our purchases of short-term and long-term investments of $150.2 million and purchases of property and equipment of $2.2 million, offset by $10.7 million in proceeds from maturities of short-term investments.

Net Cash (Used in) Provided by Financing Activities

Net cash used in financing activities was $1.5 million for the year ended December 31, 2023, resulting from $1.3 million of payments for tax withholdings related to the vesting of restricted stock units and $1.0 million of payments of offering costs, offset by $0.8 million in proceeds from the exercise of stock options.

Net cash provided by financing activities was $101.7 million for the year ended December 31, 2022, resulting from net proceeds of $99.8 million received in connection with the IPO, including the partial exercise by the underwriters of their option to purchase additional shares and net proceeds of $4.7 million received in connection with the Concurrent Private Placement, partially offset by $2.8 million in payments of IPO costs.

Funding Requirements

As of December 31, 2023, our cash, cash equivalents and investments were $127.5 million. We believe that our existing cash, cash equivalents and investments will enable us to fund our operating expenses and capital expenditure requirements into the fourth quarter of 2025. We have based this estimate on assumptions that may prove to be wrong, and we could expend our capital resources sooner than we expect.

We expect to incur significant expenses and operating losses for the foreseeable future as we advance our drug candidates through clinical development, seek regulatory approval and pursue commercialization of any approved drug candidates. We expect that our research and development and general and administrative costs will increase in connection with our planned research and clinical activities. In addition, we expect to continue to incur additional costs associated with operating as a public company. If we receive regulatory approval for any of our drug candidates, we expect to incur significant commercialization expenses related to drug manufacturing, sales, marketing and distribution, depending on where we choose to commercialize. We may also require additional capital to pursue in-licenses or acquisitions of other drug candidates.

Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical drug candidates, we are unable to accurately predict the amount of our operating expenditures. Our future capital requirements will depend on many factors, including but not limited to:

- the scope, timing, progress, results and costs of preclinical and clinical development activities;
- the costs, timing and outcome of regulatory review of drug candidates;
- the costs of future activities, including drug sales, medical affairs, marketing, manufacturing and distribution, for any drug for which we receive marketing approval;
- the costs of establishing and maintaining arrangements with third party manufacturers for the commercial supply of products that receive marketing approval, if any;
- the revenue, if any, received from commercial sale of our products, should any drug candidates receive marketing approval;
- the cash requirements of any future acquisitions or discovery of drug candidates;
- the cost and timing of attracting, hiring and retaining skilled personnel to support our operations and continued growth;
- the cost of implementing operational, financial and management systems;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our ability to establish and maintain collaborations, strategic partnerships or marketing, distribution, licensing or other strategic arrangements with third parties on favorable terms, if at all; and
- the timing, receipt and amount of sales of, or milestone payments related to or royalties on, current or future drug candidates, if any.

A change in the outcome of any of these or other variables with respect to the development of ACR-368, the ACR-368 OncoSignature, ACR-2316, or any drug or development candidate we may develop in the future could significantly change the costs and timing associated with our development plans. Further, our operating plans may change in the future, and we may need additional funds to meet operational needs and capital requirements associated with such operating plans.

Until such time, if ever, as we can generate substantial drug revenues to support our expenses, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations and other similar arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be or could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise funds through collaborations, or other similar arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, drug candidates or grant licenses on terms that may not be favorable to us and/or may reduce the value of our common stock. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our drug development or future commercialization efforts or grant rights to develop and market our drug candidates even if we would otherwise prefer to develop and market such drug candidates ourselves.

Contractual Obligations

Leases

We lease laboratory and office space in Watertown, Massachusetts. This lease is classified as an operating lease, and will expire in April 2028, with an option to extend the term for an additional five years at then-market rental rates. Additionally, we also lease laboratory and office space in Lund, Sweden. This lease is classified as an operating lease. The term of the lease commenced in October 2020 and expired in September 2023, with an option to extend the term for an additional three years. In September 2023, the Company modified the term of the lease agreement. The modification extended the lease term for an additional quarter, resulting in a de minimis impact to the ROU asset and corresponding lease liability. In addition, the Company entered into an operating lease agreement in August 2023 for office and laboratory space located in Lund, Sweden. This lease commenced on December 15, 2023 and has an initial term of three years, with an option to extend the term for an additional three years. Future minimum commitments under these leases are $5.5 million as of December 31, 2023. Of the $5.5 million, $1.2 million is due in 12 months or less. See Note 7 in our consolidated financial statements appearing at the end of this Annual Report on Form 10-K for more information on our lease obligations.

License Agreement

We may incur contingent royalty and milestone payments that we are required to make under our license agreement with Lilly, pursuant to which we have in-licensed certain intellectual property. We are required to pay Lilly aggregate development and commercial milestone payments of up to $168.0 million, of which $5.0 million is due prior to NDA. Due to the uncertainty of the achievement and timing of the events requiring payment under our license agreement with Lilly, the amounts to be paid by us are not fixed or determinable at this time. We are also obligated to pay a tiered percentage royalty on annual net sales ranging from a low single-digit up to a maximum of 10%, subject to certain specified reductions. For additional information, see the section titled "Business—Licensing and Collaborations."

Companion Diagnostic Agreement

We may incur contingent milestone payments that we are required to make under our companion diagnostic agreement with Akoya pursuant to which we agreed to co-develop, validate, and commercialize our proprietary ACR-368 OncoSignature test. We are obligated to pay Akoya up to an aggregate of $17.3 million upon the achievement of specified development milestones. Due to the uncertainty of the achievement and timing of the events requiring payment under our companion diagnostic agreement with Akoya, the amounts to be paid by us and when are not determinable at this time. As of March 28, 2024, development milestones have been achieved under our companion diagnostic agreement, resulting in payments of $8.3 million by us to Akoya. For additional information, see the section titled "Business—Licensing and Collaborations."

Purchase and Other Obligations

We enter into contracts in the normal course of business with CROs and other third-party vendors for clinical trials and testing and manufacturing services. These contracts do not contain minimum purchase commitments and are cancelable by us upon written notice. Payments due upon cancellation consist of payments for services provided or expenses incurred, including non-cancelable obligations of our service provided up to one year after the date of cancellation.

Critical Accounting Policies and Significant Judgments and Estimates

Our consolidated financial statements are prepared in accordance with accounting principles generally accepted in the United States, or U.S. GAAP. The preparation of our consolidated financial statements and related disclosures requires us to make estimates, assumptions and judgments that affect the reported amount of assets, liabilities, costs and expenses, and the disclosure of contingent assets and liabilities in our consolidated financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 2 in our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses as of each balance sheet date. This process involves reviewing open contracts and purchase orders, communicating with our personnel and with vendors to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary.

We base our expenses related to research and development activities on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid balance accordingly. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Although we do not expect our estimates to be materially different from amounts incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts incurred.

Stock-Based Compensation Expense

We measure stock-based compensation based on the grant date fair value of the stock-based awards and recognize stock-based compensation expense on a straight-line basis over the requisite service period of the awards, which is generally the vesting period of the respective award. Forfeitures are accounted for as they occur. For non-employee awards, compensation expense is recognized as the services are provided, which is generally ratably over the vesting period. At inception, prior to the issuance of any stock option grants, we adopted the guidance of Accounting Standards Update, or ASU, No. 2018-07, *Compensation—Stock Compensation* (Topic 718): *Improvements to Non-employee Share-based Payment Accounting*, ASU 2018-07, and account for awards to non-employees using the grant date fair value without subsequent periodic remeasurement.

Stock-based compensation expense is classified in our consolidated statements of operations and comprehensive loss based on the function to which the related services are provided or in the same manner in which the grantee's payroll costs are classified or in which the grantee's service payments are classified.

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model, which requires inputs based on certain subjective assumptions, including the expected stock price volatility, the expected term of the option, the risk-free interest rate for a period that approximates the expected term of the option, and our expected dividend yield. Since there is limited historical data of our share price on the public market, we determined the volatility for awards granted based on an analysis of reported data for a group of guideline companies that issued options with substantially similar terms. The expected volatility has been determined using a weighted-average of the historical volatility measures of this group of guideline companies. We expect to estimate

expected volatility based on the group of guideline companies until we have adequate historical data regarding the volatility of our own traded stock price. The expected term of our stock options granted to employees and non-employees has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. We have not paid, and do not anticipate paying, dividends on our common stock; therefore, the expected dividend yield is assumed to be zero.

Prior to our IPO, there was no public market for our common stock, and consequently, the estimated fair value of our common stock was determined by our board of directors as of the date of each option grant, with input from management, considering third-party valuations of our common stock as well as our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent third-party valuation through the date of the grant.

Following our IPO, in connection with the accounting for granted stock options and other awards we may grant, the fair value of our common stock is determined based on the quoted market price of our common stock.

Recent Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position, results of operations and cash flows is disclosed in Note 2 to our consolidated financial statements appearing at the end of this Annual Report.

Emerging Growth Company and Smaller Reporting Company Status

The JOBS Act provides that, among other things, an "emerging growth company" can take advantage of an extended transition period for complying with new or revised accounting standards. This provision allows an emerging growth company to delay the adoption of some accounting standards until those standards would otherwise apply to private companies. As an emerging growth company, we have elected not to "opt out" of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards and, as a result, we will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for private companies on a case-by-case basis until such time that we either (i) irrevocably elect to "opt out" of such extended transition period or (ii) no longer qualify as an emerging growth company. As a result, our consolidated financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates. We may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for private companies. We intend to rely on certain of the other exemptions and reduced reporting requirements provided by the JOBS Act. As an emerging growth company, we are not required to, among other things, (i) provide an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b), and (ii) comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding a supplement to the auditor's report providing additional information about the audit and the financial statements (auditor discussion and analysis).

We will remain an emerging growth company until the earlier to occur of (1) the last day of our fiscal year (a) following the fifth anniversary of the closing of our IPO, (b) in which we have total annual gross revenues of at least $1.235 billion or (c) in which we are deemed to be a "large accelerated filer" under the rules of the SEC, which means the market value of our common shares that is held by non-affiliates exceeds $700 million as of the last day of our second quarter, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

We are also a "smaller reporting company," meaning that the market value of our stock held by non-affiliates is less than $700 million and our annual revenue was less than $100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than $250 million or (ii) our annual revenue is less than $100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700 million.

