

**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, 2022

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 001-40522

**Monte Rosa Therapeutics, Inc.**

(Exact name of Registrant as specified in its Charter)

**Delaware**

(State or other jurisdiction of  
incorporation or organization)

**84-3766197**

(I.R.S. Employer  
Identification No.)

**645 Summer Street, Suite 102**

**Boston, Massachusetts**

(Address of principal executive offices)

**02210**

(Zip Code)

Registrant's telephone number, including area code: (617) 949-2643

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 \$0.0001 per share	GLUE	The Nasdaq Global Select 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 ☐

Non-accelerated filer ☒

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 equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on NASDAQ on June 30, 2022, was \$302.6 million.

The number of shares of Registrant's Common Stock outstanding as of March 10, 2023 was 49,359,033.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of registrant's definitive proxy statement for its annual meeting of shareholders to be filed within 120 days after the close of the registrant's fiscal year are incorporated by reference to into Part III of this annual report on Form 10-K.



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## SPECIAL NOTE REGARDING FORWARD LOOKING STATEMENTS

This Annual Report on Form 10-K, or Annual Report, contains forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, or the or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. All statements other than statements of historical facts contained in this Annual Report are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “may”, “will”, “should”, “expects”, “intends”, “plans”, “anticipates”, “believes”, “estimates”, “predicts”, “potential”, “continue” or the negative of these terms or other comparable terminology. These statements are not guarantees of future results or performance and involve substantial risks and uncertainties. Forward-looking statements in this Annual Report include, but are not limited to, statements about:

- the initiation, timing, progress, results, costs, and any expectations and/or predictions of success of our current and future research and development programs and preclinical studies, including our expectations for our molecular glue degraders, or MGDs, molecules, including our GSPT1-directed MGD MRT-2359;
- the initiation, timing, progress, results, costs, and any expectations and/or predictions of success of our current and any future clinical trials, including statements regarding the nature of or the timing for when any results of any clinical trials will become available;
- our ability to continue to develop our proprietary platform, called QuEEN™, and to expand our proteomics and translational medicine capabilities;
- the potential advantages of our platform technology and product candidates;
- the extent to which our scientific approach and platform technology may target proteins that have been considered undruggable or inadequately drugged;
- our plans to submit IND applications to the FDA for future product candidates;
- the potential benefits of strategic collaborations and our ability to enter into strategic collaborations with third parties who have the expertise to enable us to further develop our biological targets, product candidates and platform technologies;
- our ability to obtain and maintain regulatory approval of our product candidates;
- our ability to maintain and expand, including through third-party vendors, our library of MGDs
- our ability to manufacture, including through third-party manufacturers, our product candidates for preclinical use, future clinical trials and commercial use, if approved;
- our ability to commercialize our product candidates, including our ability to establish sales, marketing and distribution capabilities for our product candidates;
- the rate and degree of market acceptance of our product candidates;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- our ability to establish and maintain intellectual property rights covering our current and future product candidates and technologies;
- the implementation of our business model and strategic plans for our business, product candidates, and technology;
- estimates of our future expenses, revenues, capital requirements, and our needs for additional financing;
- our ability to obtain funding for our operations necessary to complete further development and commercialization of our product candidates;
- our financial performance;
- developments in laws and regulations in the United States and foreign countries;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;

- the impact of the COVID-19 pandemic on our business and operations; and
- other risks and uncertainties, including those listed under Item 1A, “Risk Factors.”

Any forward-looking statements in this Annual Report reflect our current views with respect to future events and with respect to our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those described under Item 1A, “Risk Factors” and elsewhere in this Annual Report. Given these uncertainties, you should not place undue reliance on these forward-looking statements.

All of our forward-looking statements are as of the date of this Annual Report only. In each case, actual results may differ materially from such forward-looking information. We can give no assurance that such expectations or forward-looking statements will prove to be correct. An occurrence of or any material adverse change in one or more of the risk factors or risks and uncertainties referred to in this Annual Report or included in our other public disclosures or our other periodic reports or other documents or filings filed with or furnished to the Securities and Exchange Commission, or the SEC, could materially and adversely affect our business, prospects, financial condition and results of operations. Except as required by law, we do not undertake or plan to update or revise any such forward-looking statements to reflect actual results, changes in plans, assumptions, estimates or projections or other circumstances affecting such forward-looking statements occurring after the date of this Annual Report, even if such results, changes or circumstances make it clear that any forward-looking information will not be realized. Any public statements or disclosures by us following this Annual Report that modify or impact any of the forward-looking statements contained in this Annual Report will be deemed to modify or supersede such statements in this Annual Report.

We may from time to time provide estimates, projections and other information concerning our industry, the general business environment, and the markets for certain diseases, including estimates regarding the potential size of those markets and the estimated incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties, and actual events, circumstances or numbers, including actual disease prevalence rates and market size, may differ materially from the information reflected in this Annual Report. Unless otherwise expressly stated, we obtained this industry, business information, market data, prevalence information and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data, and similar sources, in some cases applying our own assumptions and analysis that may, in the future, prove not to have been accurate.

### **TRADEMARKS**

Solely for convenience, our trademarks and trade names in this report are sometimes referred to without the ® and ™ symbols, but such references should not be construed as any indicator that we will not assert, to the fullest extent under applicable law, our rights thereto.

## SUMMARY OF RISK FACTORS ASSOCIATED WITH OUR BUSINESS

Our business is subject to numerous material and other risks and uncertainties that you should be aware of in evaluating our business. These risks are described more fully in Part II, “Item 1A—Risk Factors,” and include, but are not limited to, the following:

- We are a biotechnology company with a limited operating history and have not generated any revenue to date from drug sales, and may never become profitable.
- We have incurred significant operating losses since our inception and anticipate that we will incur continued losses for the foreseeable future.
- We are very early in our development efforts. All but one of our programs are still in the preclinical stages of drug development. If we are unable to commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.
- Our approach to the discovery and development of product candidates based on our QuEEN™ platform is novel, which makes it difficult to predict the time, cost of development and likelihood of successfully developing any product candidates.
- We may not be successful in our efforts to identify or discover additional product candidates or we may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.
- Even if we receive marketing authorization for our product candidates, we will be subject to extensive 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 product candidates.
- If we are unable to obtain and maintain patent and other intellectual property protection for our technology and product candidates or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and drugs similar or identical to ours, and our ability to successfully commercialize our technology and drugs may be impaired, and we may not be able to compete effectively in our market.
- Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.
- Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.
- Our executive officers, directors, principal stockholders and their affiliates exercise significant influence over our company, which will limit our stockholders' ability to influence corporate matters and could delay or prevent a change in corporate control.

# PART I

## Item 1. Business

### Overview

We are a clinical-stage biotechnology company developing a portfolio of novel and proprietary molecular glue degraders, or “MGDs”. MGDs are small molecule drugs that employ the body’s natural protein destruction mechanisms to selectively degrade therapeutically-relevant proteins. MGDs function by inducing the engagement of an E3 ligase, such as cereblon, with defined structural features on surfaces of target proteins. These target proteins are also referred to as neosubstrates. The E3 ligase then tags the target protein for degradation by adding a molecular mark known as ubiquitin. We have developed a proprietary and industry leading platform, called QuEEN™ (an abbreviation for “Quantitative and Engineered Elimination of Neosubstrates”) to enable our unique target-centric MGD discovery and development approach and our rational design of MGD product candidates. We believe our MGDs provide significant advantages over existing therapeutic modalities, including other protein degradation approaches. To date, our QuEEN™ platform has identified numerous proteins for potential targeting by our MGDs. We identify therapeutically-relevant target proteins amenable to our approach using our artificial intelligence or “AI” / machine learning or “ML” engines, as well as multiple experimental approaches. We are continuously increasing our understanding of how MGDs function and we are using this understanding to develop design principles for the engineering of new MGDs. This growing expertise manifests in our expanding MGD library as well as our discovery and development pipeline. Using our insights, knowhow, and technology platform we have generated a library of MGDs that forms the basis for our MGD programs. At present, our library comprises a diverse set of rationally designed small molecules representing more than 400 unique low molecular weight scaffolds and about 35,000 different MGD molecules, and our goal is to expand to about 40,000 compounds by the end of 2023. We also use our insights and learnings to continuously update and improve QuEEN™, consistently increasing the power of the platform.

We prioritize our product development on therapeutic target proteins backed by strong biological and genetic rationale, with the goal of discovering and developing novel medicines. We are focused on developing solutions to clinically important indications, including oncology, inflammation, immunology, and others.

Our most advanced product candidate, MRT-2359, is an orally bioavailable MGD targeting the translation termination factor protein GSPT1. MRT-2359 is currently in clinical development for potential use in MYC-driven tumors, including metastatic non-small cell lung cancer, or NSCLC, small cell lung cancer, or SCLC and high-grade neuroendocrine tumors. Our pre-clinical studies have shown that through a functional association between GSPT1 and the MYC family of transcription factors, GSPT1 serves as a key regulator of MYC-induced protein translation, and that the degradation of GSPT1 using our MGDs creates a potential vulnerability in multiple MYC-driven tumors. The U.S. Food and Drug Administration or the “FDA” cleared the company’s investigational new drug application or “IND” for MRT-2359 in September 2022, and we initiated a phase 1/2 clinical trial for the treatment of MYC-driven and high-grade neuroendocrine tumors in October 2022. In January 2023, MRT-2359 received Fast Track designation from the FDA for the treatment of patients with previously treated, NSCLC with L-MYC or N-MYC expression. Beyond GSPT1, we are advancing our pipeline of assets towards the clinic. Specifically, our VAV1, NEK7 and CDK2 programs are now in lead optimization and continue to advance towards development candidate selection. Our pipeline further includes multiple additional undisclosed discovery phase programs.

Our proprietary QuEEN™ platform uniquely enables us to rationally design and develop our diverse library of MGDs and to deploy them against target proteins identified through our AI/ML approach. Many of these target proteins are considered inadequately drugged or completely undruggable by other therapeutic modalities. Our resulting MGDs are designed to reprogram the E3 ligase to bind to and induce the degradation of a therapeutically-relevant target protein. Central to our QuEEN™ platform is a detailed understanding of the molecular interactions promoted by our MGDs between E3 ligases and structural features on the surface of therapeutically-relevant proteins, which we refer to as degrons.

Key components of our QuEEN™ platform are:

- *AI/ML engines:* Our proprietary AI/ML engines enable us to a) determine structural features on protein surfaces that serve as MGD-dependent points of interaction between an E3 ligase and a therapeutically-relevant protein; b) create ternary complex models of an E3 ligase, an MGD, and a target protein or



neosubstrate in order to rapidly guide the design and optimization of novel MGDs, as well as perform *in silico* screening of such; and c) connect MGDs and their biological activity to disease-relevant biomarkers.

- *Proprietary MGD library*: A wholly-owned, proprietary, diverse, and continuously growing chemical library of currently around 35,000 MGDs that we have rationally designed based on our growing expertise in molecular glue anatomy and design. Library compounds currently represent more than 400 unique low molecular weight scaffolds with favorable binding affinities for an E3 ubiquitin ligase.
- *High throughput proximity screening and chemo-proteomics capabilities*: Our specialized and tailored suite of biochemical, structural biology, cellular, proteomics and *in silico* tools that enable and accelerate the discovery and optimization of MGD product candidates that efficiently recruit target proteins to E3 ligases.

By capturing our insights and experience with the identification of target proteins amenable to our approach as well as the discovery and development of MGDs through QuEEN™, we are constantly increasing the power of the platform.

Our lead candidate, MRT-2359, is an orally bioavailable MGD of the translation termination factor protein GSPT1. MRT-2359 was identified using QuEEN™ and is currently in development as a potential treatment for cancers dependent on or characterized by the expression of high levels of MYC family genes (c-MYC, N-MYC and L-MYC). The MYC transcription factors are some of the most frequently mutated, translocated and highly expressed oncogenes in human cancers. For example, we estimate 15% of NSCLC, and over 70% of SCLC, express high levels of L- or N-MYC. MYC-driven cancer cells are highly addicted to protein translation, and we have shown in extensive pre-clinical studies that due to the key role of GSPT1 in protein synthesis, selective GSPT1 degradation by MRT-2359 in cells expressing high levels of L- or N-MYC leads to cell death. Further, we have demonstrated in these MYC-driven preclinical models that MRT-2359 potently and selectively induces GSPT1 degradation, leading to tumor regression after oral administration. Based on these preclinical results, we initiated clinical trials with MRT-2359 in October 2022. The Phase 1/2, open-label, multicenter study will primarily assess the safety, tolerability, pharmacokinetic or “PK”, pharmacodynamic or “PD” and preliminary clinical activity of MRT-2359 in patients with previously treated selected solid tumors, including NSCLC, SCLC, high-grade neuroendocrine cancer of any primary site, diffuse large B-cell lymphoma or “DLBCL” and solid tumors with L-MYC or N-MYC amplification. We expect to disclose initial clinical data including PK, PD, safety and available initial efficacy from the Phase 1 arm of the ongoing Phase 1/2 clinical trial evaluating MRT-2359 in the second half of 2023.

In addition to our GSPT1 program, our QuEEN™ platform has produced multiple additional pipeline and discovery stage programs targeting therapeutically-relevant proteins otherwise considered undruggable or inadequately drugged. We have been able to identify selective MGDs for CDK2, an oncology target and key driver of cancers such as breast, ovarian, and uterine cancer. We have also identified target proteins outside of oncology, including target proteins with indications in inflammation and autoimmune diseases, as exemplified by our NEK7 and VAV1 programs. NEK7 is a key component of the NLRP3 inflammasome, a central regulator of cellular inflammatory responses to pathogens, damage and stress. Aberrant NLRP3 inflammasome activation is implicated in the pathogenesis of multiple autoimmune diseases, including Crohn’s disease, diabetes, gout, liver diseases, and neurodegenerative diseases. VAV1 is a central signaling protein in B and T cells, and its degradation may serve to de-activate immune cells involved in autoimmune diseases such as multiple sclerosis, myasthenia gravis, and rheumatoid arthritis. Our CDK2, NEK7 and VAV1 programs are currently in lead optimization. We also continue to progress our discovery stage programs, including a program targeting therapeutically-relevant proteins in hemoglobinopathies such as Sickle Cell Disease or “SCD”, and multiple other undisclosed target proteins. Our focus is on target proteins that have been considered undruggable or insufficiently drugged, that are highly credentialed preclinically or clinically, and that can potentially move into the clinic in indications with high unmet need and substantial commercial potential.

We are led by an experienced team of drug discovery and development experts with deep experience in targeted protein degradation, molecular glues, chemistry, structural biology, data science, disease biology, translational medicine, and clinical development.

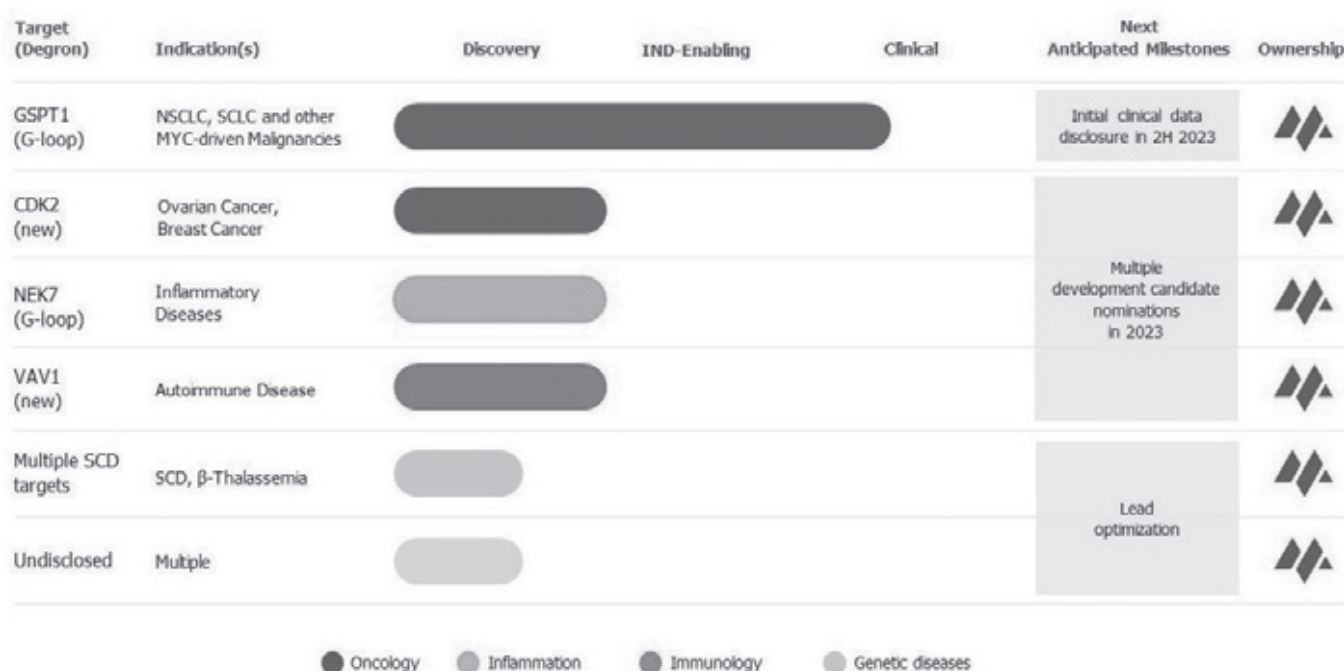
Monte Rosa Therapeutics AG, a Swiss operating company, was incorporated under the laws of Switzerland in April 2018. Monte Rosa Therapeutics, Inc. was incorporated in the State of Delaware in November 2019. The Company is headquartered in Boston, Massachusetts with research operations in both Boston and Basel, Switzerland. Our principal executive office is located at 645 Summer Street, Boston, MA 02210 and our telephone number is (617) 949-2643. Information about us is available on our corporate websites at [www.monterosatx.com](http://www.monterosatx.com). Information available on our website is not a part of, and is not incorporated into, this Annual Report. We trade on the Nasdaq Global Select Market under the ticker symbol “GLUE”.