If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Under SEC rules and regulations, because we are considered to be a "smaller reporting company," we are not required to provide the information required by this item in this report.

Item 8. Financial Statements and Supplementary Data.

Our consolidated financial statements, together with the reports of our independent registered public accounting firms, appear beginning on page F-1 of this Annual Report on Form 10-K for the years ended December 31, 2023 and 2022.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and our Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rule 13a-15(e) and 15d-15(e) of the Exchange Act of 1934, as amended) as of December 31, 2023. Based on that evaluation, management, including our Chief Executive Officer and Chief Financial Officer have concluded that as of December 31, 2023, our disclosure controls and procedures were effective at a reasonable assurance level.

The Company's disclosure controls and procedures are designed to provide reasonable assurance that information required to be disclosed by us in reports that we file or submit under the Exchange Act (i) is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms; and (ii) accumulated and communicated to management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely discussions regarding required disclosure. We believe that a control system, no matter how well designed and operated, cannot provide absolute assurance that the objectives of the control system are met, and no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within a company have been detected.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over our financial reporting, as such term is defined in Rule 13a-15(f) and 15d-15(f) under the Exchange Act. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of the effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies and procedures included in such controls may deteriorate. Our management conducted an assessment of the effectiveness of our internal control over financial reporting based on the criteria set forth in "Internal Control - Integrated Framework (2013)" issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on this assessment, our management concluded that, as of December 31, 2023, our internal control over financial reporting was effective.

Remediation of Previously Identified Material Weaknesses

A "material weakness" is a deficiency, or combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. Prior to the completion of our IPO in November 2022, we had been a private company and therefore had not designed or maintained internal controls over financial reporting commensurate with the financial reporting requirements of an SEC registrant. We previously disclosed in our 2022 Annual Report on Form 10-K the following material weaknesses, of which one was partially remediated as disclosed in our Form 10-Q for the quarter ended June 30, 2023:

- We did not design and maintain an effective control environment commensurate with the financial reporting requirements of a public company. Specifically, we lacked a sufficient complement of resources with (i) an appropriate level of accounting knowledge, experience and training to appropriately analyze, record and disclose accounting matters timely and accurately as a public company, and (ii) an appropriate level of knowledge and experience to establish effective processes and controls. Additionally, the lack of a sufficient number of professionals resulted in an inability to consistently design and maintain formal accounting policies, procedures and controls or establish appropriate authorities and responsibilities in pursuit of our financial reporting objectives, as demonstrated by, among other things, insufficient segregation of duties in our finance and accounting functions.

- We did not design and maintain effective controls in response to the risks of material misstatement. Specifically, changes to existing controls or the implementation of new controls were not sufficient to timely respond to changes to the risks of material misstatement to financial reporting due to changes in the complexity in the business.

These material weaknesses contributed to the following additional material weaknesses:

- We did not design and maintain effective controls over the preparation and review of account reconciliations and journal entries necessary to achieve complete, accurate and timely financial accounting, reporting and disclosures.
- We did not design and maintain effective controls over information technology general controls for information systems that are relevant to the preparation of its financial statements. Specifically, we did not design and maintain: (i) program change management controls to ensure that program and data changes are identified, tested, authorized and implemented appropriately; (ii) user access controls to ensure appropriate segregation of duties and to adequately restrict user and privileged access to appropriate personnel; (iii) computer operations controls to ensure that processing and transfer of data, and data backups and recovery are monitored; and (iv) program development controls to ensure that new software development is tested, authorized and implemented appropriately.

With the oversight of the Audit Committee of our Board of Directors, we have continued throughout the year ended December 31, 2023 to dedicate significant resources and efforts to improve our control environment and to take steps to remediate our material weaknesses identified above by implementing and maintaining changes to our internal control over financial reporting.

Remediation Actions Completed During Current Year

The following remediation efforts were established in the year ended December 31, 2023:

- Hired finance and accounting personnel, including Chief Financial Officer;
- Engaged third-party professionals to assist with technical accounting assessments, financial reporting assistance and timeliness of identification, assessment, and response to the risk of material misstatement;
- Established more robust accounting policies and procedures, such as implementing and documenting controls over the preparation and review of account reconciliations and journal entries;
- Performed a gap analysis to identify where new process controls are needed and to enhance existing controls to accurately build financial accounting, reporting, and disclosure procedures to document routine reconciliations and journal entries in a timely fashion;
- Further formalized the design and operational effectiveness of controls over balance sheet account reconciliations and journal entries;
- Designed and implemented an upgrade to our financial systems to support key processes and controls;
- Continued execution of information technology general controls for information systems that are relevant to the preparation of its financial statements; and
- Continued execution of controls previously designed and implemented to maintain an effective control environment commensurate with the financial reporting requirements of a public company, and to respond to the risks of material misstatement.

We completed the design, testing and evaluation of new and enhanced internal controls and determined that, as of December 31, 2023, the controls were designed and had operated effectively for a sufficient period of time for our management to conclude that the material weakness identified prior to our IPO had been remediated.

Further, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm.

Attestation Report of the Registered Public Accounting Firm

This Annual Report does not include an attestation report of our registered public accounting firm due to an exemption provided by the JOBS Act for "emerging growth companies."

Changes in Internal Control Over Financial Reporting

Other than the applicable remediation efforts described in "Remediation of Previously Identified Material Weaknesses" above, Management determined that, as of December 31, 2023, there were no changes in our internal control over financial reporting (as defined

in Rules 13a-15(f) and 15d-15(f)) that occurred during the year then ended that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2023.

Item 11. Executive Compensation.

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2023.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2023.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2023.

Item 14. Principal Accounting Fees and Services.

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2023.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(1) For a list of the financial statements included herein, see Index to the Consolidated Financial Statements on page F-1 of this Annual Report on Form 10-K, incorporated into this Item by reference.

(2) Financial statement schedules have been omitted because they are either not required or not applicable or the information is included in the consolidated financial statements or the notes thereto.

(3) Exhibits:

Exhibit Number	Description
3.1	Second Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K (File No. 001-41551) filed with the SEC on November 17, 2022).
3.2	Amended and Restated Bylaws (incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K (File No. 001-41551) filed with the SEC on November 17, 2022).
4.1*	Description of registrant's securities.
4.2	Amended and Restated Investors' Rights Agreement, by and among the Registrant and certain of its stockholders, dated November 9, 2021 (incorporated by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-1 (File No. 333-267911), filed with the SEC on October 17, 2022).
10.1+	2019 Stock Incentive Plan and Forms of Stock Option Agreement and Notice of Exercise (incorporated by reference to Exhibit 10.1 to the Company's Registration Statement on Form S-1 (File No. 333-267911), filed with the SEC on October 17, 2022)
10.2+	2022 Equity Incentive Plan and Forms of Stock Option Grant Notice, Stock Option Agreement, Notice of Exercise, Restricted Stock Unit Grant Notice and Restricted Stock Unit Award Agreement (incorporated by reference to Exhibit 10.2 to the Company's Registration Statement on Form S-1/A (File No. 333-267911), filed with the SEC on November 3, 2022).
10.3+	2022 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.3 to the Company's Registration Statement on Form S-1/A (File No. 333-267911), filed with the SEC on November 3, 2022).
10.4+	Acrivon Therapeutics Inc. 2023 Inducement Plan (incorporated by reference to Exhibit 4.3 to the Company's Registration Statement on Form S-8 (File No. 333-273908) filed with the SEC on August 11, 2023).
10.5+	Form of Indemnification Agreement with Executive Officers and Directors (incorporated by reference to Exhibit 10.4 to the Company's Registration Statement on Form S-1 (File No. 333-267911), filed with the SEC on October 17, 2022).
10.6+	Non-Employee Director Compensation Policy (incorporated by reference to Exhibit 10.11 to the Company's Registration Statement on Form S-1 (File No. 333-267911), filed with the SEC on October 17, 2022).
10.7+	Employment Offer Letter Agreement, dated October 5, 2020, and Letter Amendment to Employment Offer Letter Agreement, dated August 5, 2022, by and between the Registrant and Eric Devroe (incorporated by reference to Exhibit 10.10 to the Company's Registration Statement on Form S-1 (File No. 333-267911), filed with the SEC on October 17, 2022).
10.8†	License Agreement, by and between the Registrant and Eli Lilly and Company, dated January 27, 2021 (incorporated by reference to Exhibit 10.5 to the Company's Registration Statement on Form S-1 (File No. 333-267911), filed with the SEC on October 17, 2022).
10.9†	OncoSignature Companion Diagnostic Agreement, by and between the Registrant and Akoya Biosciences, Inc., dated June 17, 2022 (incorporated by reference to Exhibit 10.6 to the Company's Registration Statement on Form S-1 (File No. 333-267911), filed with the SEC on October 17, 2022).
10.10†	Patent License Agreement, by and between the Registrant and Peter Blume-Jensen, dated April 12, 2018 (incorporated by reference to Exhibit 10.7 to the Company's Registration Statement on Form S-1 (File No. 333-267911), filed with the SEC on October 17, 2022).
10.11+	Executive Employment Agreement, by and between the Registrant and Peter Blume-Jensen, dated October 5, 2020 (incorporated by reference to Exhibit 10.8 to the Company's Registration Statement on Form S-1 (File No. 333-267911), filed with the SEC on October 17, 2022).
10.12+	Employment Offer Agreement, dated March 30, 2022, and Amendment to Employment Offer Letter Agreement, dated August 5, 2022, by and between the Registrant and Rasmus Holm-Jorgensen (incorporated by reference to Exhibit 10.12 of the Company's Annual Report on Form 10-K (File No. 001-41551) filed with the SEC on March 28, 2023).
10.13*+	Amended and Restated Executive Employment Agreement, dated May 30, 2023, by and between the Registrant and Kristina Masson.
10.14†	First Amendment to OncoSignature Companion Diagnostic Agreement, by and between the Registrant and Akoya Biosciences, Inc., dated December 21, 2022 (incorporated by reference to Exhibit 10.14 of the Company's Annual Report on Form 10-K (File No. 001-41551) filed with the SEC on March 28, 2023).
10.15*†	Second Amendment to OncoSignature Companion Diagnostic Agreement, by and between Acrivon Therapeutics, Inc. and Akoya Biosciences, Inc., dated June 19, 2023.
10.16*†	Third Amendment to OncoSignature Companion Diagnostic Agreement, by and between the Registrant and Akoya Biosciences, Inc., dated December 4, 2023.
21.1*	List of Subsidiaries
23.1*	Consent of PricewaterhouseCoopers LLP, independent registered accounting firm
24.1	Power of Attorney (included on signature page)

31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1**	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2**	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
97.1*	Policy on Recoupment of Incentive Compensation.
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.
101.SCH	Inline XBRL Taxonomy Extension Schema With Embedded Linkbase Documents
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

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* Filed herewith.
+ Indicates management contract or compensatory plan or arrangement.
† Certain confidential information contained in this exhibit, indicated by asterisks, has been omitted pursuant to Item 601(b)(10)(iv) or Item 601(a)(5), as applicable, of Regulation S-K.
** The certifications furnished in Exhibits 32.1 and 32.2 hereto are deemed to accompany this Annual Report on Form 10-K and are not deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liability of that section, nor shall they be deemed incorporated by reference into any filing under the Securities Act or the Exchange Act, irrespective of any general incorporation language contained in such filing.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

Acrivon Therapeutics, Inc.

Date: March 28, 2024 By: /s/ Peter Blume-Jensen
Peter Blume-Jensen, M.D., Ph.D.
Chief Executive Officer and President

Date: March 28, 2024 By: /s/ Rasmus Holm-Jorgensen
Rasmus Holm-Jorgensen
Chief Financial Officer

POWER OF ATTORNEY

KNOW ALL BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Peter Blume-Jensen and Rasmus Holm-Jorgensen, and each of them, as his or her true and lawful agents, proxies and attorneys-in-fact, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Peter Blume-Jensen Peter Blume-Jensen, M.D., Ph.D.	Chief Executive Officer, President and Chairman of the Board *(Principal Executive Officer)*	March 28, 2024
/s/ Rasmus Holm-Jorgensen Rasmus Holm-Jorgensen	Chief Financial Officer *(Principal Financial and Accounting Officer)*	March 28, 2024
/s/ Derek DiRocco Derek DiRocco, Ph.D.	Director	March 28, 2024
/s/ Kristina Masson Kristina Masson, Ph.D., M.B.A.	Executive Vice President, Business Operations, Director	March 28, 2024
/s/ Sharon Shacham Sharon Shacham, Ph.D., M.B.A.	Director	March 28, 2024
/s/ Michael Tomsicek Michael Tomsicek, M.B.A.	Director	March 28, 2024
/s/ Charles Baum Charles Baum, M.D., Ph.D.	Director	March 28, 2024
/s/ Ivana Magovcevic-Liebisch Ivana Magovcevic-Liebisch, Ph.D., J.D.	Director	March 28, 2024

/s/ Santhosh Palani Santhosh Palani, Ph.D., C. F.A.	Director	March 28, 2024

INDEX TO THE CONSOLIDATED FINANCIAL STATEMENTS

Consolidated Financial Statements for the Years Ended December 31, 2023 and 2022:

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Acrivon Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Acrivon Therapeutics, Inc. and its subsidiaries (the "Company") as of December 31, 2023 and 2022, and the related consolidated statements of operations and comprehensive loss, of convertible preferred stock and stockholders' equity (deficit) and of cash flows for the years then ended, including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2023 and 2022, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 28, 2024

We have served as the Company's auditor since 2022.

ACRIVON THERAPEUTICS, INC.
CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share data)

	December 31, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 36,015	$ 29,519
Short-term investments	91,443	98,232
Prepaid expenses and other current assets	2,234	4,344
Total current assets	129,692	132,095
Property and equipment, net	3,479	2,092
Operating lease right-of-use assets	4,429	4,770
Long-term investments	—	41,881
Restricted cash	414	388
Deferred offering costs	251	—
Total assets	$ 138,265	$ 181,226
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 5,048	$ 904
Accrued expenses and other current liabilities	7,378	4,886
Operating lease liabilities, current	877	726
Total current liabilities	13,303	6,516
Operating lease liabilities, long-term	3,767	4,235
Total liabilities	17,070	10,751
Commitments and contingencies (Note 12)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized as of December 31, 2023 and 2022, respectively; 0 shares issued and outstanding as of December 31, 2023 and 2022.	—	—
Common stock, par value $0.001; 500,000,000 shares authorized as of December 31, 2023 and 2022, respectively; 22,522,644 and 21,920,402 shares issued and outstanding as of December 31, 2023 and 2022, respectively.	23	22
Additional paid-in capital	237,675	226,580
Accumulated other comprehensive loss	(83)	(95)
Accumulated deficit	(116,420)	(56,032)
Total stockholders' equity	121,195	170,475
Total liabilities and stockholders' equity	$ 138,265	$ 181,226

The accompanying notes are an integral part of these consolidated financial statements.

ACRIVON THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(in thousands, except share and per share data)

	Year Ended December 31,	
	2023	2022
Operating expenses:		
Research and development	$ 46,024	$ 23,949
General and administrative	21,079	8,708
Total operating expenses	67,103	32,657
Loss from operations	(67,103)	(32,657)
Other income, net	6,715	1,490
Net loss	$ (60,388)	$ (31,167)
Net loss per share—basic and diluted	$ (2.74)	$ (7.56)
Weighted-average common stock outstanding—basic and diluted	22,078,190	4,121,912
Comprehensive loss:		
Net loss	(60,388)	(31,167)
Other comprehensive income (loss):		
Unrealized gain (loss) on available-for-sale investments, net of tax	12	(95)
Comprehensive loss	$ (60,376)	$ (31,262)

The accompanying notes are an integral part of these consolidated financial statements.

ACRIVON THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
(in thousands, except share data)

	Convertible Preferred Stock		Common Stock					
	Shares	Amount	Shares	Amount	Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity (Deficit)
Balance at December 31, 2021	27,471,911	$ 122,518	1,769,561	$ 2	$ 1,054	$ —	$ (24,865)	$ (23,809)
Issuance of common stock upon completion of initial public offering, net of commissions, underwriting discounts and offering costs	—	—	8,585,540	9	96,160	—	—	96,169
Issuance of common stock upon concurrent private placement, net of placement agent fee	—	—	400,000	—	4,650	—	—	4,650
Exercise of common stock options	—	—	25,039	—	24	—	—	24
Conversion of convertible preferred stock to common stock	(27,471,911)	(122,518)	11,140,262	11	122,507	—	—	122,518
Stock-based compensation expense	—	—	—	—	2,185	—	—	2,185
Unrealized loss on available-for-sale investments, net of tax	—	—	—	—	—	(95)	—	(95)
Net loss	—	—	—	—	—	—	(31,167)	(31,167)
Balance at December 31, 2022	—	$ —	21,920,402	$ 22	$ 226,580	$ (95)	$ (56,032)	$ 170,475
Exercise of common stock options	—	—	292,444	—	775	—	—	775
Issuance of common stock upon vesting of restricted stock units, net of shares withheld for tax	—	—	309,798	1	(1,298)	—	—	(1,297)
Stock-based compensation expense	—	—	—	—	11,618	—	—	11,618
Unrealized gain on available-for-sale investments, net of tax	—	—	—	—	—	12	—	12
Net loss	—	—	—	—	—	—	(60,388)	(60,388)
Balance at December 31, 2023	—	$ —	22,522,644	$ 23	$ 237,675	$ (83)	$ (116,420)	$ 121,195

The accompanying notes are an integral part of these consolidated financial statements.

ACRIVON THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,	
	2023	2022
Cash flows from operating activities:		
Net loss	$ (60,388)	$ (31,167)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	536	364
Stock-based compensation expense	11,618	2,185
Non-cash lease expense	778	731
Net amortization of premiums and accretion of discounts on investments	(3,323)	(698)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	2,110	(3,539)
Accounts payable	3,609	(245)
Accrued expenses and other liabilities	3,173	2,919
Operating lease liabilities	(754)	(667)
Net cash used in operating activities	(42,641)	(30,117)
Cash flows from investing activities:		
Purchases of short-term and long-term investments	(56,528)	(150,178)
Proceeds from maturities of short-term investments	108,533	10,668
Purchases of property and equipment	(1,288)	(2,166)
Net cash provided by (used in) investing activities	50,717	(141,676)
Cash flows from financing activities:		
Proceeds from initial public offering of common stock, net of commissions and underwriting discounts	—	99,808
Proceeds from issuance of common stock upon Concurrent Private Placement, net of placement agent fee	—	4,650
Proceeds from exercise of stock options	775	24
Payments of offering costs	(1,032)	(2,773)
Payments of tax withholdings related to vesting of restricted stock units	(1,297)	—
Net cash (used in) provided by financing activities	(1,554)	101,709
Net increase (decrease) in cash, cash equivalents, and restricted cash	6,522	(70,084)
Cash, cash equivalents and restricted cash at beginning of period	29,907	99,991
Cash, cash equivalents and restricted cash at end of period	$ 36,429	$ 29,907
Supplemental disclosure of non-cash investing and financing activities:		
Conversion of convertible preferred stock to common stock	$ —	$ 122,518
Purchases of property and equipment included in accounts payable	$ 635	$ —
Supplemental cash flow information:		
Right-of-use assets obtained in exchange for operating lease liability	$ 437	$ —
Deferred offering costs in accounts payable and accrued expenses and other current liabilities	$ 85	$ 866
Reconciliation of cash, cash equivalents, and restricted cash:		
Cash and cash equivalents	$ 36,015	$ 29,519
Restricted cash	414	388
Total cash, cash equivalents, and restricted cash	$ 36,429	$ 29,907

The accompanying notes are an integral part of these consolidated financial statements.

1. Nature of the Business

Acrivon Therapeutics, Inc., (the "Company") is a clinical stage biopharmaceutical company developing oncology medicines that the Company matches to patients whose tumors are predicted to be sensitive to each specific medicine by utilizing its proteomics-based patient responder identification platform. The Company's pipeline includes the Phase 2 lead program, ACR-368, referred to as prexasertib, a precision oncology asset, as well as ACR-2316, a selective, dual WEE1/PKMYT1 inhibitor, and additional programs targeting these two critical nodes in the DNA Damage Response, or DDR, pathways.