## Our product pipeline

We have leveraged our QuEEN™ platform to generate our pipeline of product candidates with the potential to treat a diverse range of diseases through targeted protein degradation. Our current programs are focused on delivering therapies to target proteins that have been considered undruggable or inadequately drugged in well-characterized biological pathways across clinical indications in oncology, inflammation, immunology and other diseases with high unmet needs. We currently retain exclusive worldwide rights to the programs shown in the Figure 1 below.

**Figure 1: Monte Rosa Proprietary Pipeline**



## Our strategy

Our mission is to discover and develop a portfolio of novel small molecule MGDs that selectively eliminate therapeutically-relevant proteins to benefit patients in a broad range of indications with significant unmet medical need. We believe the product candidates identified through our proprietary QuEEN™ platform can provide distinct advantages over other modalities to address target proteins that have been considered undruggable or inadequately drugged.

Conventional small molecule inhibitor drugs generally work by interfering with the activity of a target protein through an interaction between the drug and a defined binding pocket on the target protein, typically an enzymatically active site of a protein. This limits the application of such drugs to proteins with a succinct binding pocket. Within this field, as binding pockets tend to be highly conserved within protein classes and families, achieving selectivity can be challenging. Even where a protein's active site can be targeted, potentially with specificity, protein inhibition does not always provide the desired functional outcome.

MGDs on the other hand, provide for therapeutic opportunities not constrained by some of the key limitations of conventional small molecule inhibitor drugs. MGDs provide an opportunity to target a vast universe of target proteins not limited to those with a defined binding pocket, in a highly selective way, due to the diversity of surfaces that can be targeted, resulting in reversible elimination of a target protein. More specifically, because MGDs work by inducing protein-protein interactions between target proteins and an E3 ligase, they do not require a defined binding pocket on the target protein of interest. Thus, MGDs offer a unique opportunity to unlock significant target space and enable us to address target proteins that have been considered undruggable or inadequately drugged. The interaction surfaces we utilize are often not conserved within protein classes and families, allowing us to potentially achieve significant selectivity for our MGD product candidates that we believe is superior to classical small molecule inhibitor drugs. Lastly, we focus on target proteins where experimental evidence suggests that removal of the target is superior to transiently inhibiting it, in particular proteins that have a scaffolding function.

Through our ability to produce potentially highly selective MGDs with fine-tuned speed and depth of degradation, we believe we can generate MGD product candidates with a wide therapeutic window that may be beneficial in a broad range of indications, including oncology, immunology, inflammation, metabolic diseases and diseases of the central nervous system or CNS.

Our precision oncology programs are focused on the elimination of proteins that are highly validated driver oncogenes in cancer cells (“oncogene addiction”), that define a cancer lineage dependence (“lineage addiction”), or that create a vulnerability specific to tumor cells (“synthetic lethality”). By tuning the speed and depth of degradation and leveraging our proprietary pharmacogenomic tools, we optimize our oncology MGDs to selectively target biomarker-positive cells. Our platform enables us to potentially tune the activity (depth and speed of degradation) of our MGDs to the most relevant tumor lineages to achieve maximal phenotypic effects.

In immunology, we are uniquely able to target highly credentialed immune signaling proteins in pathologically relevant immune pathways. These proteins may have a scaffolding role (e.g. NEK7), or an active site that is hard to target (e.g. VAV1), or may be considered to be undruggable by conventional small molecules. We prioritize target proteins that are validated through preclinical or clinical (including human genetic) evidence. We have shown that we are able to optimize our MGD product candidates to induce deep and selective degradation of immune-pathway relevant proteins.

Key elements of our strategy include:

- *Continue to advance our GSPT1-directed MGD program through clinical development and towards seeking regulatory approval.* We have generated data in preclinical models that demonstrate the potential of our GSPT1-directed MGDs to confer antitumor activity across multiple tumor types that are characterized by the expression of high levels of the MYC family of transcription factors. We received FDA clearance of our IND for MRT-2359 in September 2022 and initiated patient dosing in our ongoing Phase 1/2 clinical trial in October 2022. Further, in January 2023, the FDA granted Fast Track designation to MRT-2359 for the treatment of patients with previously treated, metastatic NSCLC with L-MYC or N-MYC expression;
- *Continue to advance and develop our pipeline of rationally designed MGDs to transform the treatment of diseases in multiple therapeutic areas.* Through our QuEEN™ platform, we have identified a variety of degron-containing proteins that are amenable to our approach and are either undruggable or insufficiently drugged. Our programs for CDK2, VAV1 and NEK7 are all in the lead optimization stage, and we anticipate nominating multiple development candidates for these programs in 2023. MRT-2359 and our CDK2, NEK7 and VAV1 programs are all examples of our successful application of our QuEEN™ platform to the discovery of MGDs with the potential to be rapidly advanced through drug development. As we advance those programs in the clinic and to candidate selection, we continue to advance our other programs into lead optimization, and to identify new degron-containing target proteins as well as MGDs. We will continue to prioritize therapeutically-relevant target proteins backed by strong biological and genetic rationale with the goal of producing novel precision medicines. These opportunities include indications such as oncology, immunology, inflammation, as well as others;
- *Continue to enhance and expand the capabilities of our QuEEN™ platform to unlock the full therapeutic potential of our MGDs in our targeted therapeutic areas.* We employ a core set of drug discovery and development principles to guide our target protein selection across various protein classes and therapeutic areas. We are specifically focused on delivering therapies to target proteins that have been considered undruggable or inadequately drugged in preclinically and clinically well-characterized biological pathways. Our QuEEN™ platform enables us to vastly expand the degradable proteome beyond conventionally druggable target proteins. Our approach includes the computational identification of structural features on the surface of a protein that render a target protein amenable to complex formation with an E3 ligase bound by one of our MGDs. We combine our QuEEN™ platform, including our AI/ML degron discovery engine, with our proprietary library of rationally designed MGDs to selectively connect degron-containing target proteins to E3 ligase proteins, including cereblon. QuEEN™ has the potential to help us better understand the optimal pairing of degron-containing proteins with ligases to further expand our target space. We continue to invest in building our QuEEN™ platform, including expanding our proprietary MGD library as well as our proteomics, *in silico* screening, pharmacogenomics and translational medicine capabilities;
- *Expand and protect our proprietary know-how and intellectual property.* We continue to expand intellectual property around our innovations in the field of targeted protein degradation and in particular MGDs. Our intellectual property, which includes proprietary know-how, patent applications and expected patents, as well as trade secrets, applies not only to our product candidates, but also to all of our various innovations, including, for example, our drug discovery processes including our QuEEN™ platform; our AI-based E3

ligase characterization algorithms, AI-based degron discovery algorithms, AI-based novel MGD design algorithms, and *in silico* screening algorithms; our drug development tools; our growing library of MGDs; the innovative methods and approaches we have developed to rationally design MGDs to expand our library, and to certain biomarkers and therapeutic applications for our potential product candidates; and

- **Consider strategic collaborations in select therapeutic areas to fully realize the potential of our QuEEN™ platform.** Our goal is to become a fully integrated biopharmaceutical company that delivers pioneering therapies for patients. We currently retain all rights to our programs and platform. To support our goal, we will selectively explore strategic partnerships where we can leverage complementary capabilities in discovery, development, and commercialization in disease areas within and outside our core areas of therapeutic focus to bring transformative therapies to patients with high unmet medical needs.






## Background on targeted protein degradation and molecular glues

Proteins are large, complex molecules that are involved in essentially all biochemical reactions that take place in the body. Many human diseases are associated with abnormal intracellular protein behavior driven by modified functional activation or inactivation of the protein itself. Given their critical role, proteins are attractive therapeutic targets, including those that act inside the cell and on its surface. While significant progress has been made in the development of therapeutics that address malfunctioning proteins, about 75% of human proteins are still considered undruggable by traditional small molecules.

### Challenges with druggable vs. undruggable proteins

The most common methods of targeting proteins, including intracellular proteins, involve traditional small molecule inhibitors that bind to a pocket in the protein and, there, act to inhibit or modify the function of the protein. Having such a pocket is what has traditionally led to a protein being considered druggable, yet most proteins lack suitably sized and shaped binding pockets. In particular, proteins such as transcription factors, those that act as scaffolding for other proteins, and modulators of enzyme activity, all of which can play a critical role in disease, often don't have binding pockets suited for efficient ligand binding. The absence of a binding pocket presents a challenge to the development of traditional small molecule inhibitors. Other therapeutic modalities that can target such proteins, such as therapeutic antibodies, oligo-based nucleotides, and other genetic therapies, are limited in their ability to address aberrant protein behavior. Some of the therapeutic modalities have meaningfully advanced the treatment of disease and improved the quality of life for millions of patients. However, these modalities face specific challenges related to their mode of delivery, scalability, and their therapeutic application. A summary of these characteristics can be found in Figure 2.

**Figure 2: The Next Generation of Precision Medicine-Based Small Molecule Drugs; Selectively Editing the Human Proteome with Rationally Designed MGDs**

	 Traditional small molecule inhibitors	 Therapeutic Antibodies	 MGDs	 RNAi, RNA Editing	 CRISPR/Gene Therapy
Ability to access undruggable space	✗	✓	✓	✓	✓
Cellular permeability	✓	✗	✓	✓	✓
Oral bioavailability	✓	✗	✓	✗	✗
Systemic distribution	✓	✓	✓	✗	✗
CNS Penetration	✓	✗	✓	✗	✗
Manufacturing scalability	✓	✓	✓	✗	✗

## ***Molecular glues: a new approach to protein degradation***

A new and promising approach to modulating protein function using small molecules in cells was recently elucidated: protein degradation. Illustrated in Figure 3, protein degradation is one of the body's natural processes by which proteins are eliminated from human cells through the attachment of a molecular tag, called ubiquitin, to a protein by any of the approximately 600 human E3 ligases, marking the protein for degradation by the proteasome in the cell. Protein degradation can be induced by small molecule-based degraders, including both PROteolysis TARgeting Chimeras, or "PROTACs", and MGDs. It was found that lenalidomide, now an approved best-selling drug in multiple indications with 2021 global sales of \$12.8 billion, functioned as a small molecule-based degrader, or as an MGD, more specifically. In one of these indications, multiple myeloma, lenalidomide acts by causing two disease-driving transcription factors, IKZF1 and IKZF3, that lack druggable pockets, to bind to cereblon, an E3 ligase protein, resulting in their degradation. In this context, lenalidomide leads to the formation of a complex of IKZF1 and IKZF3 with cereblon by inducing surface complementarity between the components of the complex rather than by binding of the MGD into a succinct binding pocket on the protein target. We believe the targeted protein degradation approach offers many features that make it an attractive therapeutic modality:

- ***Removal of a target protein:*** partial or complete removal of a target protein can lead to more complete inhibition of signaling and metabolic pathways, thus resulting in more profound pharmacodynamic effects than traditional reversible or irreversible inhibition.
- ***Targeting Intracellular proteins:*** small molecule-based protein degraders, in particular MGDs, readily cross cell membranes or can be optimized to do so.
- ***Ease of delivery:*** small molecule-based protein degraders, in particular MGDs, can be delivered through various routes of administration, including oral.
- ***Systemic and tissue distribution:*** since most small molecule-based degraders, in particular MGDs, are low molecular weight compared to other therapeutic modalities, tissue distribution, such as into the CNS or tumor tissues, poses less of an issue.
- ***Catalytic mode of action:*** after inducing degradation of a target protein molecule, the small molecule-based protein degrader-E3 ligase complex is able to induce the degradation of another target protein molecule. Thus, the small molecule-based protein degrader acts catalytically, unlike protein inhibition, causing the removal of many target protein molecules, thereby editing the cellular proteome.
- ***Event driven pharmacology:*** unlike with inhibitors where prolonged engagement of the drug with the protein is required for efficacy, small molecule-based protein degraders only require engagement with the E3 ligase and the target protein long enough to induce tagging for degradation

As mentioned above, there are multiple advantages of the protein degradation approach, but one of the most beneficial is the potential to achieve greater therapeutic efficacy resulting from the removal of a target protein from the cellular proteome.

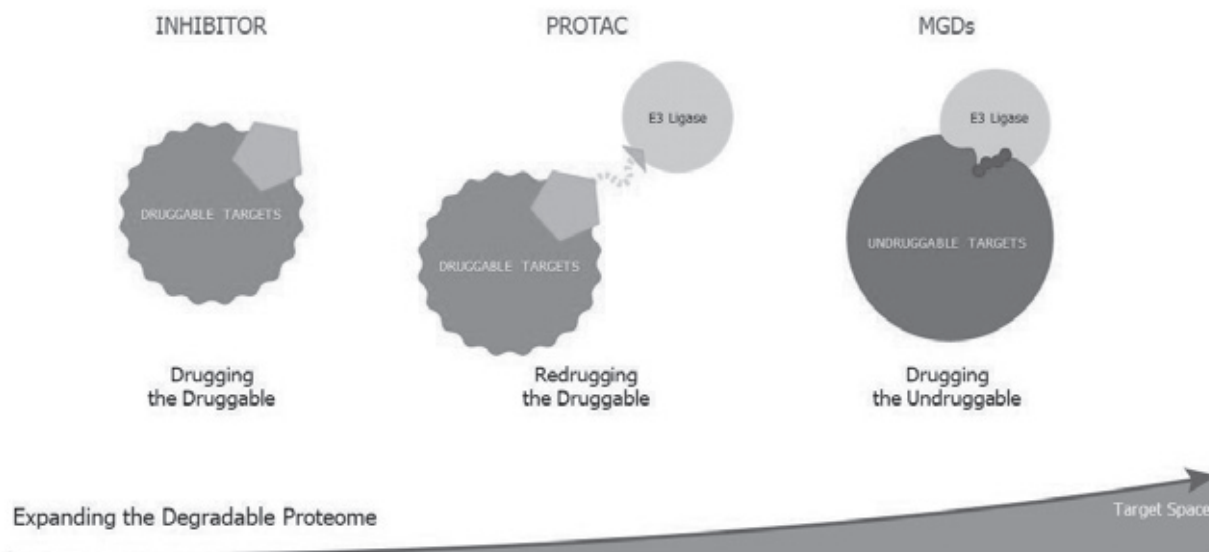
## ***Current approaches to protein degradation***

While lenalidomide is an MGD, the majority of recent drug discovery efforts in the design of protein degraders has been focused on PROTACs. These heterobifunctional degraders are composed of two separate small molecules connected by a chemical linker. One molecule binds to a necessary binding pocket on the target protein and the other to a component of the E3 ubiquitin ligase complex. Binding of the PROTAC to both the protein of interest and the E3 ligase brings the target protein into proximity of the E3 ligase, resulting in tagging of the protein of interest for degradation. While this represents a novel way to eliminate therapeutically-relevant proteins from cells, we believe an MGD approach offers the following advantages over PROTACs:

- ***Ability to target undruggable proteins:*** MGDs utilize the richness of molecular surface features across the proteome allowing access to a broader and differentiated target space. In contrast, PROTACs require identification of a small molecule that binds to a defined binding pocket of a target of interest, which today largely constrains the approach to the universe of proteins that can already be addressed with small molecule inhibitors.
- ***Favorable pharmaceutical properties:*** The relative simplicity and size of an MGD generally allows for more rapid optimization for oral bioavailability. PROTACs often have a larger size and larger molecular weight due to their complex heterobifunctional structure, which may lead to challenges to develop the molecules into drugs suitable for oral dosing.