The Company was incorporated in March 2018 under the laws of the state of Delaware, and its principal offices are in Watertown, Massachusetts. Also in March 2018, the Company formed Acrivon AB, a wholly-owned subsidiary of the Company, established in Lund, Sweden. In December 2021, the Company formed Acrivon Securities Corporation, a wholly-owned subsidiary, established in Massachusetts.

Liquidity

As an emerging growth entity, the Company has devoted substantially all of its resources since inception to organizing and staffing the Company, business planning, raising capital, establishing its intellectual property portfolio, acquiring or discovering drug candidates, research and development activities for the Company's lead candidate ACR-368, for the Company's internally discovered development candidate ACR-2316, and other compounds, establishing arrangements with third parties for the manufacture of its drug candidates and component materials, and providing general and administrative support for these operations. As a result, the Company has incurred significant operating losses and negative cash flows from operations since its inception and anticipates such losses and negative cash flows will continue for the foreseeable future.

The Company has incurred recurring losses since its inception, including net losses of $60.4 million and $31.2 million for the years ended December 31, 2023, and 2022, respectively. As of December 31, 2023 and 2022 the Company had an accumulated deficit of $116.4 million and $56.0 million, respectively. To date the Company has not generated any revenues and expects to continue generating operating losses for the foreseeable future as it continues to expand its research and development efforts.

Since its inception, the Company has funded its operations primarily with proceeds from the sales of shares of its convertible preferred stock and the issuance of convertible notes, and most recently, through an initial public offering ("IPO") and concurrent private placement. Upon the closing of the Company's IPO on November 17, 2022, only common stock remains issued and outstanding.

The Company expects that its existing cash, cash equivalents and investments of $127.5 million as of December 31, 2023, will be sufficient to fund its operating expenses and capital expenditure requirements for at least 12 months from the date these consolidated financial statements were issued.

The Company will need additional funding to support its planned operating activities. There can be no assurances, however, that the current operating plan will be achieved or that additional funding will be available on terms acceptable to the Company, or at all, considering the current interest rate environment. If the Company is unable to obtain sufficient funding, it could be required to delay its development efforts, limit activities and reduce research and development costs, which could adversely affect its business prospects.

ATM Program

On December 1, 2023, the Company filed a registration statement on Form S-3 (the "Registration Statement") with the U.S. Securities and Exchange Commission (the "SEC"), which was declared effective on December 15, 2023, which registered the offering, issuance, and sale of up to a maximum aggregate offering price of $300.0 million of common stock, preferred stock, debt securities, warrants and/or units of any combination thereof. We simultaneously entered into a sales agreement with Cowen and Company, LLC, as sales agent, to provide for the issuance and sale by the Company of up to $100.0 million of common stock from time to time in "at-the-market" offerings under the Registration Statement and related prospectus filed with the Registration Statement ("ATM Program"). As of December 31, 2023, no sales had been made pursuant to the ATM Program.

Initial Public Offering, Reverse Stock Split and Concurrent Private Placement

On November 17, 2022, the Company closed its IPO, pursuant to which it issued and sold 7,550,000 shares of its common stock at a public offering price of $12.50 per share for gross proceeds of $94.4 million. In connection with the IPO, the Company granted the underwriters a 30-day option to purchase 1,132,500 additional shares of common stock. On December 14, 2022, the underwriters

partially exercised the option to purchase 1,035,540 additional shares. The sale pursuant to the exercise of the underwriters' option to purchase additional shares closed on December 16, 2022, upon which the Company issued 1,035,540 shares of common stock for gross proceeds of $12.9 million. The Company received aggregate net proceeds from the IPO, including the exercise by the underwriters of their option to purchase additional shares, of $99.8 million, after deducting underwriting discounts and commissions of $7.5 million, but before deducting offering expenses payable by the Company of $3.6 million.

In connection with the IPO, the Company effected a 1-for-2.466 reverse stock split of the Company's common stock and adjusted the ratio at which the Company's preferred stock is convertible into common stock, the number of shares available for issuance under the 2019 Stock Incentive Plan ("2019 Plan") and the number of options and exercise prices of options granted under the 2019 Plan as a result of the 1-for-2.466 reverse stock split. Accordingly, all common shares, stock options, and per share information presented in the accompanying consolidated financial statements and notes thereto have been adjusted, where applicable, to reflect the reverse stock split on a retroactive basis for all periods presented. The per share par value and authorized number of shares of the Company's common stock were not adjusted as a result of the reverse stock split.

Upon the closing of the IPO, all of the Company's then-outstanding shares of convertible preferred stock converted into 11,140,262 shares of common stock at the applicable conversion ratio then in effect. Subsequent to the closing of the IPO, there were no shares of convertible preferred stock outstanding.

The Company also completed a private placement which closed concurrently with the IPO, in which the Company issued and sold 400,000 shares of its common stock at $12.50 per share to Chione Limited, an existing investor of the Company (the "Concurrent Private Placement"). The Company received aggregate net proceeds of $4.7 million from the Concurrent Private Placement, after deducting the placement agent fee.

2. Summary of Significant Accounting Policies

Basis of Presentation and Consolidation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP") and include the operations of Acrivon Therapeutics, Inc. and its wholly-owned subsidiaries. All intercompany accounts, transactions and balances have been eliminated in consolidation.

Use of Estimates

The preparation of the Company's consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the accrual of research and development expenses and the valuation of stock-based awards. The Company bases its estimates on historical experience when available, known trends and other market specific data, or other relevant factors that it believes to be reasonable under the circumstances. On an ongoing basis, management evaluates its estimates when there are changes in circumstances, facts and experience. Changes in estimates and assumptions are reflected in reported results in the period in which they become known. Actual results could differ from those estimates.

Segment Information

Operating segments are defined as components of an enterprise for which separate and discrete information is available for evaluation by the chief operating decision-maker in deciding how to allocate resources and assess performance. The Company has one operating segment. The Company's focus is the research and development of precision oncology therapies. The Company's chief operating decision maker, its chief executive officer, manages the Company's operations on a consolidated basis for the purpose of allocating resources. As the Company has one reportable segment, all required segment financial information is presented in the consolidated financial statements. As of December 31, 2023, $5.7 million and $2.2 million of the Company's long-lived assets are held in the United States and in Sweden, respectively.

Cash and Cash Equivalents

The Company considers all highly liquid investments purchased with original maturities of 90 days or less at acquisition to be cash equivalents. Cash and cash equivalents include standard checking accounts and amounts held in money market funds. Periodically, the Company maintains deposits in accredited financial institutions in excess of federally insured limits.

Restricted Cash

Cash accounts with any type of restriction are classified as restricted cash. The Company has restricted cash deposits with a bank, which serve as collateral for a letter of credit issued to the landlord of the Company's leased facility for a security deposit. The Company classified this amount as restricted cash in the accompanying consolidated balance sheets within non-current assets based on the release date of restrictions.

Deferred Offering Costs

The Company capitalizes certain legal, professional accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After consummation of an equity financing, these costs are recorded as a reduction of the proceeds from the offering in stockholders' equity as a reduction of additional paid-in capital generated as a result of the offering. Should the Company choose to not initiate such financing, the deferred offering costs would be immediately expensed as operating expenses.

Deferred offering costs associated with the ATM Program are reclassified to additional paid-in-capital on a pro-rata basis when the Company completes offerings under the ATM Program. Any remaining deferred offering costs will be expensed to the consolidated statements of operations and comprehensive loss should the planned offering be abandoned. As of December 31, 2023, $0.3 million of such deferred offering costs are capitalized.

Concentration of Credit Risk and Significant Suppliers

Financial instruments that potentially subject the Company to concentrations of credit risk consist principally of cash, cash equivalents and investments. The Company has not experienced any credit losses on its cash, cash equivalents, or investments. The Company maintains its cash, cash equivalents and investments, which at times exceed insurance limits, at major financial institutions. The Company has not experienced any losses in such accounts and management believes that such funds are not exposed to any significant credit or concentration risk. However, the Company may face exposure, including constraint on liquidity and access to capital, if there is failure by these or other financial institutions.

The Company is dependent on third-party contract research organizations ("CROs") and contract manufacturing organizations to supply certain intellectual property and services for research activities in its drug candidates. In particular, the Company relies and expects to continue to rely on a small number of these organizations to supply it with its requirements for key raw materials related to these programs. These drug candidates could be adversely affected by a significant interruption in the supply of key raw materials. Additionally, the Company relies on a single companion diagnostic collaborator to perform ACR-368 OncoSignature tests in the Company's clinical trials (see Note 12).

Comprehensive Loss

Comprehensive loss is defined as a change in equity of a business enterprise during a period resulting from transactions from non-owner sources. Comprehensive loss includes net loss and certain changes in stockholders' equity that are excluded from net loss. The Company had a net change in available-for-sale securities during the years ended December 31, 2023 and 2022, which met the criteria as other comprehensive loss and, therefore, the Company's comprehensive loss includes unrealized gains (losses) on those available-for-sale securities.

Investments

The Company classifies all investments with an original maturity of greater than three months and less than one year upon purchase as available-for-sale. Available-for-sale securities are recorded at fair value based upon market prices at period end, with the unrealized gains and losses reported in other comprehensive loss. The amortized cost of debt securities in this category is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization is included in interest income, presented within other income, net in the consolidated statements of operations and comprehensive loss. Realized gains and losses and declines in value due to credit-related factors on available-for-sale securities are included in other income, net in the consolidated statements of operations and comprehensive loss. The cost of securities sold is based on the specific identification method. Interest on securities classified as available-for-sale is included in interest income, presented within other income, net in the consolidated statements of operations and comprehensive loss. For the years ended December 31, 2023 and 2022, other income, net, of $6.7 million and $1.5 million, respectively, included interest income of $7.0 million and $1.5 million, respectively, offset by de minimis miscellaneous items.

At each balance sheet date, the Company assesses available-for-sale debt securities in an unrealized loss position to determine whether the unrealized loss or any potential credit losses should be recognized in other income, net. The Company evaluates whether it intends to sell, or it is more likely than not that it will be required to sell, the security before recovery of its amortized cost basis. The

Company also evaluates whether the decline in fair value has resulted from credit losses or other factors. In making this assessment, the Company considers the severity of the impairment, any changes in interest rates, changes to the underlying credit ratings and forecasted recovery, among other factors. The credit-related portion of unrealized losses, and any subsequent improvements, are recorded in other income, net. There have been no impairment or credit losses recognized during any of the periods presented.

Fair Value Measurements

Accounting Standards Codification ("ASC") Topic 820, *Fair Value Measurement* ("ASC 820"), establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability and are developed based on the best information available in the circumstances.

ASC 820 identifies fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 establishes a three-tier fair value hierarchy that distinguishes among the following:

Level 1—Quoted prices in active markets for identical assets or liabilities.

Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.

Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Property and Equipment, net

Property and equipment are stated at cost, less accumulated depreciation. Costs for capital assets not yet placed in service are capitalized as construction in progress and depreciated once placed in service. Costs of major additions and betterments are capitalized. Maintenance and repairs which do not improve or extend the life of the respective assets are charged to expense as incurred. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets, which range from five to seven years. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the related asset. The Company's leasehold improvements as of December 31, 2023 were de minimis. The Company had no leasehold improvements as of December 31, 2022. When an item is sold or retired, the costs and related accumulated depreciation are eliminated, and the resulting gain or loss, if any, is credited or charged to the consolidated statements of operations and comprehensive loss. Property and equipment to be disposed of are carried at fair value less costs to sell. The estimated useful lives of the Company's property and equipment are as follows:

	Estimated Useful Life (in Years)
Laboratory equipment and computer equipment	5 years
Furniture and fixtures	5-7 years
Leasehold improvements	Lesser of asset useful life or lease term

Impairment of Long-Lived Assets

The Company recognizes an impairment loss in the consolidated statements of operations and comprehensive loss only if the carrying amount of a long-lived asset is not recoverable based on its undiscounted future cash flows and in such case, measures an impairment loss as the difference between the carrying amount and the fair value of the asset.

The Company tests long-lived assets to be held and used, including property and equipment and operating lease right-of-use ("ROU") assets, for impairment whenever events or changes in circumstances indicate that the carrying amount of assets or asset groups may not be fully recoverable. Determination of recoverability is based on an estimate of undiscounted future cash flows resulting from the use of the asset and its eventual disposition. In the event that such cash flows are not expected to be sufficient to recover the carrying

amount of the assets, the assets are written down to their fair values. The Company has not recognized any impairment losses during the years ended December 31, 2023 and 2022.

Research and Development Expenses

Research and development costs include (i) employee-related expenses, including salaries, benefits, and stock-based compensation expense; (ii) external research and development expenses incurred under arrangements with third parties, such as CRO agreements and consultants; (iii) costs associated with preclinical activities; and (iv) lab supplies, lab expenses and an allocation of rent, depreciation, and infrastructure. Costs incurred in connection with research and development activities are expensed as incurred.

The Company enters into various consulting, research, and other agreements with commercial firms, researchers, universities and other external parties for the provision of goods and services. Such arrangements are generally cancelable upon reasonable notice and payment of costs incurred.

Costs are considered incurred based on an evaluation of the progress to completion of specific tasks under each contract using information and data provided by the Company's clinical sites and vendors. These costs consist of direct and indirect costs associated with specific projects, as well as fees paid to various entities that perform certain research on behalf of the Company. Depending upon the timing of payments to the service providers, the Company recognizes prepaid expenses or accrued expenses related to these costs. These accrued or prepaid expenses are based on management's estimates of the work performed under service agreements, milestones achieved, and experience with similar contracts. Milestone payments under license agreements are accrued, with a corresponding expense being recognized, in the period in which the milestone is determined to be probable of achievement and the related amount is reasonably estimable. The Company monitors each of these factors and adjusts estimates accordingly. The Company has not experienced any material differences between accrued costs and actual costs incurred since its inception.

Asset Acquisitions and Acquired In-Process Research and Development Expenses

The Company accounts for acquisitions of assets or a group of assets that do not meet the definition of a business as asset acquisitions based on the cost to acquire the asset or group of assets, which include certain transaction costs. In an asset acquisition, the cost to acquire is allocated to the identifiable assets acquired and liabilities assumed based on their relative fair values as of the acquisition date. No goodwill is recorded in an asset acquisition. Assets that are acquired in an asset acquisition for use in research and development activities that have an alternative future use are capitalized as in-process research and development ("IPR&D"). Acquired IPR&D that has no alternative future use as of the acquisition date is recognized as research and development expense as of the acquisition date. The Company will recognize additional research and development expenses in the future if and when the Company becomes obligated to make contingent milestone payments under the terms of the agreements by which it acquired the IPR&D assets.

Contingent consideration in asset acquisitions is measured and recognized when payment becomes probable and reasonably estimable. Subsequent changes in the accrued amount of contingent consideration are measured and recognized at the end of each reporting period and upon settlement as an adjustment to the cost basis of the acquired asset or group of assets, or, if related to IPR&D with no alternative future use, charged to expense. The Company did not recognize any IPR&D expense for the years ended December 31, 2023 and 2022.

Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications such as direct application fees, and legal and consulting expenses are expensed as incurred due to the uncertainty about the recovery of the expenditure. Patent-related costs are classified as general and administrative expenses within the Company's consolidated statements of operations and comprehensive loss.

Foreign Currency Transactions

The functional currency for the Company's wholly-owned foreign subsidiary, Acrivon AB, is the United States dollar. All foreign currency transaction gains and losses are recognized in the consolidated statements of operations and comprehensive loss through other income, net. The Company recognized a net foreign currency transaction gain of $0.1 million during the year ended December 31, 2023, which is primarily related to unrealized and realized foreign currency gains and losses as a result of transactions entered into by Acrivon AB in currencies other than the United States dollar. The Company did not recognize any material foreign currency transaction gain or loss during the year ended December 31, 2022.

Leases

Effective on January 1, 2021, the Company accounts for leases in accordance with Accounting Standards Update ("ASU") No. 2016-02, *Leases*, as subsequently amended (collectively, "ASC 842"). In accordance with ASC 842, the Company determines whether an arrangement is or contains a lease at inception. A contract is or contains a lease if the contract conveys the right to control the use of an identified asset for a period of time in exchange for consideration. The Company classifies leases at the lease commencement date, when control of the underlying asset is transferred from the lessor to the lessee, as operating or finance leases and records a ROU asset and a lease liability on the consolidated balance sheets for all leases with an initial lease term of greater than 12 months. The Company has elected to not recognize leases with a lease term of 12 months or less, but payments are recognized as expense on a straight-line basis over the lease term.

The Company enters into contracts that contain both lease and non-lease components. Non-lease components may include maintenance, utilities, and other operating costs. For leases of real estate, the Company combines the lease and associated non-lease components in its lease arrangements as a single lease component. Variable costs, such as utilities or maintenance costs, are not included in the measurement of right-of-use assets and lease liabilities, but rather are expensed when the event determining the amount of variable consideration to be paid occurs.

Finance and operating lease assets and liabilities are recognized at the lease commencement date based on the present value of the lease payments over the lease term using the discount rate implicit in the lease if readily determinable. If the rate implicit is not readily determinable, the Company utilizes its incremental borrowing rate, which reflects the fixed rate at which the Company could borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment. ROU assets are further adjusted for initial direct costs, prepaid rent, or incentives received. Operating lease payments are expensed using the straight-line method as an operating expense over the lease term. The Company's lease terms may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. Finance lease assets are amortized to depreciation expense using the straight-line method over the shorter of the useful life of the related asset or the lease term. Finance lease payments are bifurcated into (i) a portion that is recorded as interest expense using the effective interest method and (ii) a portion that reduces the finance liability associated with the lease.

In addition, the Company examines other contracts with suppliers, vendors and outside parties to identify whether such contracts contain an embedded lease and, as applicable, records such embedded leases in accordance with ASC 842.

Stock-Based Compensation

The Company accounts for all stock-based payment awards granted to employees and non-employees as stock-based compensation expense at fair value, based on the date of the grant, and recognizes compensation expense for those awards over the requisite service period, which is generally the vesting period of the respective award. The Company's stock-based payments include stock options and grants of common stock. The measurement date for employee awards is the date of grant, and stock-based compensation costs are recognized as expense over the employees' requisite service period, which is the vesting period, on a straight-line basis. The Company adopted ASU No. 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* ("ASU No. 2018-07") at inception of the 2019 Stock Incentive Plan, prior to the issuance of any stock option grants. The measurement date for non-employee awards is the date of grant, and stock-based compensation costs for non-employees are recognized as expense over the vesting period on a straight-line basis. The Company accounts for forfeitures as they occur. Stock-based compensation expense is classified in the accompanying consolidated statements of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipients service payments are classified.

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model, which requires inputs based on certain subjective assumptions. Prior to the IPO, the Company's board of directors ("Board") determined the fair value of the Company's common stock, taking into consideration its most recently available third-party valuations of common stock as well as additional factors which may have changed since the date of the most recent contemporaneous valuation through the grant date. The Company has historically been a private company and lacks company-specific historical and implied volatility information. Following the IPO, the fair value of the Company's common stock is determined based on the quoted market price of common stock. The Company estimates its expected stock volatility based on the historical volatility of a publicly traded set of representative companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. The expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends on common stock and does not expect to pay any cash dividends in the foreseeable future.

Net Loss per Share

Basic net loss per share is computed by dividing net loss by the weighted-average number of common shares outstanding during the period. Diluted net loss per share is computed using the weighted-average number of common shares outstanding during the period and, if dilutive, the weighted-average number of potential shares of common stock. Net loss per share attributable to common stockholders is calculated using the two-class method, which is an earnings allocation formula that determines net loss per share for the holders of the Company's common shares and participating securities. The Company's convertible preferred stock contained participation rights in any dividend paid by the Company and was deemed to be a participating security. Net loss attributable to common stockholders and participating preferred shares, if any, are allocated to each share on an as-converted basis as if all of the earnings for the period had been distributed. The participating securities did not include a contractual obligation to share in losses of the Company and are not included in the calculation of net loss per share in the periods in which a net loss is recorded.