- *Broader tissue distribution:* The physicochemical properties of PROTACs may also limit the drug distribution within the body, thereby reducing the potential in certain therapeutics areas such as central nervous systems disorders. MGDs are more traditional small molecules and hence do not have these issues.
- *No observable hook effect:* MGDs show a more typical concentration response where increasing concentrations elicit increasing efficacy caused by the catalytic interaction. In contrast, PROTACs require a precise concentration range to elicit efficacy due to the loss of degradation potential at higher concentrations caused by their heterobifunctional structure (also known as “hook effect”).

**Figure 3: Molecule Glue Degraders; Expanding Target Space, Fostering a New Generation of Drugs**



In summary, and as shown in Figure 3, MGDs are non-heterobifunctional and do not require an active site or binding pocket on target proteins. We believe these properties potentially expand the universe of amenable target proteins while also maintaining the favorable drug-like properties of small molecule therapeutics.

## Our approach





We design and develop molecular glue degraders or MGDs in a rational and iterative approach using our industry-leading and dynamic QuEEN™ platform.

MGDs are small molecule-based protein degraders designed to modify an E3 ligase's binding specificity and thus can employ the body's natural mechanisms of protein destruction to selectively eliminate therapeutically-relevant proteins. Lenalidomide and pomalidomide are two approved drugs that were found to function as MGDs by causing the degradation of therapeutically-relevant proteins through the induced interaction with the E3 ligase cereblon, and provide clinical validation to the MGD approach.

Following the discovery that the clinically and commercially successful lenalidomide and pomalidomide were in fact MGDs, it was believed that the discovery of MGDs will mostly be through serendipitous findings, that MGDs could not be rationally designed and optimized to high levels of selectivity and achieve drug-like properties through conventional medicinal chemistry efforts, and that the target protein space for this approach is limited. Our QuEEN™ platform was designed and built to address these issues. With QuEEN™ we can discover and develop MGD product candidates that are potentially potent, selective and have favorable drug like properties in a target-centric, prospective and rational way against a wide variety of target proteins.

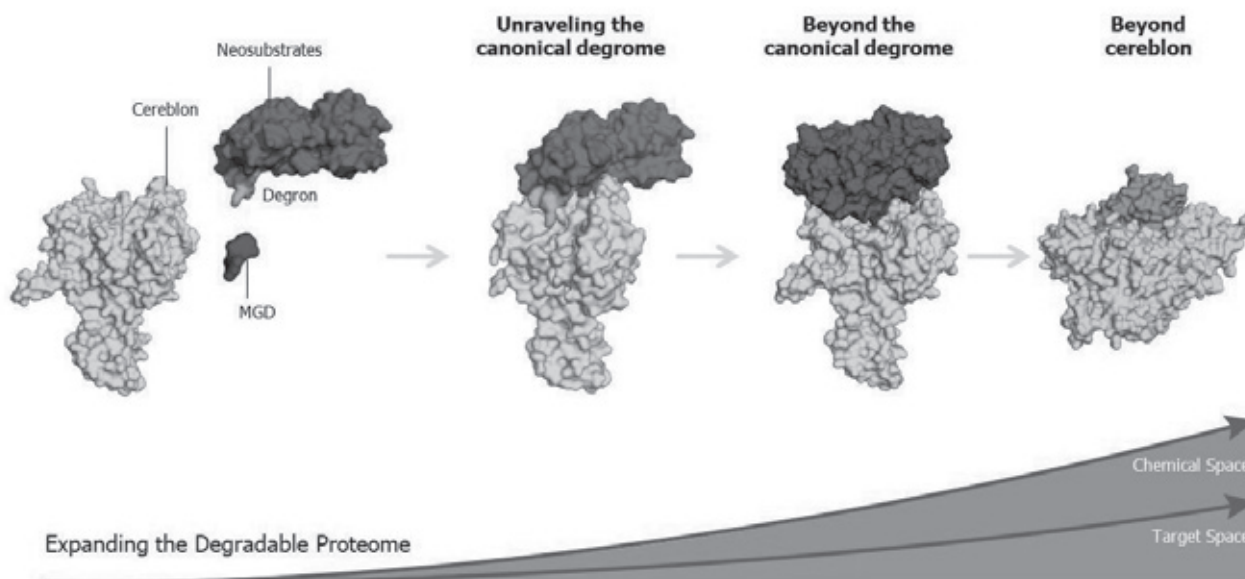
**Figure 4: QuEEN™ is Redefining the Rules of MGD Discovery**



Traditional thinking		Monte Rosa Therapeutics approach
'Target space is limited'		QuEEN™ has vastly expanded the degradable target space across a broad range of undruggable protein classes
'MGDs are identified by serendipity'		QuEEN™ enables target centric and systematic discovery of MGDs
'Med Chem rules don't apply to MGDs'		AI-driven and/or structure-based design allow rational Med Chem optimization of MGDs
'MGDs are not selective'		High specificity achievable even within same protein class, families and isoforms

We believe our platform will continue to deliver MGD product candidates with the potential to address target proteins that have been considered undruggable or inadequately drugged, while possessing attractive pharmaceutical properties. Our initial programs are utilizing cereblon as the E3 ligase system to tag target proteins. Through our AI/ML platform and proprietary MGD library we have expanded and continue to expand chemical and target space. Further, we have started using the platform to leverage other E3 ligases as well.

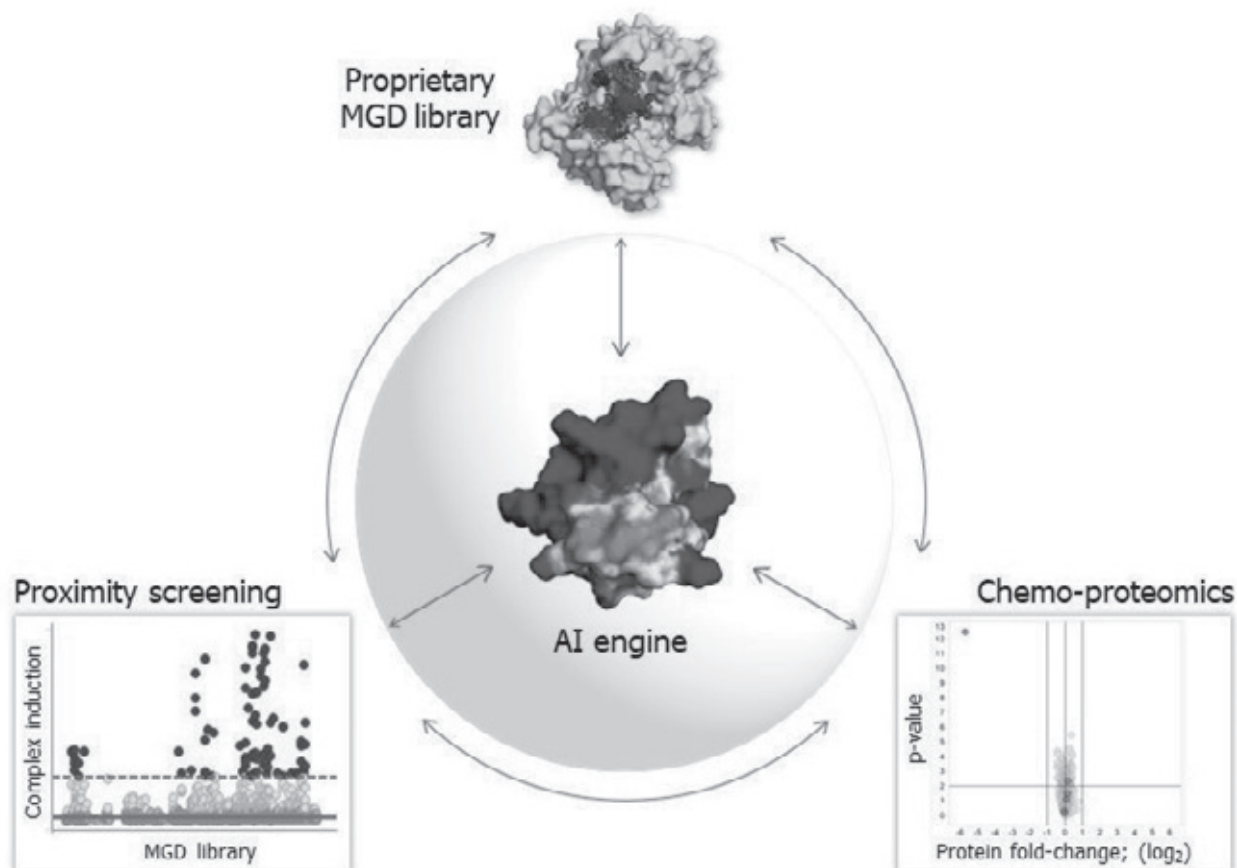
**Figure 5: Our Rational Approach to Unleash the Full Potential of MGDs**



Our proprietary and industry-leading QuEEN™ platform was built to support our target-centric approach to the discovery and development of MGD drugs that degrade a wide landscape of therapeutically-relevant target proteins by (i) systematically identifying degrons and other surface features on target proteins that may enable degradation through our approach; and (ii) rationally designing MGDs that can be optimized towards high potency and selectivity, with favorable pharmaceutical properties. Our proprietary library of rationally designed MGDs currently includes about 35,000 unique small molecules built around 400 cereblon binding scaffolds. Through our platform, we have built expertise that allows us to induce a high degree of surface complementarity between the E3 ligase and a target protein, potentially leading to high potency and selectivity for the therapeutically-relevant

target proteins we select. Figure 6 provides a schematic overview of some of the most unique and critical features of our QuEEN™ platform.

**Figure 6: Monte Rosa's QuEEN™ Discovery Platform; An Industry Leading Target-Centric Approach to MGD Discovery and Development**



Our proprietary and industry leading Quantitative and Engineered Elimination of Neosubstrates platform, or QuEEN™ platform, encapsulates our team's deep and growing expert knowledge and discovery capabilities across biology, chemistry and computational sciences, from which we are generating our library and pipeline of MGD product candidates. Central to our QuEEN™ platform is a detailed understanding of the molecular interactions promoted by our MGDs between E3 ligases and therapeutically-relevant target proteins, which have been considered undruggable or inadequately drugged. We believe this depth of knowledge allows us to leverage our platform to rationally design MGDs with favorable pharmaceutical properties that have the potential to translate into clinical success across multiple therapeutic areas. Our capabilities have been developed through key features of our QuEEN™ platform, which include our AI/ML engines, proprietary MGD library, and our high throughput proximity screening and chemo-proteomics capabilities, as described above.

Our process of degron discovery and MGD design is highly iterative and interdisciplinary, and is guided by our experience and powerful AI modeling. Computational predictions and analyses guide our high throughput screening and chemo-proteomics, which in turn provide more information to feed back into the AI engine, and all the accumulated knowledge is used to guide our MGD library expansion. For example, MGD discovery and development for a protein target can pass from degron identification, to MGD hit identification, to *in silico* improvement, to a round of chemo-proteomics validation, to chemical library alterations and back, until we reach the desired selectivity and degradation.

#### **Our Proprietary MGD library**

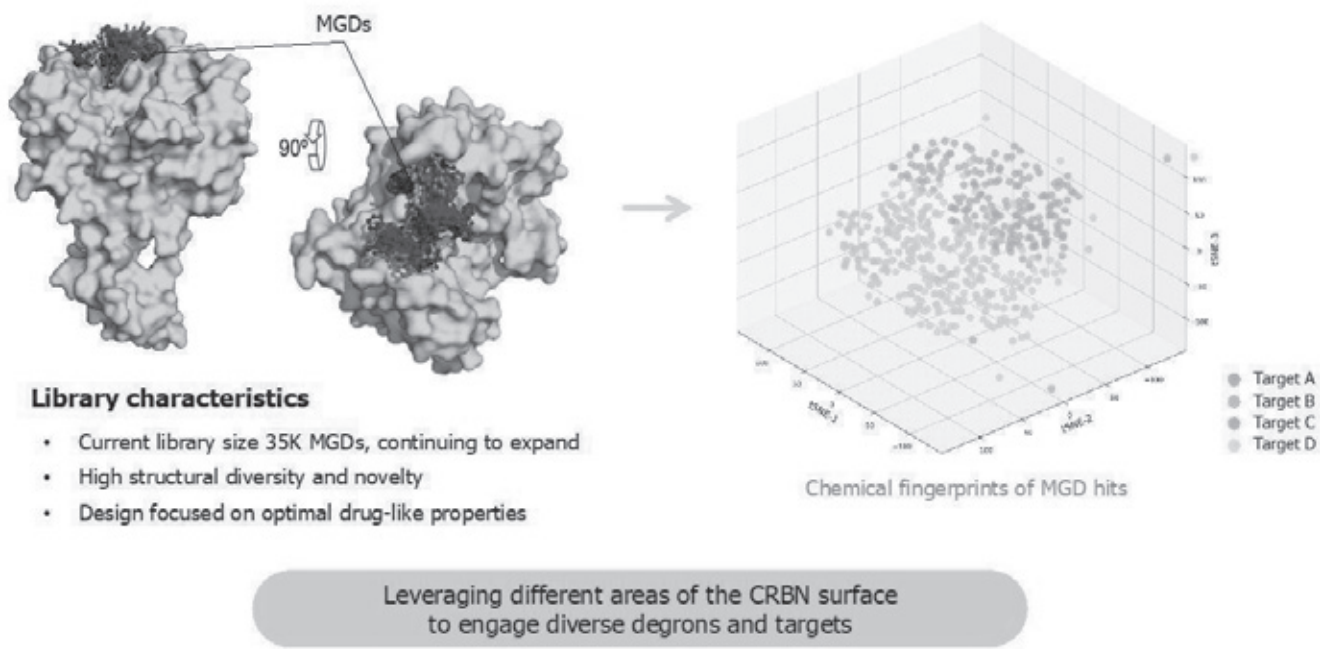
We continue to expand our highly diverse library of MGDs based on our growing expertise in MGD design and development captured in QuEEN™. We discover and develop lead MGDs for degron-containing target proteins by



applying our MGD library, computational chemistry tools, proximity screening tools, our chemo-proteomic capabilities and our knowledge of the cereblon-binding site and variations in degron structures. Our proprietary MGD library currently consists of over 400 unique scaffolds, each designed to probe different three-dimensional spaces. These scaffolds have been utilized to create a highly diverse proprietary library, currently consisting of approximately 35,000 unique MGDs. As shown in Figure 7, our MGDs are characterized by high structural diversity and leverage different areas of the cereblon surface to engage diverse degrons and target proteins. Our diverse library has given rise to multiple series of MGDs for each of the target proteins currently being studied across our disclosed and undisclosed portfolio.

With our experienced team of data scientists, structural biologists, biochemists, biologists and chemists, we have innovated proprietary tools designed to broadly match our MGDs against degron-containing target proteins. Our MGD design capabilities are driven by both *in silico* and laboratory-based assays that predict and assess the ability of our MGDs to induce the binding of target proteins to E3 ligase components, such as cereblon, and directly measure target degradation.

**Figure 7: Monte Rosa Proprietary MGD Library: A Cereblon-Centric Library Characterized by Novelty and Structural Diversity**



### ***Our AI/ML engine Rhapsody enables in silico discovery of novel and highly selective MGDs***

We have developed sophisticated and proprietary AI-powered algorithms to design novel MGDs, create ternary complex models for virtual screening and structure activity relationship or SAR optimization, and an *in silico* screening engine to identify and prioritize hits. Our pipeline integrates flexibility and active learning to quickly create ternary complex models for each target protein, enabling modeling, SAR engineering, and virtual screening. Our platform also leverages ensembles, molecular dynamics and quantum mechanics to identify and prioritize MGDs for synthesis and testing. We have named this engine Rhapsody™.

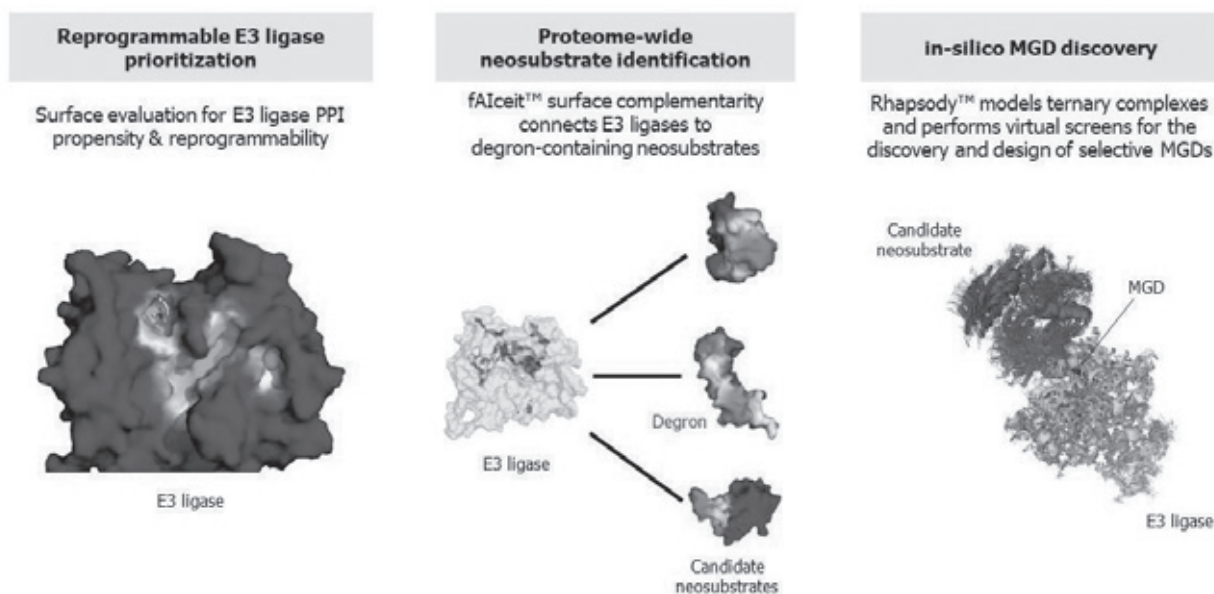
For hit expansion and MGD optimization, Rhapsody is used to generate an *in silico* model of the MGD-specific, MGD-induced ternary complex. The engine includes modules for *in silico* docking, molecular fingerprinting, and SAR cliff discovery, enumeration, expansion, and generation, synthesis filtering, and structure- and ligand based virtual screening. Evaluation of the model allows us to rapidly predict which parts of the MGD anatomy are involved in target recruitment and which parts may be modified. This enables us to maintain or enhance the target-specific potency of the MGD, while optimizing its selectivity, and its other chemical and biological properties.

Rhapsody results are used to create and identify novel MGDs that are predicted to induce neosubstrate-specific ternary complex formation, are available for rapid synthesis, and can be prioritized for follow-up experiments. Many of these tools have been built around cereblon as an E3 ligase and are being applied to additional E3 ligases.

## ***Our AI/ML engines OneVision and fAlceit identify reprogrammable E3 ligases and glueable target proteins***

We have developed sophisticated and proprietary AI-powered algorithms to mine databases of protein sequences and structures, including structures determined from x-ray crystallography and structures from predicted protein folding. We have identified topological, structural and sequence features associated with published, or canonical, as well as newly discovered, or non-canonical, degrons and encoded these features in OneVision™ and fAlceit™, part of our suite of AI-powered algorithms that include modules leveraging highly customized geometric deep learning, deep neural networks, and molecular dynamics. We use OneVision to characterize E3 ligase surfaces, such as for propensity to form protein-protein interactions and the presence of small molecule ligand-binding pockets. Using both protein amino acid sequences and three-dimensional protein structures as inputs, we have deployed fAlceit to identify degrons with an initial focus on identification of degrons predicting putative neosubstrates of cereblon. Using fAlceit to computationally predict the presence of structural features with a high potential to function as a degron along with the presence of a surface complementary to cereblon, we have identified a variety of proteins with the potential to be neosubstrates, and many of them are target proteins in disease relevant pathways.

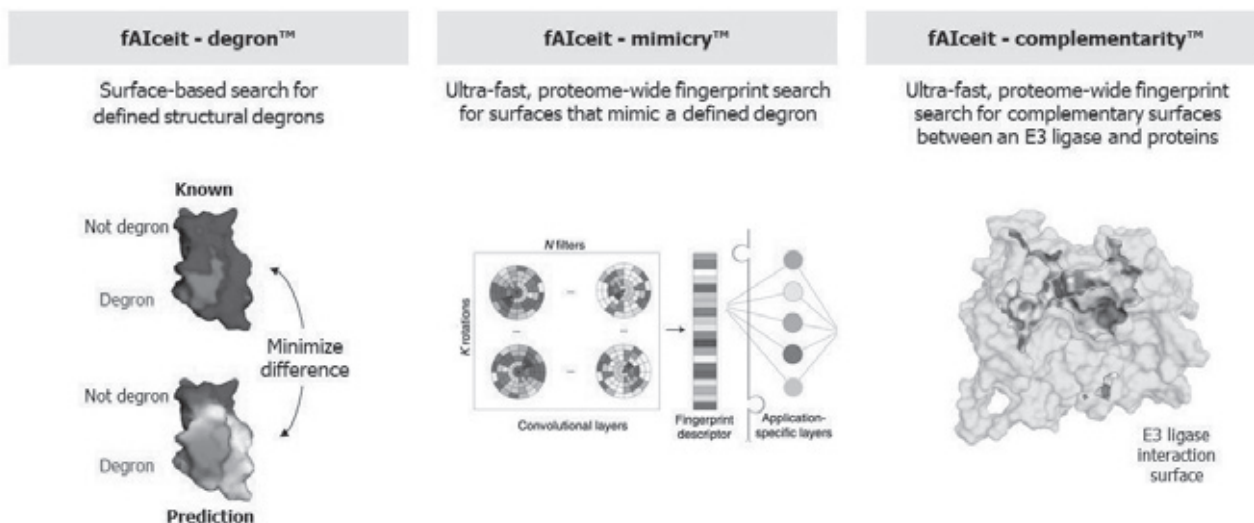
**Figure 8: Monte Rosa's Proprietary AI/ML Engine allows for Discovery of Glueable Target Proteins and Highly Selective MGDs**



A key feature of the fAlceit process is the ability to integrate new discoveries from our proximity screening platform: as we characterize the activity of our expanding MGD library, fAlceit learns more degron features and, projecting these features into the entire proteome, identifies more potential neosubstrates targetable by our

MGDs. We are also applying fAIceit to identify candidate complementary target proteins to E3 ligases beyond cereblon prioritized by OneVision.

**Figure 9: Monte Rosa's Protein Surface Exploration AI Engines**



## High throughput proximity screening and chemo-proteomics capabilities

### Quantitative biochemical and cellular assays

We have developed a suite of assays that have been tailored to measure specific steps of the MGD-induced protein degradation cascade. With our set of assays, we can measure ternary complex formation and screen for MGDs which have the most efficient binding characteristics. We have developed a Homogeneous Time Resolved Fluorescence, or HTRF, assay to measure ternary complex formation, whereby the close proximity of cereblon and the target protein are detected by fluorescent energy transfer between antibodies binding to the two proteins. We have used these types of assays to screen multiple target proteins using our proprietary MGD library. Our studies have validated the ability of MGDs to drive ternary complex formation in a concentration dependent manner. By measuring the dependency of ternary complex formation on MGD concentration, we generate concentration dependent curves, enabling us to calculate objective measures of potency such as the  $EC_{50}$ , or the concentration at which the effect is half of the maximum.

We have also developed multiple assays to measure degradation of target proteins in cells. The HiBiT cellular assay is one example of a high-throughput assay that we have used to screen our proprietary MGD chemical library and identify MGDs that promote cellular target degradation in a selective manner. The assay measures the decrease in luminescence signal by using an endogenous HiBiT tag fused to the target of interest. Preclinical studies using our MGDs have shown these compounds can drive target degradation in a concentration dependent manner. By measuring the dependency of target protein levels on MGD concentration, we generate concentration dependent curves, enabling us to calculate objective measures of potency such as the  $DC_{50}$ , or the concentration at which the degradation is half of the maximum, and the  $D_{max}$ , the maximum amount of target protein that is degraded.

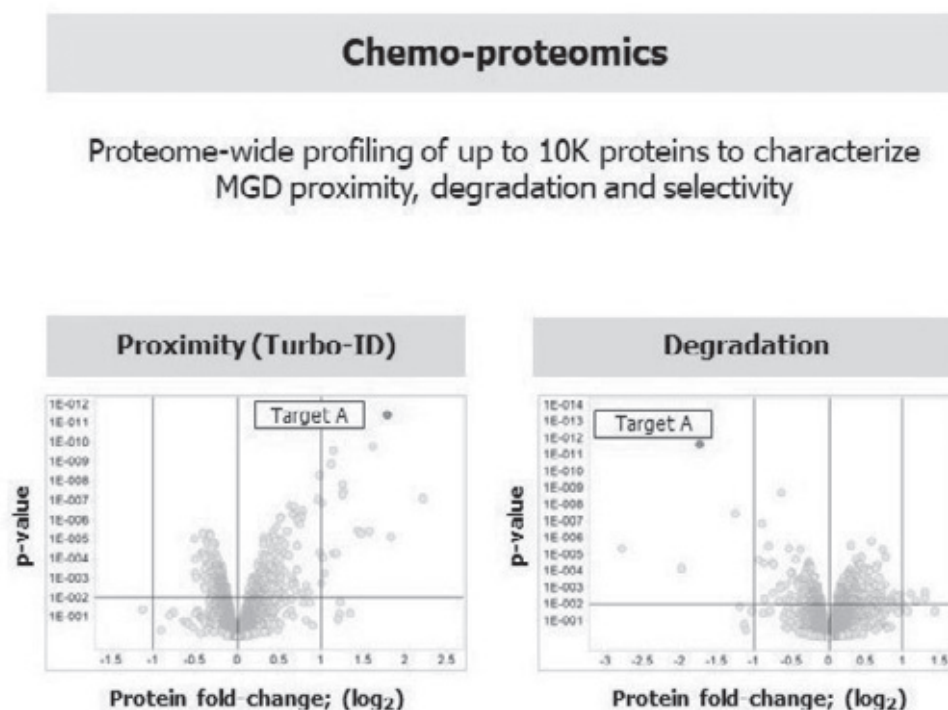
We are using our tailored suite of biochemical and cellular assays to screen, identify and rapidly optimize our MGDs. We have demonstrated that multiple target proteins from our degron database can be engaged and/or degraded using MGDs from our proprietary MGD library.

### Quantitative chemo-proteomics profiling assays

Utilizing our expertise in mass-spectrometry-based proteomics, we have developed a suite of high throughput quantitative profiling assays to assess multiple parameters, including cellular target degradation, selectivity of degradation and ternary complex formation in cells, the latter allowing us to identify potential neosubstrates not yet predicted by our *in silico* approach. We utilize this information in multiple ways, including:

- *To assess target degradation and determine the selectivity of our MGDs:* Proteome wide changes in expression levels of proteins after treatment with a MGD are measured. Downregulation of protein levels is suggestive of degradation.
- *To validate complex formation of our MGDs in cells:* Proteins that are induced by the MGD to be proximal to the E3 ligase are tagged and enriched using a Turbo-ID proximity assay. This induced spatial proximity is suggestive of cellular ternary complex formation.
- *To identify novel neosubstrates:* Screening of our MGD library with the proximity-based assay provides additional unbiased data to identify novel degrons and train our computational degron prediction algorithms to further expand the target space.
- Additionally, we have created BaseCamp and Degron Pages, our suite of custom software tools for data processing, storage, analysis, and visualization. Through a web interface, these software tools enable every Monte Rosa scientist easy access to proximity platform screening results, Rhapsody *in silico* MGD designs and screening predictions, and the fAlceit degron interface identification. Using these proprietary tools, every scientist is empowered as an investigator to discover connections between MGDs, degrons, and diseases.

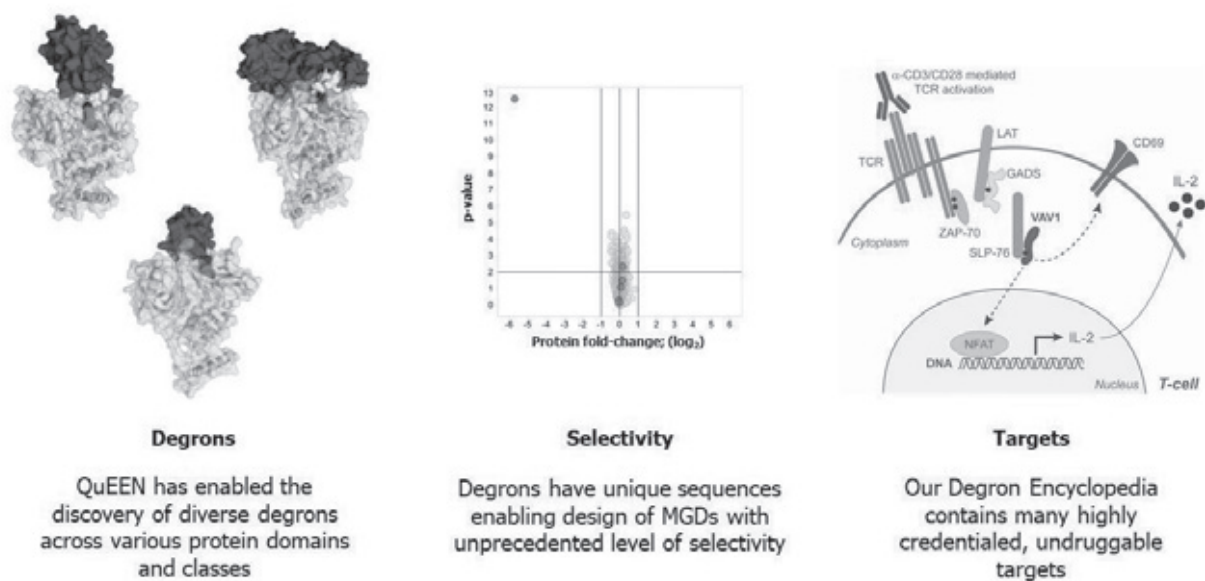
**Figure 10: Our Chemoproteomics Platforms Accelerates Degron and MGD Discovery and Validation**



As shown in Figure 11, our QuEEN™ platform has enabled us to discover a broad landscape of degrons and degron-containing proteins. We have used our AI engine and a rational design approach to discover MGDs that are exquisitely selective. All combined, this allows us to potentially eliminate therapeutically-relevant target proteins in pathways that are highly relevant for diseases with high unmet need in oncology, immunology, inflammation as well as other diseases.



**Figure 11: Discovering Diverse Degrons and Developing Highly Selective MGDs Against Them**



### QuEEN™ expansion

Our QuEEN™ platform was originally focused on identifying and developing MGDs that induce the binding of degron-containing neosubstrates to cereblon as a means of targeting them for degradation. We are expanding the scope of QuEEN™ to grow the cereblon target space and to leverage additional E3 ligases for targeted protein degradation.

- **Expand the cereblon neosubstrate universe:** As we rationally designed our MGD compound library to increase diversity, we found in preclinical studies that there are novel degrons with a diversity of amino acid sequences and 3-dimensional structures that can be targeted, and we have shown we can induce efficient protein degradation through these previously undisclosed degrons. We have used our proprietary AI-driven algorithms to predict the existence of degrons from the primary sequences and the topology of proteins and are using our rational design approach to expand chemical diversity of our MGD library so to be able to target this diverse set of cereblon-accessible degrons.
- **Utilize additional E3 ligases:** We believe that we will be able to reprogram other E3 ligases through the discovery of ligase specific MGDs as well as specific ligase-accessible degrons, thus enabling us to generate ternary complexes with a further subset of the approximately 600 E3 ligases

Expanding the universe of neosubstrates or target proteins and recruitment of such to additional E3 ligases through the continued identification of degrons has the potential to bring more therapeutically-relevant target proteins into the universe of degradable targets, which we anticipate will allow us to address additional therapeutic target proteins that are undruggable or insufficiently drugged.