Diluted net loss per share is computed using the more dilutive of (a) the two-class method or (b) the if-converted method. The Company allocates earnings first to preferred stockholders based on dividend rights and then to common and preferred stockholders based on ownership interests. The weighted-average number of common shares included in the computation of diluted net loss per share gives effect to all potentially dilutive common equivalent shares, including outstanding stock options and preferred stock.

Common stock equivalent shares are excluded from the computation of diluted net loss per share if their effect is antidilutive. In periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders since dilutive common shares are not assumed to have been issued if their effect is antidilutive. The Company reported a net loss attributable to common stockholders for the years ended December 31, 2023 and 2022.

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or the Company's tax returns. Under this method, deferred tax assets and liabilities are determined based on the differences between the consolidated financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established.

The Company accounts for uncertain tax positions recognized in the consolidated financial statements by prescribing a "more likely than not" threshold for financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. There are no unrecognized tax benefits included in the Company's consolidated balance sheets as of December 31, 2023 and 2022. The Company's policy is to recognize interest and penalties related to income tax matters in income tax expense. The Company has not recognized interest or penalties in its consolidated statements of operations and comprehensive loss since inception.

Recently Adopted Accounting Pronouncements

ASU 2016-13, Financial Instruments–Credit Losses

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments–Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"), and also issued subsequent amendments to the initial guidance: ASU 2018-19, ASU 2019-04, ASU 2019-05, ASU 2020-02 and ASU 2020-03 (collectively, "Topic 326"). Topic 326 significantly changes the impairment model for most financial assets and certain other instruments. Topic 326 requires immediate recognition of estimated credit losses expected to occur over the remaining life of many financial assets, which will generally result in earlier recognition of allowances for credit losses on loans and other financial instruments. The measurement is based on relevant information, including historical experience, current conditions and reasonable and supportable forecasts that affect the collectability of the reported amount and requires disclosure requirements related to credit risks. The Company adopted this accounting standard as of January 1, 2023, with no material impact on its consolidated financial statements and related disclosures.

Recently Issued Accounting Pronouncements Not Yet Adopted

ASU 2023-06, *Disclosure Improvements*

In October 2023, the FASB issued ASU 2023-06, *Disclosure Improvements: Codification Amendments in Response to the SEC's Disclosure Update and Simplification Initiative.* The amendments clarify or improve disclosure and presentation requirements on

various disclosure areas, including the statement of cash flows, earnings per share, debt, equity, and derivatives. The amendments will align the requirements in the FASB ASC with the SEC's regulations. The amendments in this ASU will be effective on the date the related disclosures are removed from Regulation S-X or Regulation S-K by the SEC, and will not be effective if the SEC has not removed the applicable disclosure requirement by June 30, 2027. Early adoption is prohibited. As the Company is currently subject to these SEC requirements, ASU 2023-06 is not expected to have a significant impact on the Company.

ASU 2023-07, Segment Reporting (Topic 280)

In November 2023, the FASB issued ASU 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures,* which requires public entities to disclose information about their reportable segments' significant expenses on an interim and annual basis. All disclosure requirements under ASU 2023-07 are also required for public entities with a single reportable segment. The ASU is effective for annual periods beginning after December 15, 2024 and for interim periods within fiscal years beginning after December 15, 2025. Early adoption is permitted. The Company is currently evaluating the effect of this update on its consolidated financial statements and related disclosures.

ASU 2023-09, Income Taxes (Topic 740)

In December 2023, the FASB issued ASU 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures*, which requires disclosure of disaggregated income taxes paid, prescribes standard categories for the components of the effective tax rate reconciliation, and modifies other income tax-related disclosures. The ASU is effective for annual periods beginning after December 15, 2024 and allows for adoption on a prospective basis, with a retrospective option. The Company is currently evaluating the effect of this update on its consolidated financial statements and related disclosures.

3. Investments

The following table summarizes the amortized cost and estimated fair value of the Company's U.S. Treasury securities and U.S. government-sponsored enterprise securities, which are considered to be available-for-sale investments and were included in short-term investments as of December 31, 2023 and in short and long-term investments as of December 31, 2022 (in thousands):

	December 31, 2023			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Short-term investments:				
U.S. Treasury securities	$ 41,470	$ 22	$ (19)	$ 41,473
U.S. government-sponsored enterprise securities	50,056	—	(86)	49,970
	$ 91,526	$ 22	$ (105)	$ 91,443

	December 31, 2022			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Short-term investments:				
U.S. Treasury securities	$ 32,174	$ 3	$ (34)	$ 32,143
U.S. government-sponsored enterprise securities	66,106	68	(85)	66,089
Long-term investments:				
U.S. Treasury securities	7,242	—	(4)	7,238
U.S. government-sponsored enterprise securities	34,686	—	(43)	34,643
	$ 140,208	$ 71	$ (166)	$ 140,113

Certain short-term debt securities with original maturities of less than 90 days are included in cash and cash equivalents on the consolidated balance sheets and are not included in the tables above. As of December 31, 2023 and 2022, all short-term investments had contractual maturities within one year. As of December 31, 2022, all long-term investments had contractual maturities between one to two years.

The aggregate fair value of available-for-sale securities held by the Company in an unrealized loss position for less than 12 months as of December 31, 2023 was $59.9 million. The unrealized losses on the Company's investments of $0.1 million and $0.2 million as of December 31, 2023 and 2022, respectively, were caused by interest rate increases which resulted in the decrease in market value of these securities. There were no available-for-sale securities in a continuous unrealized loss position for greater than 12 months. Because the decline in fair value is attributable to changes in interest rates and not credit quality, and because the Company does not intend to sell the investments and it is not more likely than not that the Company will be required to sell the investments before recovery of their amortized cost bases, which may be maturity, there are no allowances for credit losses as of December 31, 2023.

4. Fair Value Measurement

The following tables present information about the Company's financial assets measured at fair value on a recurring basis (in thousands):

		Fair Value Measurements at December 31, 2023 Using:		
Assets:	**Total**	**Level 1**	**Level 2**	**Level 3**
Cash equivalents:				
Money market funds	$ 31,191	$ 31,191	$ —	$ —
Short-term investments:				
U.S. Treasury securities	41,473	41,473	—	—
U.S. government-sponsored enterprise securities	49,970	—	49,970	—
Total assets	$ 122,634	$ 72,664	$ 49,970	$ —

		Fair Value Measurements at December 31, 2022 Using:		
Assets:	**Total**	**Level 1**	**Level 2**	**Level 3**
Cash equivalents:				
Money market funds	$ 24,082	$ 24,082	$ —	$ —
Short-term investments:				
U.S. Treasury securities	32,143	32,143	—	—
U.S. government-sponsored enterprise securities	66,089	—	66,089	—
Long-term investments:				
U.S. Treasury securities	7,238	7,238	—	—
U.S. government-sponsored enterprise securities	34,643	—	34,643	—
Total assets	$ 164,195	$ 63,463	$ 100,732	$ —

The Company classifies its money market funds and U.S. Treasury securities as Level 1 assets under the fair value hierarchy as these assets have been valued using quoted market prices in active markets without any valuation adjustment. The Company classifies its U.S. government-sponsored enterprise securities as Level 2 assets under the fair value hierarchy as these assets have been valued using information obtained through a third-party pricing service as of the balance sheet date, using observable market inputs that may include trade information, broker or dealer quotes, bids, offers, or a combination of these data sources.

During the years ended December 31, 2023 and 2022, there were no transfers between levels. The Company uses the carrying amounts of its restricted cash, prepaid expenses and other current assets, accounts payable and accrued expenses to approximate their fair values due to the short-term nature of these amounts.

5. Property and Equipment, net

Property and equipment, net consisted of the following (in thousands):

	December 31,	
	2023	**2022**
Laboratory and computer equipment	$ 2,955	$ 2,340
Furniture and fixtures	172	172
Construction in progress	1,308	—
Total property and equipment	4,435	2,512
Less: accumulated depreciation	(956)	(420)
Property and equipment, net	$ 3,479	$ 2,092

Depreciation expense related to property and equipment for the years ended December 31, 2023 and 2022 was $0.5 million and $0.4 million, respectively.

6. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31,	
	2023	2022
Accrued compensation and benefits	$ 3,860	$ 2,662
Accrued research and development expenses	2,661	790
Accrued legal, accounting and other professional fees	667	648
Accrued other	190	44
Accrued offering costs	—	673
Deferred sublease income	—	69
Total accrued expenses and other current liabilities	$ 7,378	$ 4,886

7. Leases

In September 2020, the Company entered into an operating lease agreement, denominated in Swedish Krona, for office and laboratory space located in Lund, Sweden. The term of the lease commenced in October 2020 and expired in September 2023, with an option to extend the term for an additional three years. In September 2023, the Company modified the lease agreement. The modification extended the lease term for an additional quarter, resulting in a de minimis impact to the ROU asset and corresponding lease liability.

In December 2020, the Company entered into a lease agreement for laboratory and office space located at 480 Arsenal Way, Watertown, Massachusetts (the "Arsenal Way Lease"). The term of the lease commenced in April 2021. The lease has an initial term from the rent commencement date, which is a month after the lease commencement date, of approximately seven years, with an option to extend the term for an additional five years at then-market rental rates. In connection with the execution of the lease agreement, the Company delivered a letter of credit of $0.3 million to the landlord, which is included in restricted cash in the accompanying consolidated balance sheets. The landlord contributed an aggregate of $0.7 million toward the cost of tenant improvements for the premises. Under the terms of the lease, the base rent is $1.0 million, subject to a 3% annual rent increase, plus an allocation of operating expenses and taxes.

In May 2021, the Company entered into an agreement to sublease 6,330 rentable square feet of its Arsenal Way Lease to a subtenant through March 2023. Sublease income was recognized on a straight-line basis over the term of the sublease agreement. Sublease rent income, including common area maintenance charges, was $0.2 million and $0.8 million for the years ended December 31, 2023 and 2022, respectively, which was allocated and recorded as a reduction to general and administrative expenses and research and development expenses. The Company was not relieved of its primary obligation under the Arsenal Way Lease as a result of the sublease.

In August 2023, the Company entered into an operating lease agreement, denominated is Swedish Krona, for office and laboratory space located in Lund, Sweden. The term of the lease commenced in December 2023. The lease has an initial term of three years, with an option to extend the term for an additional three years. Lease payments are made on a quarterly basis.