### Our Precision Medicine Approach for MYC-driven Cancers

**MRT-2359, a highly selective and orally bioavailable GSPT1-directed molecular glue degrader (MGD) in development for the treatment of MYC-driven cancers**

#### Overview

MRT-2359 is an orally bioavailable MGD that we have shown using extensive in vitro and in vivo studies to induce the degradation of GSPT1. GSPT1 (also known as eRF3a) is a translation termination factor that helps catalyze the termination of protein synthesis, facilitating the release of mRNA and newly synthesized protein from the ribosomal protein synthesis machinery. We have identified GSPT1 as a potential therapeutic vulnerability for MYC-driven cancers. MRT-2359, our GSPT1-directed MGD, is designed to preferentially affect growth and survival of cancer cells addicted to protein translation, such as those driven by high expression and activity of MYC family transcription factors. *In vivo*, once daily oral dosing of MRT-2359 led to a potent anti-tumor activity in

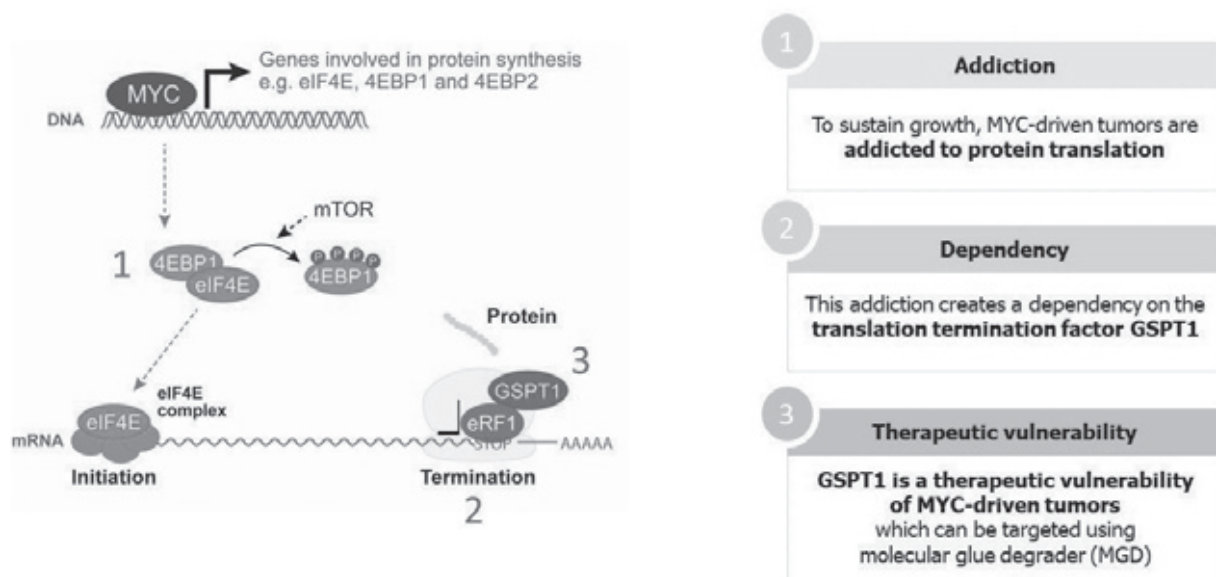
MYC-driven, cell-line-derived xenograft models as well as patient-derived xenograft models of NSCLC and SCLC. MRT-2359 is currently in a Phase 1/2 clinical trial for the treatment of MYC-driven and high-grade neuroendocrine tumors (ClinicalTrials.gov Identifier: NCT05546268).

#### *Development of GSPT1-directed MGDs to Target Downstream Vulnerabilities of MYC Activation*

In humans, the MYC family transcription factors comprises three proteins, c-MYC, L-MYC, and N-MYC. Upon activation in tumor cells, MYCs can function as oncogenic transcription factors. The MYC family transcription factors have long been recognized as drivers of multiple human cancers and are among the most frequently mutated, translocated and highly expressed oncogenes in human cancers. However, despite 40 years of drug discovery efforts, MYC has remained largely recalcitrant to new drug development and no approved therapies directly or indirectly targeting MYC family transcription factors have been developed to date.

It is well established that abnormal activation of MYC through translocation or high levels of expression results in uncontrolled cell growth that is associated with high rates of protein synthesis and ramp up of the protein translation machinery. MYC-driven tumors are therefore widely believed to be addicted to protein translation, and this addiction to protein translation creates an inherent dependency on critical components of the translation machinery, such as GSPT1, illustrated in Figure 12. As part of our research program, we identified GSPT1 as a potential novel vulnerability of MYC-driven cancers and, based on this observation, we believe that targeting GSPT1 with MGDs represents a viable approach for the treatment and management of patients with MYC-driven cancers. We believe that the administration of our GSPT1-directed MGD product candidate, MRT-2359, has the potential to address a critical downstream vulnerability of oncogenic MYC activation and provide a unique opportunity for therapeutic intervention.

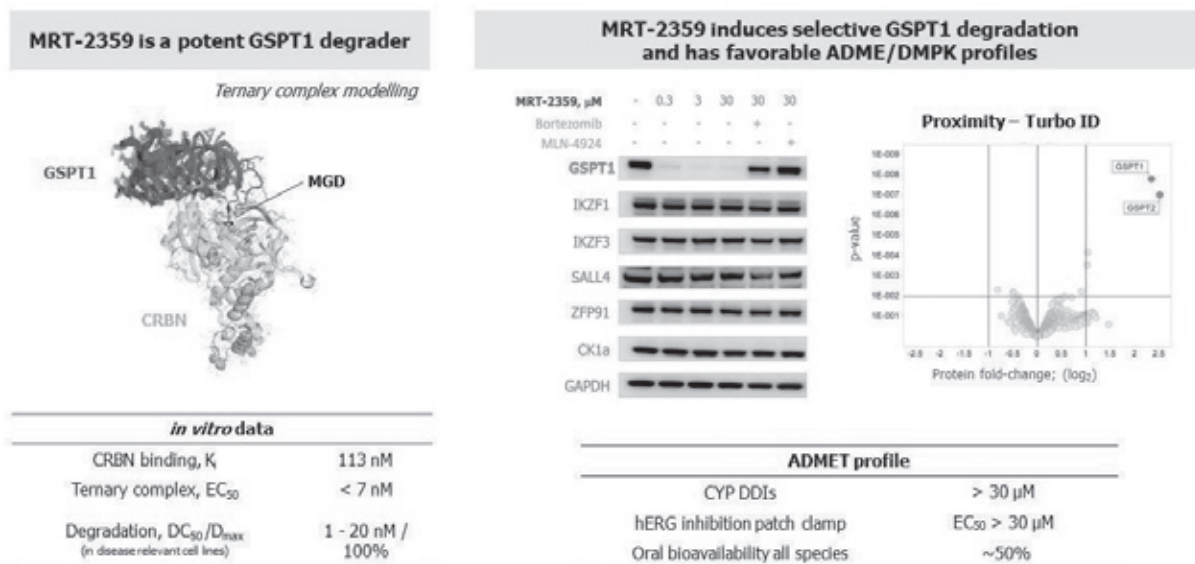
**Figure 12: The Role of GSPT1 in MYC-driven, Translationally Addicted Cancer Cells**



#### *Targeting GSPT1 with MRT-2359 (preclinical data and studies)*

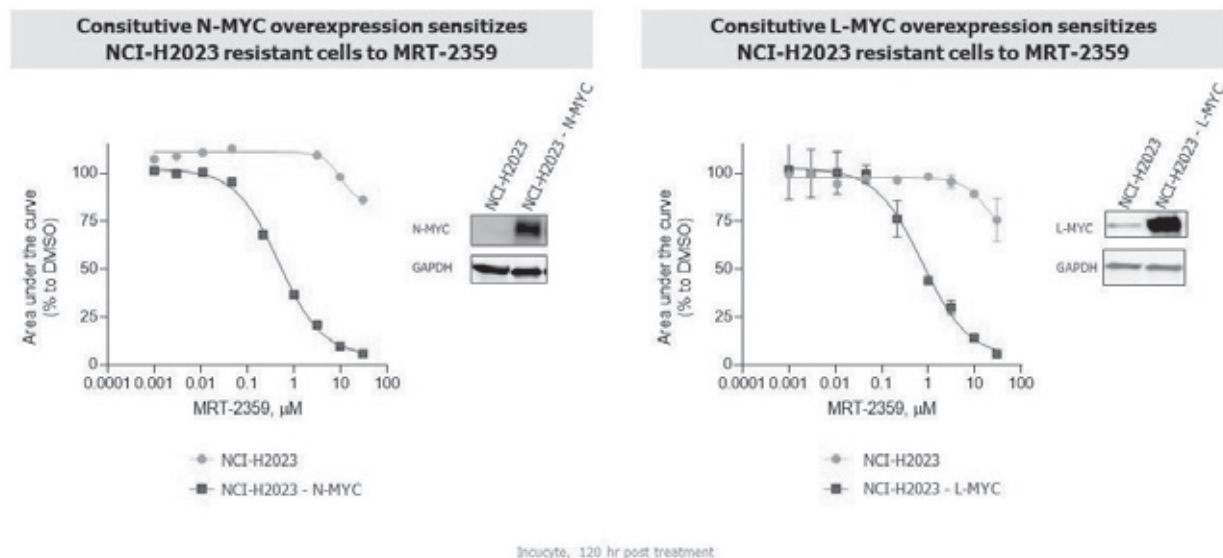
MRT-2359 is a potent and selective GSPT1-directed MGD discovered and rationally designed using our QuEEN™ platform. Key features and parameters of MRT-2359 are provided in Figure 13.

**Figure 13: MRT-2359 is a Selective and Orally Bioavailable GSPT1-directed MGD Rationally Designed Using our QuEEN™ Discovery Engine**



As shown in Figure 14, the sole ectopic overexpression of N-MYC or L-MYC was sufficient to sensitize initially insensitive NSCLC cells (NCI-H2023) to MRT-2359, corroborating a pivotal role of GSPT1 for the survival of MYC-driven cancer cells and demonstrating the potential of MRT-2359 to selectively inhibit growth and survival of L- and N-MYC expressing tumor cells. We believe these studies establish a causal link between N-MYC and L-MYC expression and the sensitivity to MRT-2359 not seen for other agents.

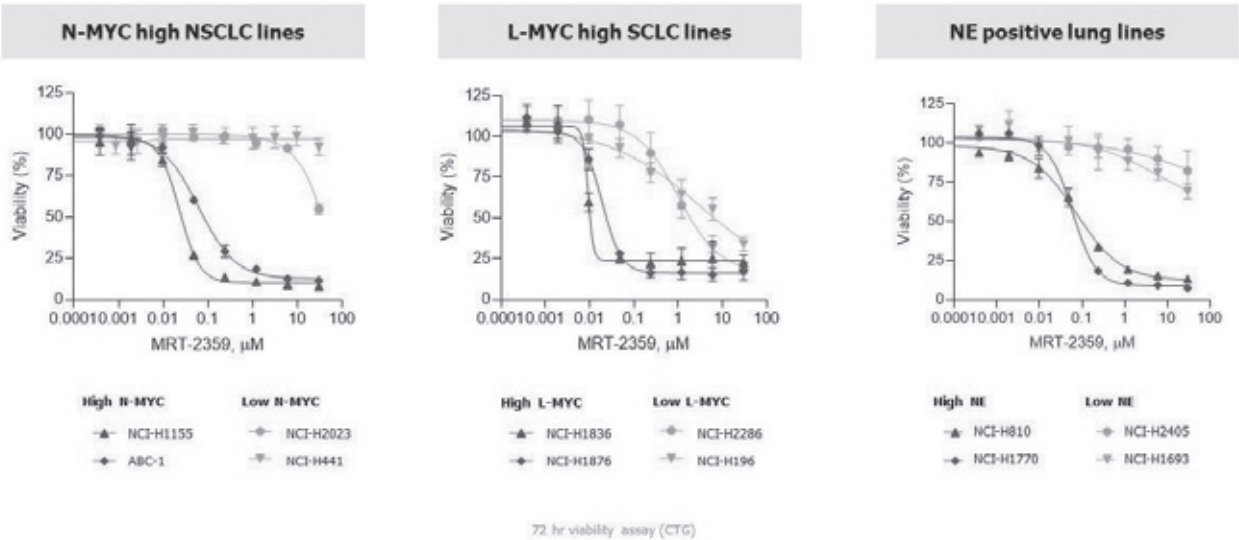
**Figure 14: Overexpression of N-MYC or L-MYC is Sufficient to Sensitize Initially Resistant NSCLC Cells to MRT-2359**



Preferential activity of MRT-2359 on growth and survival of MYC-driven cells was further validated in a panel of representative lung cancer cell lines. As shown in Figure 15, MRT-2359 profoundly and preferentially affected growth and survival of MYC-driven cell lines, such as high N- and L-MYC expressing NSCLC and SCLC lines, compared to their MYC low expressing counterparts. Similar observations were made in neuroendocrine or NE positive versus negative lung cancer cell lines.

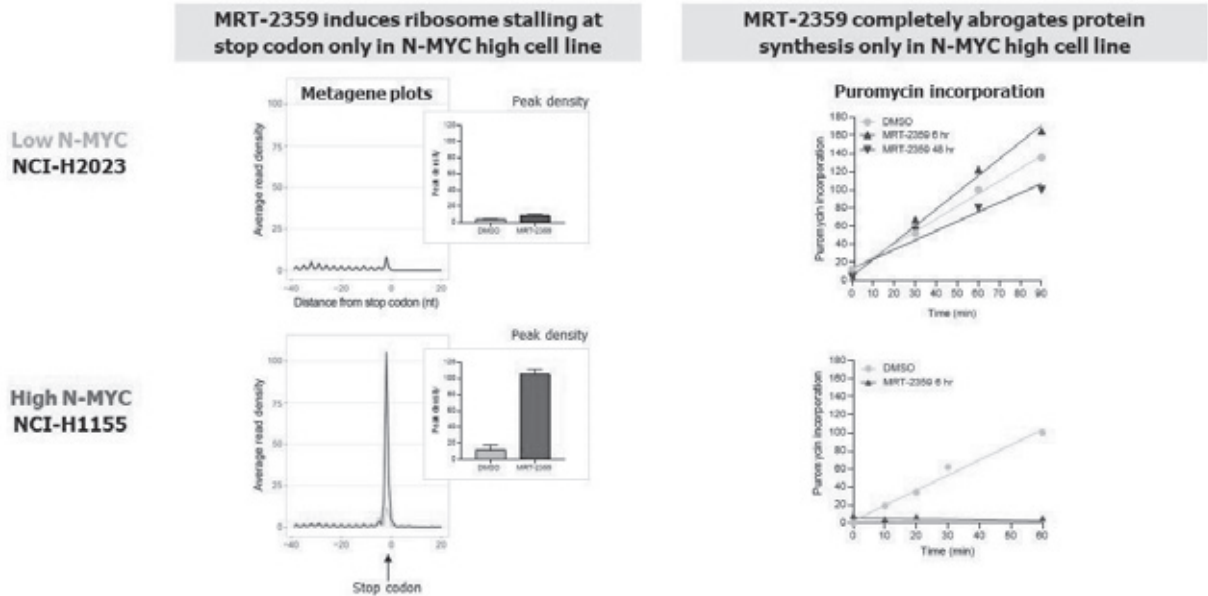


**Figure 15: Preferential Activity of MRT-2359 in MYC High NSCLC, SCLC or Neuroendocrine (NE) Positive Cancer Lines**



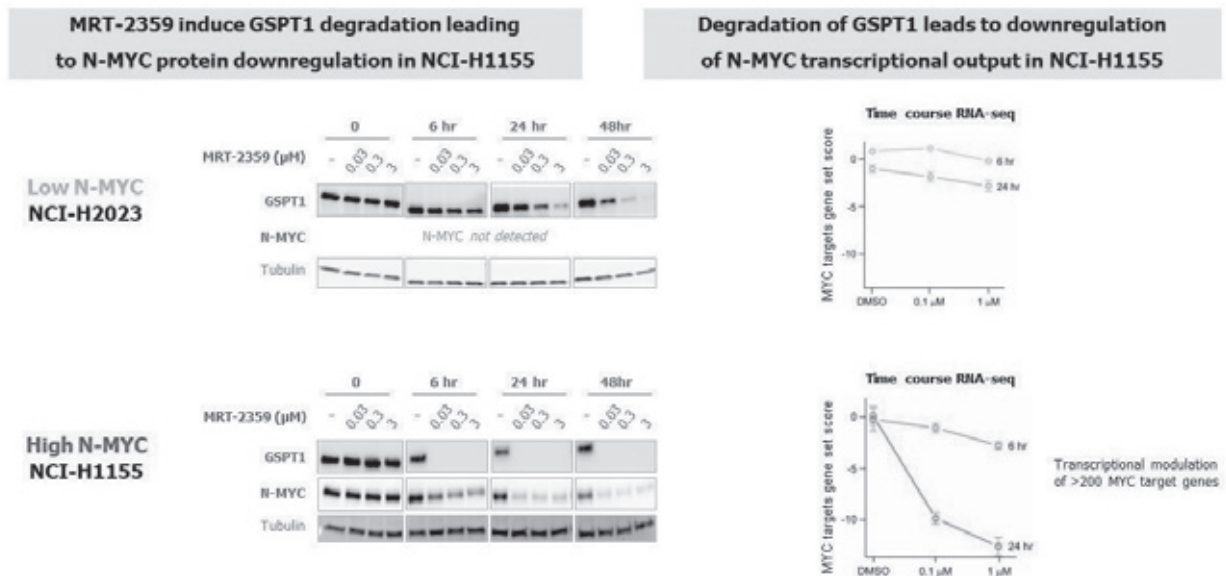
As shown in Figure 16, MRT-2359 induced significant ribosomal stalling at the stop codon of mRNA transcripts only in the MYC high cell lines such as the NSCLC cell lines NCI-H1155. Only minimal effects on ribosomes were seen in the MYC low cell line NCI-H2023. In addition, MRT-2359 rapidly and completely abrogated protein synthesis in NCI-H1155 cells while exhibiting only marginal effects on translation in NCI-H2023 cells.

**Figure 16: MRT-2359 Strongly and Preferentially Impaired Protein Translation in the N-MYC High Compared to the MYC Low NSCLC Cancer Cell Line**



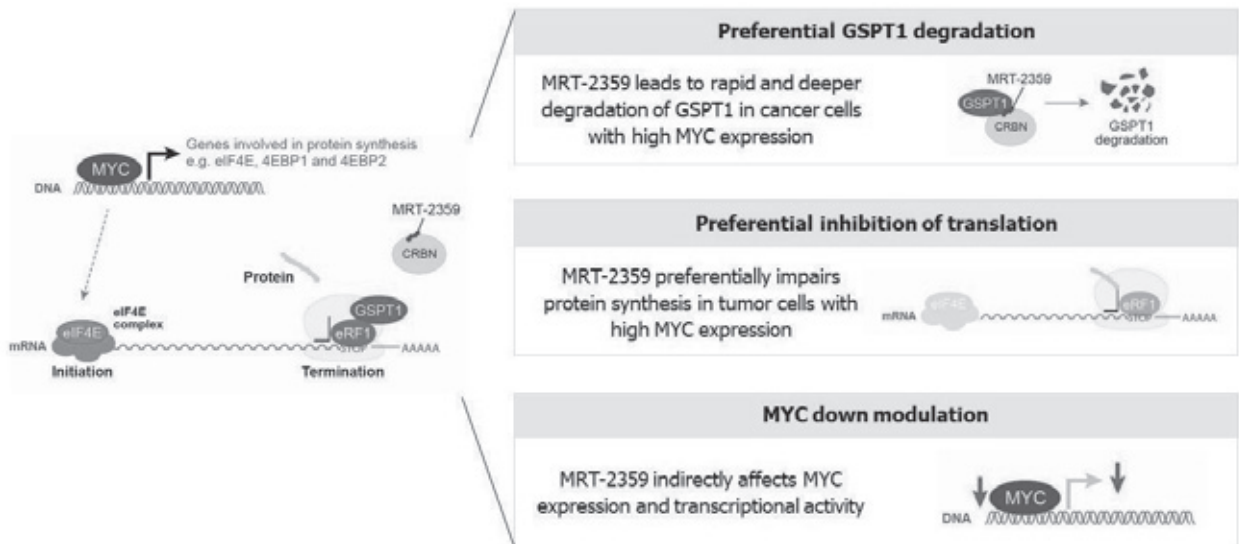
As shown in Figure 17, down modulation of the N-MYC oncogene and of its downstream target genes was observed in the NCI-H1155 cell line following MRT-2359 induced degradation of GSPT1. Further, N-MYC could not be detected in the NCI-H2023 cell line, and no significant effects were detectable on N-MYC downstream target genes after degradation of GSPT1.

**Figure 17: MRT-2359 Downmodulated N-MYC and Its Downstream Target Genes in the N-MYC High Compared to the MYC Low NSCLC Cancer Cell Lines**



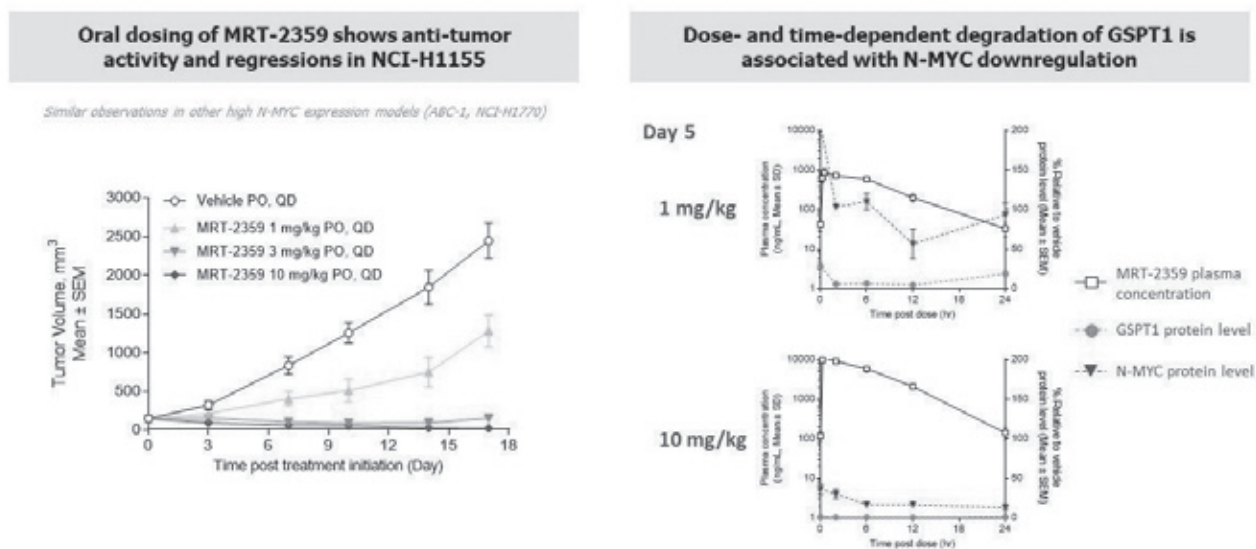
Collectively, we believe that the inhibition of growth and survival of MYC-driven versus MYC-independent tumor cells results from a combination of (i) preferential degradation of GSPT1, (ii) preferential ribosome stalling and protein synthesis inhibition and (iii) downregulation of MYC-induced transcription in MYC-addicted but not MYC-independent tumor cells, as depicted in Figure 18.

**Figure 18: Three Mechanisms Driving Preferential Activity in MYC High Cancer Lines**



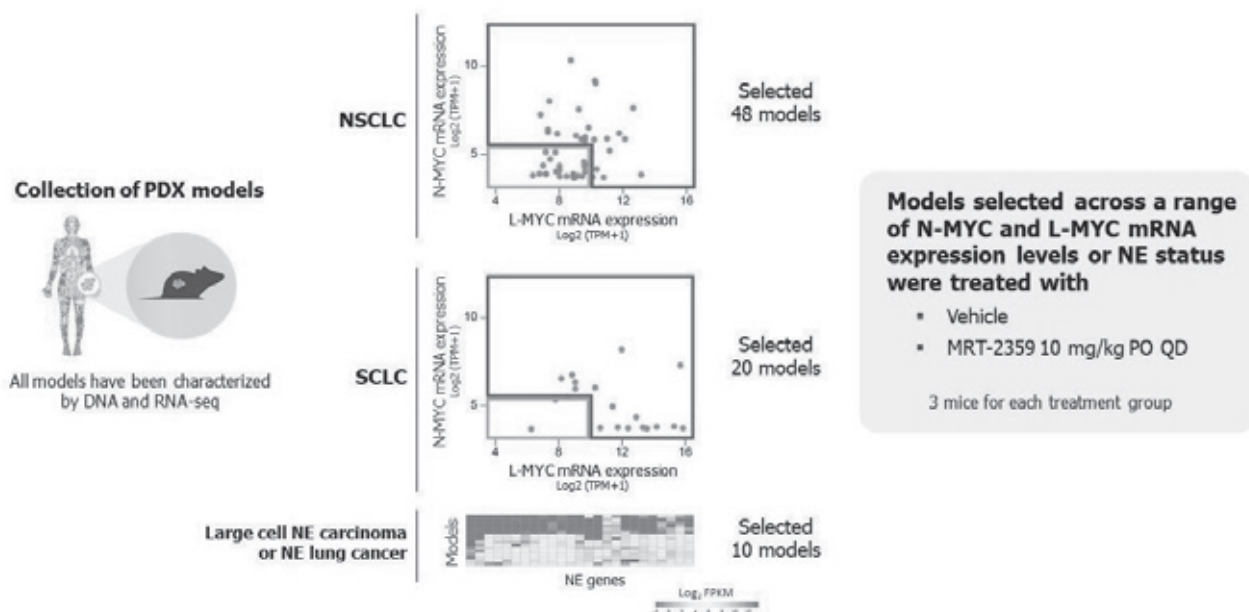
As shown in Figure 19, MRT-2359 demonstrated significant dose-dependent anti-tumor activity *in vivo*, including regressions, in an NCI-H1155 cell line-based xenograft model. In this study, MRT-2359 was dosed orally (PO) once daily (QD) at 1, 3 and 10 mg/kg. Figure 19 also shows that anti-tumor activity was accompanied by a dose-dependent reduction of levels of both GSPT1 and N-MYC protein following the administration of 5 consecutive doses of MRT-2359 at 1 and 10 mg/kg.

**Figure 19: Anti-tumor Activity and Effects on GSPT1 and N-MYC of MRT-2359 in the N-MYC High NCI-H1155 NSCLC Xenograft Model**



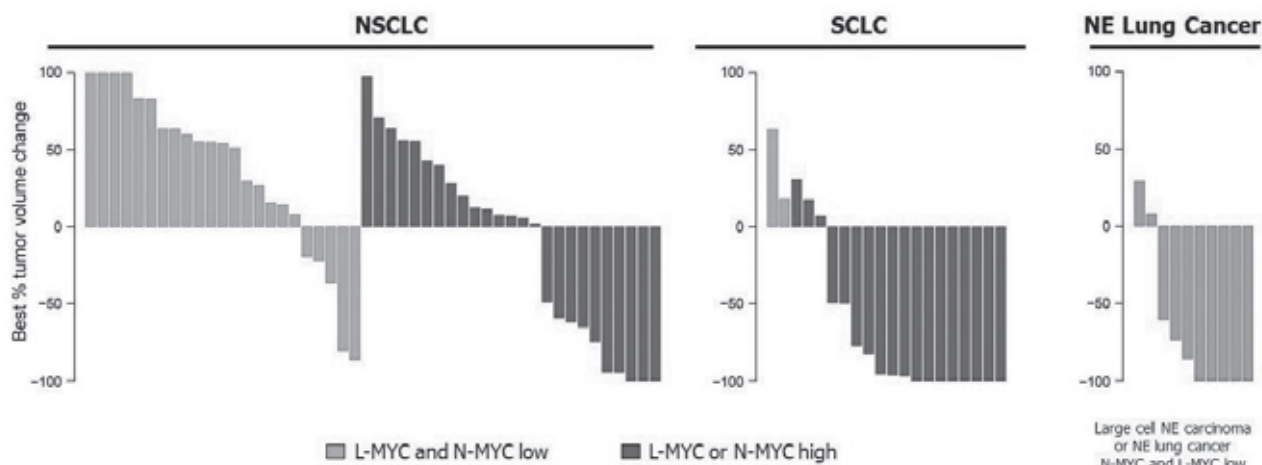
The anti-tumor activity of MRT-2359 was further assessed in 78 fully annotated lung cancer patient-derived xenograft or PDX models. As shown in Figure 20, models were selected across a wide range of L- and N-MYC mRNA expression levels or based on their NE status.

**Figure 20: MRT-2359 Mouse-trial in NSCLC, SCLC and Lung NE Patient-derived Xenografts**



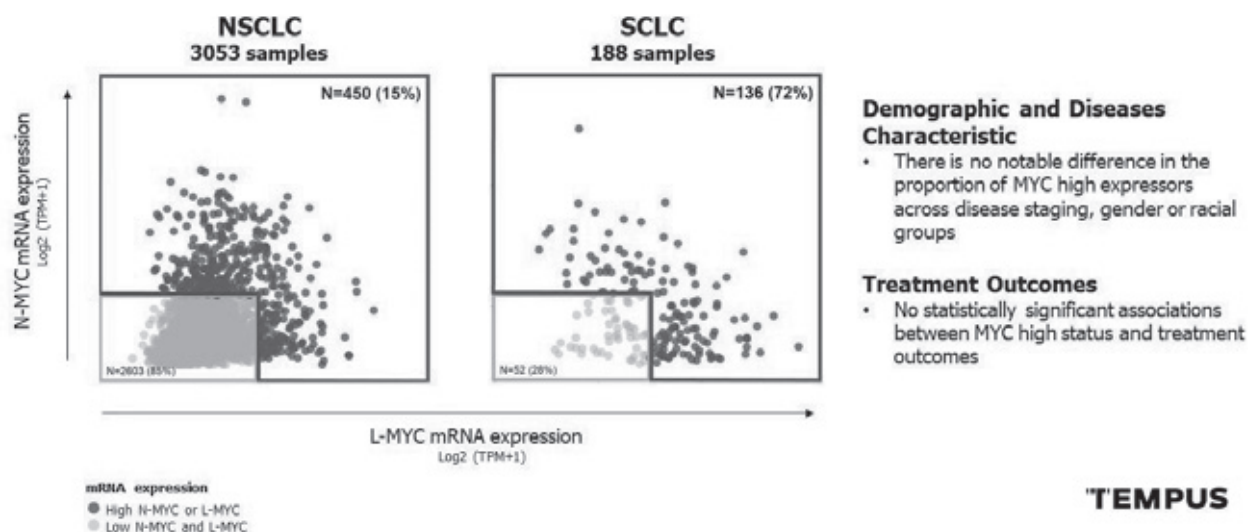
As shown in Figure 21, oral dosing of MRT-2359 demonstrated preferential activity in models expressing high levels of L- and N-MYC within both NSCLC and SCLC PDXs, including numerous instances of tumor regressions. Similar levels of anti-tumor activity were observed in neuroendocrine lung cancer PDX models.

**Figure 21: MRT-2359 Demonstrated Preferential Anti-tumor Activity in MYC High or Neuroendocrine (NE) Lung Cancer PDXs**



As shown in Figure 22, we analyzed the expression of both L-MYC and N-MYC in samples from patients with both NSCLC and SCLC using real world genomic data and determined the frequency to be 15% and 72% respectively. (Figures adapted from real world molecular and genomic data analysis on 3241 lung cancers in collaboration with Tempus Labs, Inc.).

**Figure 22: Real-world Data Analysis of L-MYC and N-MYC mRNA Expression and Amplification in Lung Cancer**



### Non-small cell lung cancer

There are an estimated 238,000 new cases of lung cancer diagnosed in the United States each year, and lung cancer causes 127,000 deaths annually in the United States. NSCLC accounts for 80% to 85% of lung cancer cases.

While targeted therapies have been developed for patients with certain tumors, less than thirty percent of patients are eligible for these therapies. Patients who are ineligible or resistant to these therapies can be treated with immune checkpoint inhibitors that lead to significant improvements in progression free survival and overall survival compared to standard chemotherapy. However, despite the availability of these therapies, very few patients are cured of their disease and the prognosis in NSCLC remains poor, with an average five-year survival rate for newly diagnosed patients with NSCLC of 28 percent. Accordingly, there is an unmet medical need for the treatment of patients with NSCLC.

As shown above in Figure 22, our data as well as data from the analyses of molecular data from NSCLC tumors found that around 15% of NSCLC tumors have elevated L- or N-MYC expression. We believe that our preclinical data, presented above, supports that these tumors will be sensitive to our GSPT1-directed MGD, MRT-2359.

#### *Small cell lung cancer*

SCLC is estimated to represent approximately 15% of all lung cancers, accounting for 30,000 new cases a year in the United States. SCLC is a rapidly progressive disease with short overall survival after initial therapeutic responses. SCLC is derived from neuroendocrine cells and is distinguished clinically from NSCLC by its rapid doubling time and the early development of metastases. Most patients have metastatic disease at the time of their initial diagnoses.

Unlike in NSCLC, which has seen a steady stream of new drug approvals over the last 2 decades, the progress and consequent improvement in treatment outcomes in SCLC have been more modest. The 5-year survival rate for patients with extensive stage SCLC, which accounts for 80% of all patients diagnosed, remains at 3% with a median survival between 10-13 months. Patients with limited stage SCLC can be treated with combined chemoradiation; however, the 5-year survival rates fluctuate between 30% to 40%. Most patients with SCLC are responsive to chemotherapy, but eventually relapse. In extensive stage SCLC, immune checkpoint inhibitors atezolizumab and durvalumab have been approved for use in conjunction with chemotherapy. Overall response rates for chemotherapy, with or without immunotherapy, are around 60%; however, the median progression-free survival ranges from 4-5 months and the overall survival ranges from 10-13 months. Upon relapse, patients are offered alternative therapies based on their quality and duration of response to initial treatment, but most are chemotherapy-based. Expected outcomes in previously treated patients remain unsatisfactory with response rates between 25% to 35%, which creates a significant unmet need for development of new therapies. There are no targeted therapeutics available for SCLC patients.