The Company recognizes monthly operating lease expense on a straight-line basis over the term of the lease as research and development or general and administrative expenses in the consolidated statements of operations and comprehensive loss. Variable lease expense relates primarily to office lease common area maintenance, insurance, and property taxes, is expensed as incurred, and is excluded from the calculation of the lease liabilities and right-of-use-assets.

The following table summarizes the presentation of the Company's operating leases on its consolidated balance sheets (in thousands):

Leases	Balance sheet classification	December 31, 2023	December 31, 2022
Assets:			
Operating lease assets	Operating lease right-of-use assets	$ 4,429	$ 4,770
Total lease assets		$ 4,429	$ 4,770
Liabilities:			
Current:			
Operating lease liabilities	Operating lease liability, current	$ 877	$ 726
Noncurrent:			
Operating lease liabilities	Operating lease liability, long-term	3,767	4,235
Total lease liabilities		$ 4,644	$ 4,961

The components of lease cost under ASC 842 included within research and development expenses and general and administrative expenses in the Company's consolidated statements of operations and comprehensive loss were as follows (in thousands):

	For the Year Ended December 31,	
Lease cost	2023	2022
Operating lease cost	$ 1,140	$ 1,143
Variable lease cost	492	519
Sublease income	(134)	(537)
Total lease cost	$ 1,498	$ 1,125

As of December 31, 2023 and 2022, the weighted-average remaining lease term for operating leases was 4.2 years and 5.3 years, respectively, and the weighted-average discount rate was 8.30% and 7.86%, respectively. Cash paid for amounts included in the measurement of lease liabilities was $1.1 million for each of the years ended December 31, 2023 and 2022.

Future minimum annual lease commitments under the Company's non-cancelable operating leases as of December 31, 2023 were as follows (in thousands):

Year ended December 31,	Amount
2024	$ 1,221
2025	1,315
2026	1,349
2027	1,200
2028	404
Total lease payments	5,489
Less: interest	(845)
Present value of operating lease liabilities	$ 4,644

8. Stockholders' Equity

Prior to the IPO, the voting, dividend and liquidation rights of the holders of the Company's common stock were subject to and qualified by the rights, powers and preferences of the holders of the Preferred Stock as set forth above and described in the Company's final prospectus for the IPO filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act on November 16, 2022.

In October 2022, the Board approved the amended and restated certificate of incorporation, which was filed upon the closing of the IPO and which authorized the Company to issue up to 10,000,000 shares of preferred stock, with a par value of $0.001. There are no shares of preferred stock issued or outstanding as of December 31, 2023.

As of December 31, 2023 and 2022, the Company's Amended and Restated Certificate of Incorporation authorized the Company to issue 500,000,000 shares of common stock, with a par value of $0.001.

The holders of the common stock are entitled to one vote for each share of common stock held at all meetings of stockholders (and written actions in lieu of meetings), and there are not any cumulative voting rights. The number of authorized shares of common stock may be increased or decreased by the affirmative vote of the holders of shares of capital stock of the Company; however, the

issuance of common stock may be subject to the vote of the holders of one or more series of preferred stock that may be required by terms of the Amended and Restated Certificate of Incorporation.

As of December 31, 2023 and 2022, the Company had reserved the following shares of common stock for the potential exercise of stock options, vesting of restricted stock units, as well as the remaining shares available for issuance under the 2022 Stock Option Incentive Plan (the "2022 Plan"), the 2022 Employee Stock Purchase Plan (the "2022 ESPP"), and the 2023 Inducement Plan (the "Inducement Plan"):

	December 31,	
	2023	2022
Options to purchase common stock	3,117,042	3,300,935
Unvested restricted stock units	1,759,918	1,787,152
Remaining shares reserved for future issuance	2,107,745	733,636
Total	6,984,705	5,821,723

9. Stock-Based Compensation

2022 Equity Incentive Plan

In October 2022, the Board adopted, and in November 2022 its stockholders approved, the 2022 Plan, which replaced the 2019 Plan and became effective immediately prior to and contingent upon the execution of the underwriting agreement related to the Company's IPO. No further shares were issued under the 2019 Plan as of the effective date of the 2022 Plan. The 2022 Plan allows the Company to make equity-based and cash-based incentive awards to its officers, employees, directors, and consultants. The 2022 Plan provides for the grant of incentive stock options, non-qualified stock options, stock appreciation rights, restricted stock awards, restricted stock units ("RSUs") and other stock-based awards. The number of shares initially reserved for issuance under the 2022 Plan was 5,606,723, which is the sum of: (i) 2,555,271 new shares, plus (ii) the number of shares that remained available for issuance under the 2019 Plan at the time the 2022 Plan became effective and (iii) up to 2,148,679 shares of common stock subject to awards granted under the 2019 Plan that, after the effective date of the 2022 Plan, expire or otherwise terminate without having been exercised in full or are forfeited to or repurchased. In addition, the number of shares reserved and available for issuance under the 2022 Plan shall automatically increase beginning on January 1, 2023 and each January 1 thereafter, by five percent of the aggregate number of shares of common stock of all classes issued and outstanding on the immediately preceding December 31 or such lesser number of shares of common stock as determined by the compensation committee.

The shares of common stock underlying any awards under the 2022 Plan and the 2019 Plan that are forfeited, canceled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, reacquired by the Company prior to vesting, satisfied without the issuance of stock, expire, or are otherwise terminated (other than by exercise) will be added back to the shares of common stock available for issuance under the 2022 Plan.

As of December 31, 2023, there were 1,369,341 shares reserved for future issuance under the 2022 Plan.

2022 Employee Stock Purchase Plan

In October 2022, the Board adopted, and in November 2022 its stockholders approved, the 2022 ESPP, which became effective immediately prior to and contingent upon the execution of the underwriting agreement related to the Company's IPO. A total of 215,000 shares of common stock were initially reserved for issuance under this plan. The number of shares of common stock that may be issued under the 2022 ESPP shall cumulatively increase beginning on January 1, 2023 and each January 1 thereafter through January 1, 2032, by one percent of the outstanding number of shares of common stock on the immediately preceding December 31 or such lesser number of shares as determined by the compensation committee.

No shares of the Company's common stock have been issued and no stock-based compensation expense has been recognized related to the 2022 ESPP. As of December 31, 2023, there were 434,204 shares reserved for future issuance under the 2022 ESPP.

2023 Inducement Plan

In June 2023, the Board adopted the Inducement Plan to facilitate the granting of equity awards as an inducement material to new employees joining the Company. The Inducement Plan is administered by the compensation committee of the Board. The Board initially reserved 450,000 common shares of the Company for issuance under the Inducement Plan. The only persons eligible to receive awards under the Inducement Plan are individuals who are new employees and satisfy the standards for inducement grants under Nasdaq Listing

Rule 5635(c)(4) or 5635(c)(3), as applicable. The terms of the Inducement Plan are identical to the terms of the 2022 Plan, except that no incentive stock options shall be awarded under the Inducement Plan.

As of December 31, 2023, there were 304,200 shares reserved for future issuance under the Inducement Plan.

Stock Options

The Company has granted stock options with service-based vesting conditions. Stock options typically vest over four years and have a maximum term of ten years. The Company typically grants stock options to employees and non-employees at exercise prices deemed by the Board to be equal to the fair value of the common stock at the time of grant.

The assumptions that the Company used in the Black-Scholes option-pricing model to determine the grant date fair value of stock options granted were as follows:

	December 31,	
	2023	2022
Risk-free interest rate range	3.40% - 4.84%	2.69% - 4.15%
Dividend yield	0.00%	0.00%
Expected life of options (years)	5.8 - 6.1	5.8 - 6.1
Volatility rate range	81.63% - 83.55%	71.06% - 82.54%
Fair value of common stock range	$3.89 - $20.50	$3.63 - $12.50

The following table summarizes the Company's stock option activity:

	Number of Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2022	3,300,935	$ 6.29	9.26	$ 18,346
Granted	297,556	10.43		
Exercised	(292,444)	2.65		
Forfeited or canceled	(189,005)	6.12		
Outstanding as of December 31, 2023	3,117,042	$ 7.04	8.34	$ 3,409
Vested and expected to vest as of December 31, 2023	3,117,042	$ 7.04	8.34	$ 3,409
Vested and exercisable as of December 31, 2023	1,313,352	$ 5.08	7.86	$ 2,342

Included in the table above are 123,825 options outstanding as of December 31, 2023 that were granted under the Inducement Plan.

The aggregate intrinsic value of options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those stock options that had exercise prices lower than the fair value of the common stock as of the end of the reporting period. The aggregate intrinsic value of options exercised during the years ended December 31, 2023 and 2022 was $2.1 million and $0.1 million, respectively.

The weighted-average grant date fair value of the Company's stock options granted during the years ended December 31, 2023 and 2022 was $7.59 and $5.52 per option, respectively. As of December 31, 2023, there was $10.5 million of unrecognized stock-based compensation expense related to stock option grants. The Company expects to recognize this amount over a weighted-average period of 2.5 years.

The total fair value of options vested during the years ended December 31, 2023 and 2022, was $4.2 million and $0.5 million, respectively.

RSUs

The Company has granted RSUs with service vesting based conditions. Unvested shares of restricted common stock may not be sold or transferred by the holder. They are legally issued and outstanding. These restrictions lapse according to the time-based vesting of each award.

A summary of the RSU activity during the year ended December 31, 2023 is as follows:

	Restricted Stock Units	Weighted-Average Grant Date Fair Value
Unvested at December 31, 2022	1,787,152	$ 12.49
Granted	563,060	$ 11.20
Vested	(566,260)	$ 12.52
Forfeited	(24,034)	$ 10.86
Unvested at December 31, 2023	1,759,918	$ 12.09

Included in the table above are 21,975 unvested RSUs as of December 31, 2023 that were granted under the Inducement Plan.

RSUs typically vest over four years. If and when an RSU vests, the Company will issue one share of common stock for each whole RSU that has vested, subject to satisfaction of the employee's tax withholding obligations. Upon vesting and settlement of RSUs, the Company may withhold the portion of those shares with a fair market value equal to the amount of the minimum statutory withholding taxes due. The withheld shares are accounted for as repurchases of common stock.