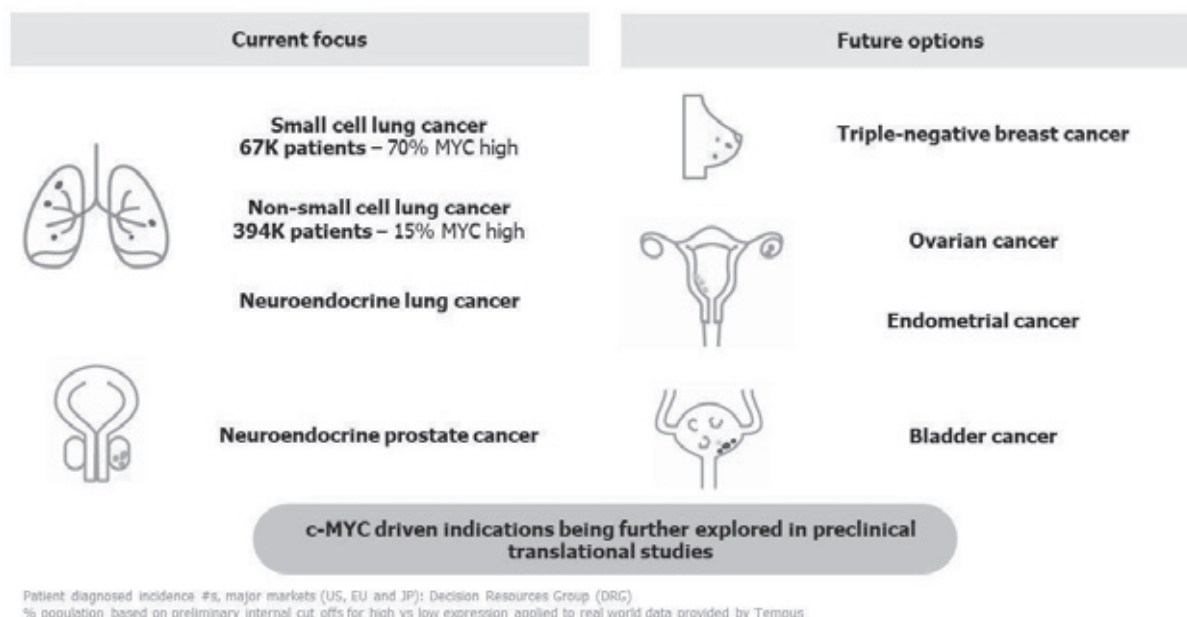
As shown above in Figure 22, our data as well as data from the analyses of molecular data from other SCLC tumors found that over half of these tumors have elevated levels of L- and N-MYC expression. We believe that our preclinical data presented above supports that these tumors will be sensitive to our GSPT1-directed MGD, MRT-2359.

#### *Potential Indications*

We believe that there are multiple other tumor types, beyond NSCLC and SCLC, in which the MYC pathway is highly activated. As shown in Figure 23, in addition to the current indications included in the MRT-2359-001 Phase 1/2 clinical study, future indications may include triple-negative breast cancer, ovarian and endometrial cancers, bladder cancer, all driven by L- and N-MYC to a substantial degree, as well as various c-MYC driven cancer types.



**Figure 23: Targeting L-/N-MYC positive and Neuroendocrine Tumors with MRT-2359**

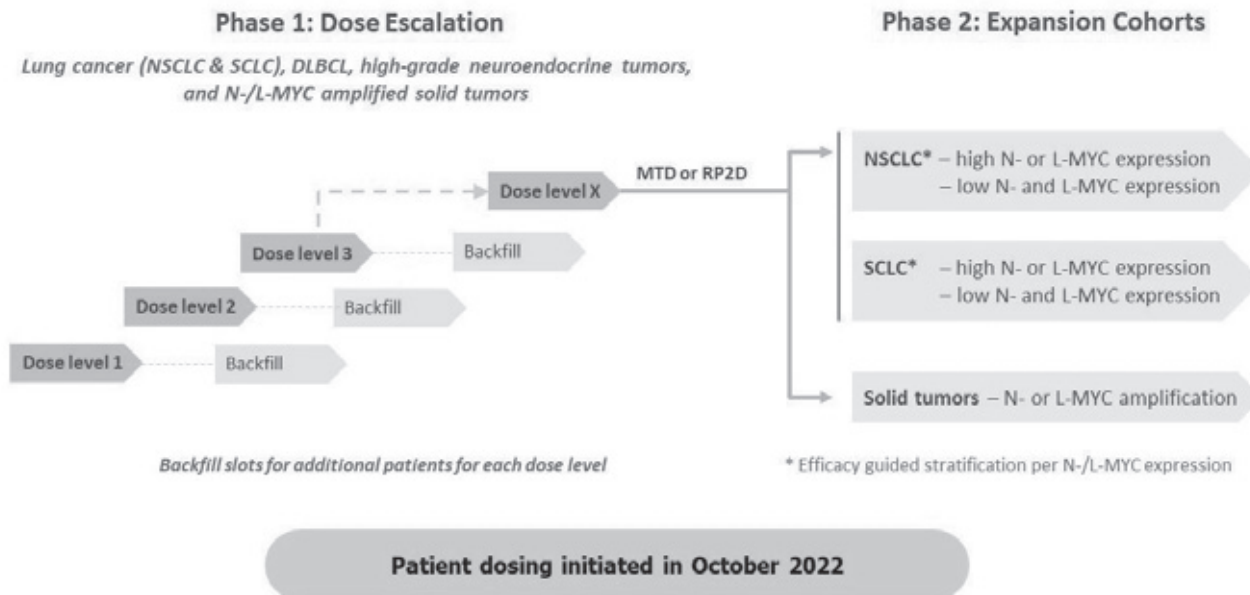


### *MRT-2359-001 Phase 1/2 Study*

Our ongoing Phase 1/2, open-label, multicenter study, illustrated in Figure 24, will primarily assess the safety, tolerability, PK, PD, and preliminary clinical activity of MRT-2359 in patients with previously treated selected solid tumors. In the Phase 1 dose escalation portion of the clinical trial, we are enrolling patients with tumors that have a significant likelihood of being MYC-driven, including patients with NSCLC, SCLC, high-grade neuroendocrine cancer of any primary site, DLBCL and patients with solid tumors that harbor L-MYC or N-MYC amplifications. In this phase of the trial, tumors will be tested retrospectively for biomarkers of MYC activation. Patients will receive escalating doses of MRT-2359 to determine the maximum tolerated dose or MTD and recommended Phase 2 dose or RP2D.

Once the MTD and/or RP2D are determined, the anti-tumor activity of MRT-2359 will be assessed in the Phase 2 portion of the study, which will enroll NSCLC and SCLC stratified per L-MYC or N-MYC expression, and solid tumors with L-MYC or N-MYC amplification. We expect to disclose initial clinical data including PK, PD, safety and available initial efficacy from the Phase 1 arm of the ongoing Phase 1/2 clinical trial evaluating MRT-2359 in the second half of 2023.

**Figure 24: MRT-2359 Clinical Study Design**

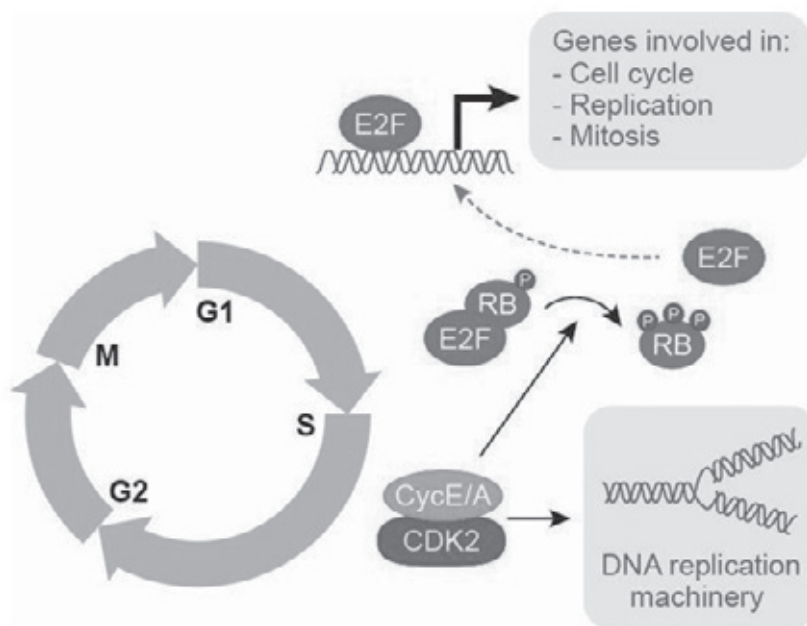


### ***CDK2-directed MGD molecules for the treatment of cancer***

Cyclin dependent kinases, or CDKs, are a family of closely related kinases that regulate progression through the cell cycle. CDK activity is modulated by specific cyclins. For example, cyclin E1 activates cyclin-dependent kinase 2, or CDK2 (Figure 25). CDK2 can be activated in tumors by the amplification or overexpression of Cyclin E1 or E2, or loss-of-function alterations of the retinoblastoma or RB1 gene. Cyclin E1 dysregulation has been found in several cancers, including ovarian and triple negative breast cancer. In addition, cyclin E1 dysregulation and CDK2 activation has also been found to be one of the mechanisms of resistance in estrogen receptor-positive breast cancer patients treated with CDK4/CDK6 inhibitors such as palbociclib. Therefore, we believe selective elimination of CDK2 using CDK2-directed MGDs may provide benefit to these patients. Previously reported small molecule inhibitors and PROTACs of CDK2 have been limited in their selectivity due to the high degree of similarity among the active sites of kinases, in particular within the CDK family itself. We have identified multiple MGD molecules that selectively promote the association of CDK2 and cereblon *in vitro*, while avoiding other CDKs. The most advanced compounds robustly and selectively induce the degradation of CDK2 in multiple cancer cell lines *in vitro* with concomitant inhibition of proliferation. Lead optimization chemistry is ongoing.



**Figure 25: CDK2 is One of the Key Regulators of the Cell Cycle**



#### *Identification of CDK2 degran CDK2-directed MGDs*

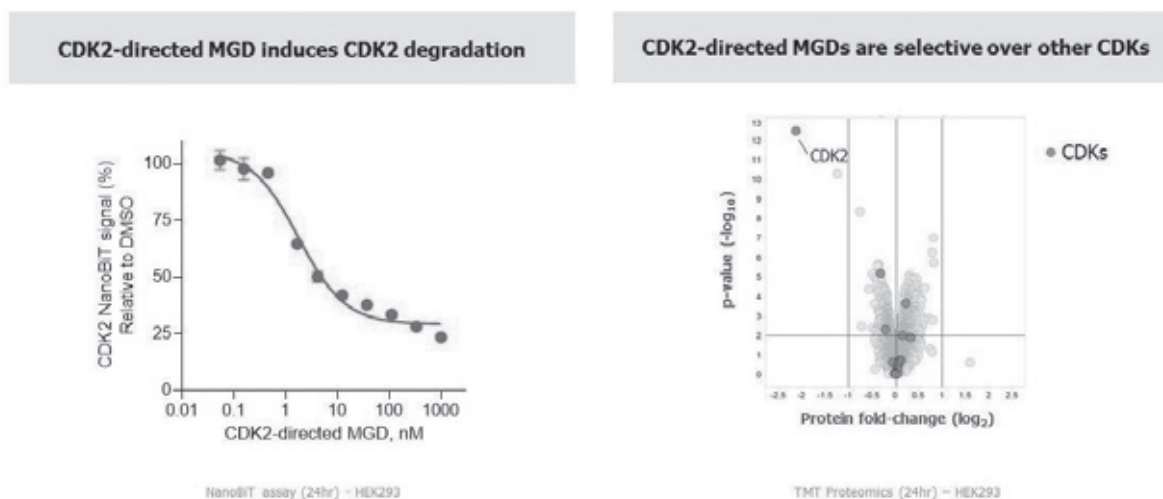
To identify molecular glue degraders targeting CDK2, we screened our proprietary MGD library in a biochemical HTRF assay to detect the formation of a ternary complex between cereblon, an MGD and CDK2. Through iterative chemistry based on the screening hits, we rapidly identified a series of MGDs that promoted the association of CDK2 with cereblon.

We confirmed that these CDK2-directed MGDs showed concentration-dependent ternary complex formation. We also assessed the biochemical selectivity of the hits over CDK1, CDK4 and CDK9 using similar HTRF assays. No ternary complex formation with these closely related kinases was observed (data not shown). Based on these initial results, we have initiated lead optimization chemistry and have successfully delivered several lead compounds from different chemical series. Using structural analysis of the interaction between cereblon, the MGD and CDK2, we have discovered a novel, previously unknown degran on CDK2.

#### *In vitro data*

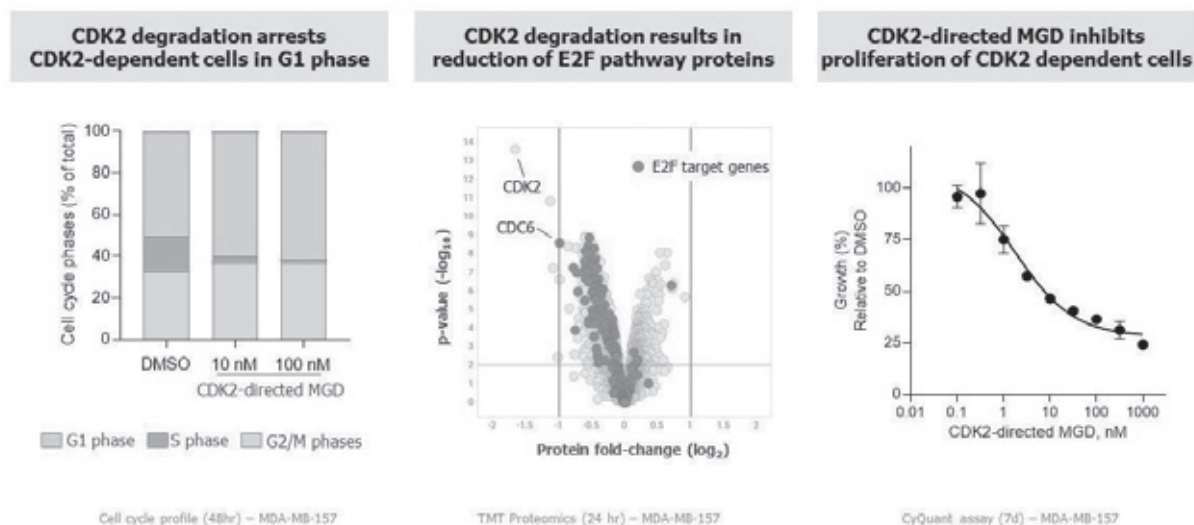
Our lead optimization process has provided several MGDs that promote ternary complex formation. In addition, we have shown specific degradation of CDK2 with our MGDs, with no significant effect on other CDKs or other kinases, as shown in Figure 26.

**Figure 26: CDK2-directed MGD Showed Selective Degradation Over the Other CDKs**



In addition, in cellular assays we have shown that a CDK2-directed MGD blocked DNA replication (S phase) in CDK2 dependent cells, induced a reduction of proteins in the E2F pathway and inhibited cellular proliferation in a concentration-dependent manner, as shown in Figure 27.

**Figure 27: CDK2-directed MGD Showed Biological Activity in a CDK2 dependent Cell Line**

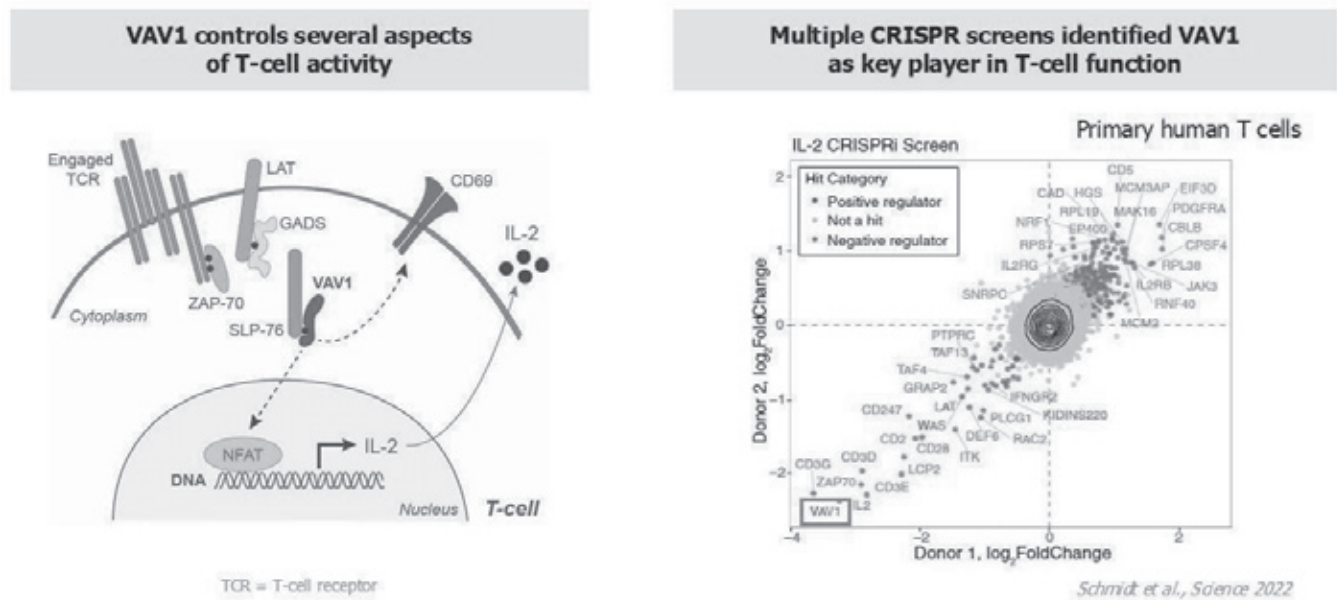


### **VAV1-directed MGD molecules for the treatment of autoimmune diseases**

VAV1, a Rho-family guanine nucleotide exchange factor, is expressed in immune cells including T and B cells and functions to mediate T and B cell receptor signaling (shown in Figure 28). Because of VAV1's function in both T and B cells, degradation could provide therapeutic benefits in multiple autoimmune diseases, including multiple sclerosis, myasthenia gravis, and rheumatoid arthritis. VAV1 degradation may also provide a benefit in the transplantation setting and graft versus host disease, preventing organ rejection. Recent studies, which included multiple whole-genome CRISPR screens in primary human T cells, have further validated VAV1's role as a key player in T-cell function, showing that the genetic elimination of VAV1 attenuated T-cell activity, exemplified by reduced IL-2 secretion in Figure 28, right panel.