The weighted-average grant date fair value of the Company's RSUs granted during the years ended December 31, 2023 and 2022 was $11.20 and $12.49 per RSU, respectively. As of December 31, 2023, there was $19.6 million of unrecognized stock-based compensation expense related to RSUs. The Company expects to recognize this amount over a weighted-average period of 2.3 years.

The total fair value of RSUs vested during the year ended December 31, 2023 was $7.1 million. No RSUs vested in 2022.

Stock-Based Compensation Expense

Stock-based compensation expense included in the Company's consolidated statements of operations and comprehensive loss is as follows (in thousands):

	Year Ended December 31,	
	2023	2022
General and administrative	$ 9,089	$ 1,396
Research and development	2,529	789
Total stock-based compensation expense	$ 11,618	$ 2,185

10. Income Taxes

The effective income tax rate differed from the amount computed by applying the federal statutory rate to the Company's loss before income taxes as follows:

	December 31,	
	2023	2022
Tax effected at statutory rate	21.0%	21.0%
State taxes	6.0%	7.0%
Stock-based compensation	(1.3%)	(0.5%)
Executive compensation	(1.7%)	(0.7%)
Federal research and development credits	4.4%	1.3%
Change in valuation allowance	(28.5%)	(28.1%)
Total	(0.1%)	—%

The Company's total deferred tax assets at December 31, 2023 and 2022 are as follows (in thousands):

	December 31,	
	2023	2022
Deferred Tax Assets		
Net operating loss carryforward	$ 9,395	$ 6,137
R&D credit carryovers	3,985	1,015
Section 174 R&D amortization	13,819	5,093
Operating lease liabilities	1,134	1,309
Accrued expenses and other current liabilities	919	528
Capitalized licenses	3,482	2,039
Other	554	226
	33,288	16,347
Valuation allowance	(31,761)	(14,562)
Deferred tax asset	1,527	1,785
Deferred Tax Liabilities		
Property and equipment	(457)	(531)
Operating lease right-of-use assets	(1,070)	(1,254)
Deferred tax liability	(1,527)	(1,785)
Net deferred tax asset	$ —	$ —

The Company has had no income tax expense due to operating losses incurred since inception. ASC 740, *Income Taxes*, requires a valuation allowance to reduce the deferred tax assets reported if, based on the weight of the evidence, it is more-likely-than-not that some portion or all of the deferred tax assets will not be realized. The Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. Based on this, the Company has provided a valuation allowance for the full amount of the net deferred tax assets as the realization of the deferred tax assets is not determined to be more likely than not. During 2023, the valuation allowance increased by $17.2 million primarily due to the increase in the Company's book loss reported in the period and the generation of additional research and development credits.

As of December 31, 2023, the Company had $33.0 million and $35.3 million of federal and state operating loss carryforwards (“NOLs”), respectively. The federal NOLs are not subject to expiration and the state NOLs begin to expire in 2038. These loss carryforwards are available to reduce future federal taxable income, if any. As of December 31, 2023, the Company also has federal and state research and development tax credit carryforwards of approximately $3.1 million and $1.2 million, respectively, to offset future income taxes, which will begin to expire beginning in December 2033. These loss carryforwards are subject to review and possible adjustment by the appropriate taxing authorities. The amount of loss carryforwards that may be utilized in any future period may be limited based upon changes in the ownership of the Company's ultimate parent.

The 2017 Tax Cuts and Jobs Act (“TCJA”) included a multitude of tax provisions, including several deferred changes that became effective for tax years ending after December 31, 2021. Included in the provisions was the TCJA’s amendment to Section 174, which now requires U.S.-based and non-U.S-based research and experimental (“R&E”) expenditures to be capitalized and amortized over a period of five or 15 years, respectively, for amounts paid in tax years starting after December 31, 2021. Prior to the TCJA amendment, Section 174 allowed taxpayers to either immediately deduct R&E expenditures in the year paid or incurred. The Company has applied this required change in accounting method beginning in 2022.

On December 18, 2015, the Protecting Americans from Tax Hikes (“PATH”) Act of 2015 was signed into law. The PATH Act has created several R&D credit provisions, including allowing qualified small business to utilize the research credit against the employer portion of payroll tax (i.e., FICA tax) not exceeding $500,000 per year. The Company does not qualify as a small business for 2023 due to gross receipts exceeding $5.0 million.

The Company follows the provisions of ASC 740-10, *Accounting for Uncertainty in Income Taxes*, which specifies how tax benefits for uncertain tax positions are to be recognized, measured, and recorded in financial statements; requires certain disclosures of uncertain tax matters; specifies how reserves for uncertain tax positions should be classified on the consolidated balance sheets; and provides transition and interim period guidance, among other provisions. As of December 31, 2023 and 2022, the Company has not recorded tax reserves associated with any unrecognized tax benefits. The Company’s policy is to recognize interest and penalties accrued on any uncertain tax positions as a component of income tax expense, if any, in its consolidated statements of operations and comprehensive loss. As of December 31, 2023, and 2022, the Company had no reserves for uncertain tax positions. For the years ended December 31, 2023 and 2022, no estimated interest or penalties were recognized on uncertain tax positions.

The Company has not conducted a study of its research and development credit carryforwards. This study may result in an adjustment to research and development credit carryforwards; however, until a study is completed, and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the consolidated balance sheets or consolidated statements of operations and comprehensive loss if an adjustment were required.

The Company's federal and Massachusetts income tax returns for the years ended December 31, 2020 to December 31, 2023 remain open and are subject to examination by the Internal Revenue Service and state taxing authorities. In addition, the Company's tax carryover attributes such as net operating losses or credits from earlier periods are also subject to examination.

11. Net Loss Per Share

Basic and diluted net loss per share attributable to common stockholders was calculated as follows (in thousands, except share and per share amounts):

	December 31,	
	2023	2022
Numerator:		
Net loss attributable to common stockholders—basic and diluted	$ (60,388)	$ (31,167)
Denominator:		
Weighted-average common stock outstanding—basic and diluted	22,078,190	4,121,912
Net loss per share—basic and diluted	$ (2.74)	$ (7.56)

The Company's potentially dilutive securities, which include stock options and RSUs, have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted-average number of common shares outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same. The Company excluded the following shares from the computation of diluted net loss per share attributable to common stockholders as of December 31, 2023 and 2022 because including them would have had an anti-dilutive effect:

	December 31,	
	2023	2022
Options to purchase common stock	3,117,042	3,300,935
Unvested restricted stock units	1,759,918	1,787,152

12. Commitments and Contingencies

Leases

The Company's commitments under its operating leases are described in Note 7.

License Agreement

In January 2021, the Company entered into a license agreement and stock issuance agreement with Eli Lilly and Company ("Lilly") (collectively, the "Lilly Agreement"), pursuant to which the Company has been granted an exclusive, royalty-bearing sublicensable license to certain patents owned or controlled by Lilly, to commercially develop, manufacture, use, distribute and sell therapeutic products containing the compound prexasertib. The license from Lilly comprises three families of patent filings all relating to ACR-368. Additionally, pursuant to the Lilly Agreement, the Company received ACR-368 drug substance and drug product to be used in future research.

As initial consideration for the license, the Company made a one-time, non-creditable, non-refundable upfront payment of $5.0 million. As additional consideration for the license, the Company is required to pay Lilly aggregate development and commercial milestone payments of up to $168.0 million, of which $5.0 million is due prior to a new drug application.

The Company is also obligated to pay a tiered percentage royalty on annual net sales ranging from single-digit up to a maximum of 10%, subject to certain specified reductions. Royalties are payable by the Company on a licensed product-by-licensed product and country-by-country basis until the later of the expiration of the last valid claim covering the licensed product in such country, expiration of all applicable regulatory exclusivities in such country for such licensed product and the tenth anniversary of the first commercial sale

of such licensed product in such country, provided, that the Company's obligation to pay royalties for a given licensed product in a given country will expire earlier upon achievement of certain sales thresholds by generic products in such country.

As of December 31, 2023, no milestone payments or royalties have been incurred related to the Lilly Agreement.

Companion Diagnostic Agreement

In June 2022, the Company entered into a companion diagnostic agreement (the "Akoya Agreement") with Akoya Biosciences, Inc. ("Akoya"), pursuant to which the Company has engaged Akoya to co-develop, validate, and commercialize the Company's proprietary ACR-368 OncoSignature test, the companion diagnostic that will be used to identify patients with cancer most likely to respond to ACR-368. Subject to the terms of the Akoya Agreement, as subsequently amended, the Company paid Akoya a one-time, non-refundable, non-creditable upfront payment in the amount of $0.6 million. The Company is obligated to pay Akoya up to an aggregate of $17.3 million upon the achievement of specified development milestones. Through December 31, 2023, the Company has made aggregate payments of $7.0 million to Akoya. During the years ended December 31, 2023 and 2022, the Company recorded research and development expenses of $6.0 million and $2.3 million, respectively. $1.3 million was due to Akoya and included in accounts payable as of December 31, 2023.

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with each of its directors and executive officers that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or services as directors or executive officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of such indemnifications. The Company is not currently aware of any indemnification claims and had not accrued any liabilities related to such obligations in its consolidated financial statements as of December 31, 2023 and 2022.

Legal Proceedings

From time to time, in the ordinary course of business, the Company is subject to litigation and regulatory examinations as well as information gathering requests, inquiries and investigations. We are not currently party to any material legal proceedings and are not aware of any pending or threatened legal proceedings against us that we believe could have an adverse effect on our business, operating results or financial condition.

Other Contracts

The Company enters into contracts in the normal course of business with various third parties for preclinical research studies, clinical trials, testing, manufacturing and other services. These contracts generally provide for termination upon notice and are cancelable without significant penalty or payment, and do not contain any minimum purchase commitments.

13. Employee Benefit Plans

Effective January 1, 2019, the Company adopted a 401(k) Plan for its employees, which is designed to be qualified under Section 401(k) of the Internal Revenue Code. Eligible employees are permitted to contribute to the 401(k) Plan within statutory and 401(k) Plan limits. Since inception of the 401(k) Plan and through the year ended December 31, 2023, the Company has not made any contributions to the 401(k) Plan.