While considered an undruggable protein, with no small molecule drugs known to inhibit its function in clinical development, we identified VAV1 as a degron-containing protein and have discovered VAV1-directed MGDs that in preclinical studies promoted the association of VAV1 and cereblon and led to the degradation of VAV1 protein. We have further optimized our lead MGDs derived from a highly selective chemical series and are currently completing lead optimization. We believe our unique ability to specifically target VAV1 provides us with a new therapeutic approach with the potential to treat a variety of autoimmune pathologies in a large patient population with significant medical needs.

Figure 28: VAV1 is a Highly Validated Target for Attenuating T-cell Activity

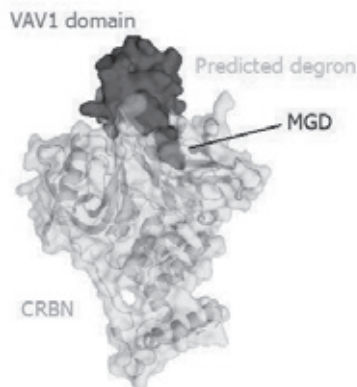


Identification of VAV1 degron and VAV1-directed MGDs

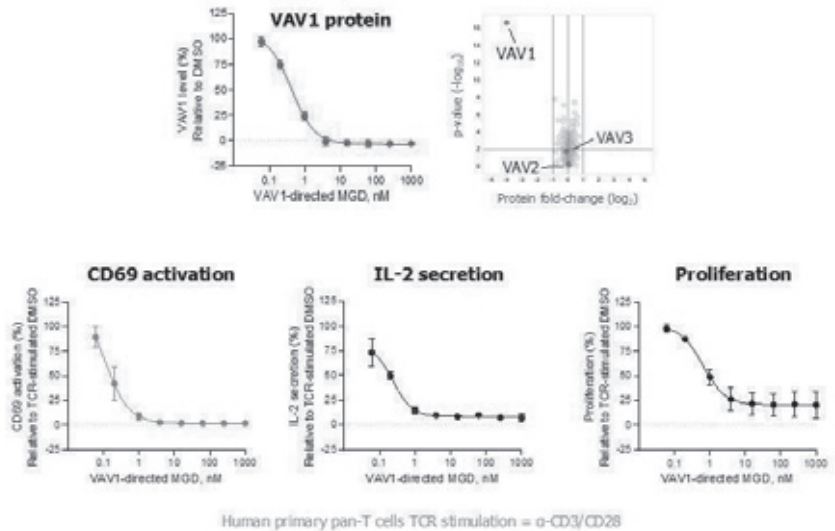
Our degron identification algorithm, fAlceit™, indicates that VAV1 contains a unique degron compared to other members of the VAV family of GEFs, suggesting we can target VAV1 selectively with our MGD molecules. As shown in Figure 29, left panel, structural analysis of the complex formed between cereblon, VAV1 and the MGD shows the predicted degron indeed participates in the protein interface. The right panel of Figure 29 shows the highly selective degradation of VAV1 in a T-cell derived cell line (Jurkat), and the dose-dependent degradation of VAV1 in human primary T-cells, with a resulting decrease in CD69 activation, IL-2 secretion, and cellular proliferation.

Figure 29: Rationally Designed Highly Selective VAV1-directed MGDs

## Degron predicted and confirmed



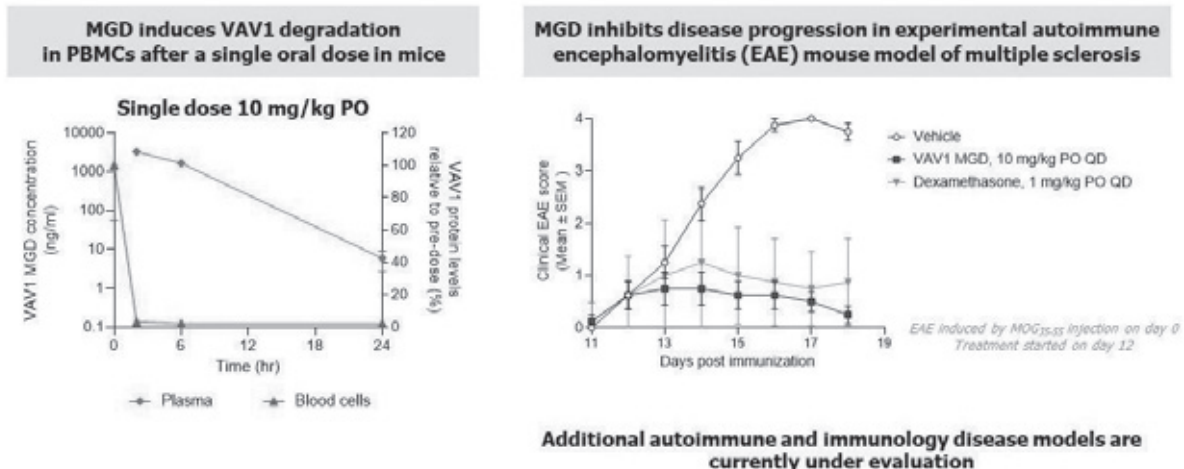
## MGD-induced degradation of VAV1 results in inhibition of TCR-mediated CD69 activation, IL-2 secretion, and proliferation



### *In vivo studies with our VAV1-directed MGDs*

Highlighted here are experiments focused on an experimental autoimmune encephalomyelitis or EAE mouse model of multiple sclerosis, where T-cells play a major role in progression of the disease. In Figure 30, left panel, following a single oral dose of a VAV1-directed MGD in mice, we see a rapid decrease in VAV1 protein, associated with the presence of the VAV1-directed MGD in plasma (green), that was sustained out to 24h post dose. In the EAE model, disease was induced at day 0. Upon disease establishment, the same VAV1-directed MGD or dexamethasone were dosed daily starting on day 12. Mice were scored for EAE clinical signs of disease (0 = no signs of disease; 1 = limp tail or hind limb weakness; 2 = limp tail and hind limb weakness; 3 = partial hind limb paralysis; 4 = complete hind limb paralysis; 5 = moribund). The right panel of Figure 30 shows that orally dosed VAV1-directed MGD inhibited disease progression in the EAE model similar to dexamethasone, a corticosteroid used broadly in auto-immune disease.

**Figure 30: VAV1-directed MGD Inhibited Disease Progression in an EAE Mouse Model**



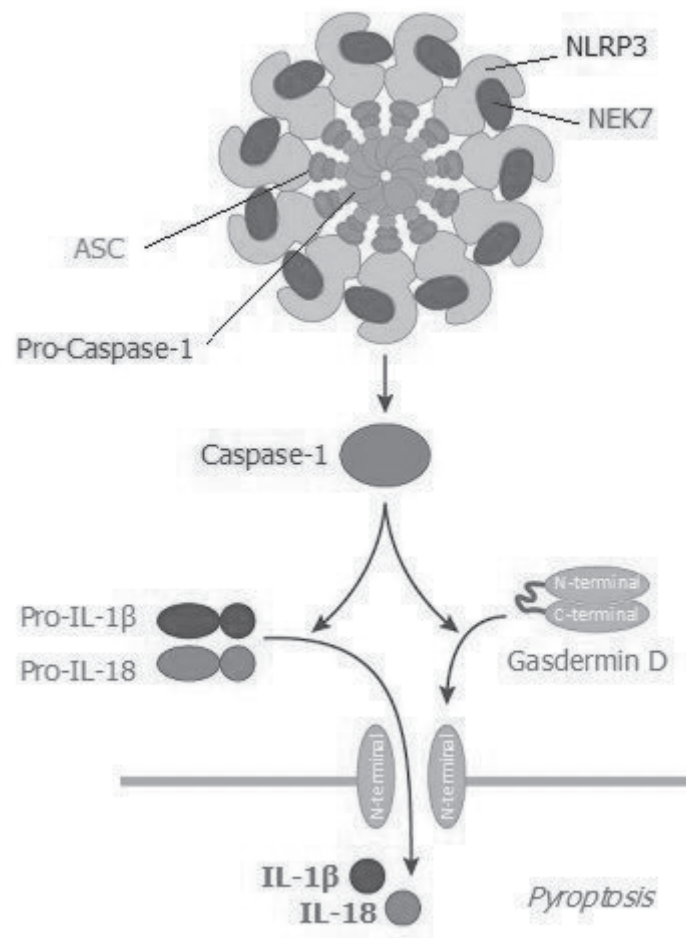
### **NEK7-directed MGDs for the treatment of inflammatory disease**

The NLRP3 inflammasome is a multiprotein complex that serves as a central node to integrate cellular signals generated by pathogens, damage and stress, and subsequently triggers the generation of pro-inflammatory cytokines, as shown in Figure 31. Aberrant NLRP3 inflammasome activation has been implicated in several autoinflammatory disorders including gout, Crohn's disease, neurodegenerative diseases, diabetes and liver

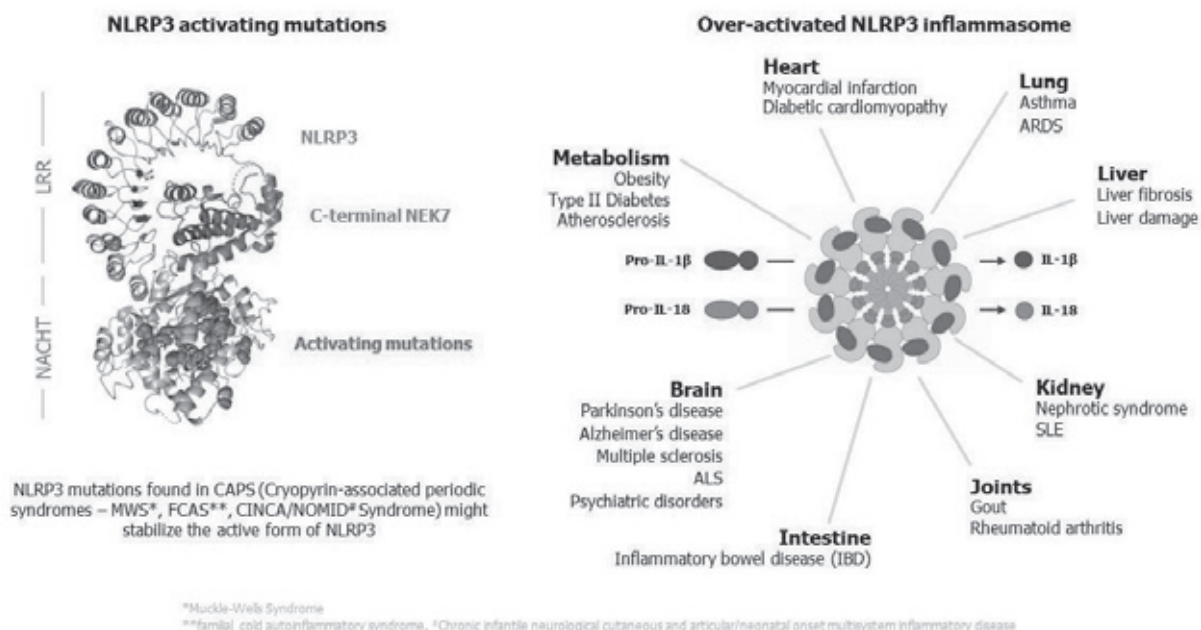
disease. Additionally, multiple activating NLRP3 mutations have been shown to be associated with Cryopyrin-associated periodic syndromes, shown in Figure 31.

NIMA-Related Kinase 7, or NEK7, a serine/threonine-protein kinase, activates the NLRP3 inflammasome in a kinase-independent manner, suggesting that degradation of NEK7 with an MGD molecule is an attractive therapeutic approach. NEK7 binding to NLRP3 is an essential step in promoting the assembly of the NLRP3 inflammasome. The assembly of NLRP3/NEK7 with ASC and pro-caspase 1 in a multi-protein complex induces cleavage of pro-caspase 1, which then activates multiple inflammatory responses including secretion of the cytokines interleukin-1 $\beta$  and interleukin-18 and the induction of pyroptosis, as depicted in figure 31. Knockout of NEK7 in animal models has been shown to decrease inflammatory signaling, which leads to decreased disease severity in models of inflammatory diseases.

**Figure 31: NEK7 is an Essential Regulator of the Inflammasome**



**Figure 32: Overactivation of the NLRP3 Inflammasome in Disease**



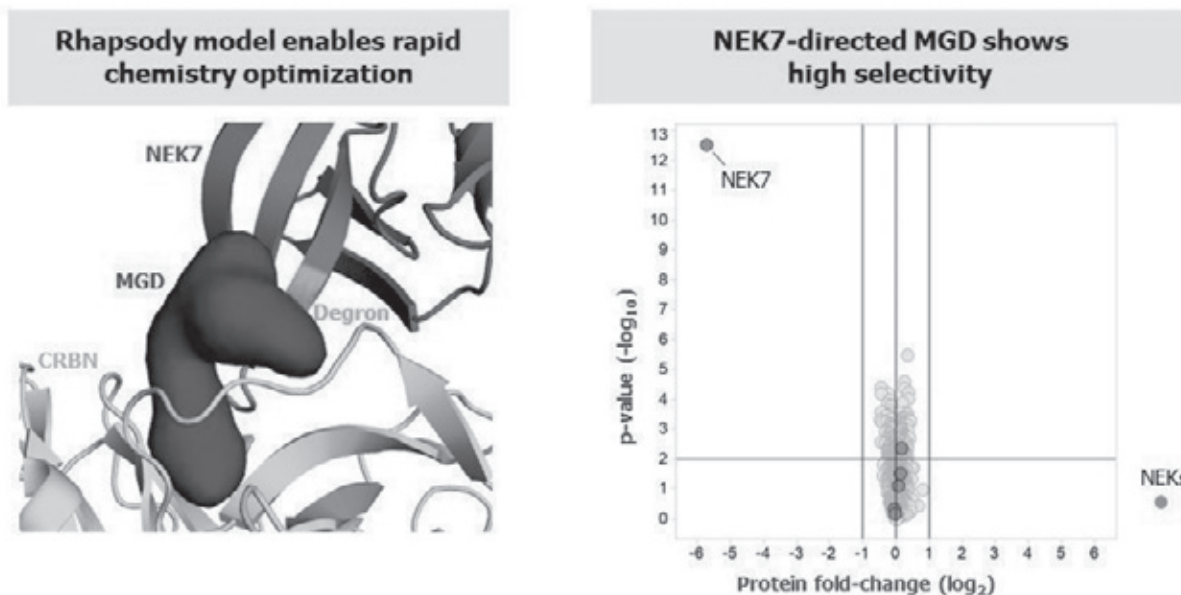
Activation of the NLRP3 inflammasome is driven through a kinase-independent function of NEK7, suggesting that inhibition of the catalytic activity of NEK7 would be ineffective in blocking NLRP3 inflammasome activation. We found that NEK7 contains a well-defined degron and have identified MGDs that are highly selective for NEK7 in *in vitro* models. We are currently optimizing MGDs that are derived from multiple chemical series in this program.

#### Identification of NEK7 degron and NEK7-directed MGDs

NEK7 contains a well-defined degron, as identified using our proprietary QuEEN™ platform (shown in Figure 33, left panel). Given the kinase-independent role of NEK7 in activating the NLRP3 inflammasome, we believe that degradation of NEK7 with our MGDs will be preferable over conventional catalytic inhibition strategies. We have generated MGDs that promoted the association of NEK7 with cereblon, and the program is currently at the lead optimization stage.



**Figure 33: Rationally Designed NEK7-directed MGD promotes selective degradation of NEK7**

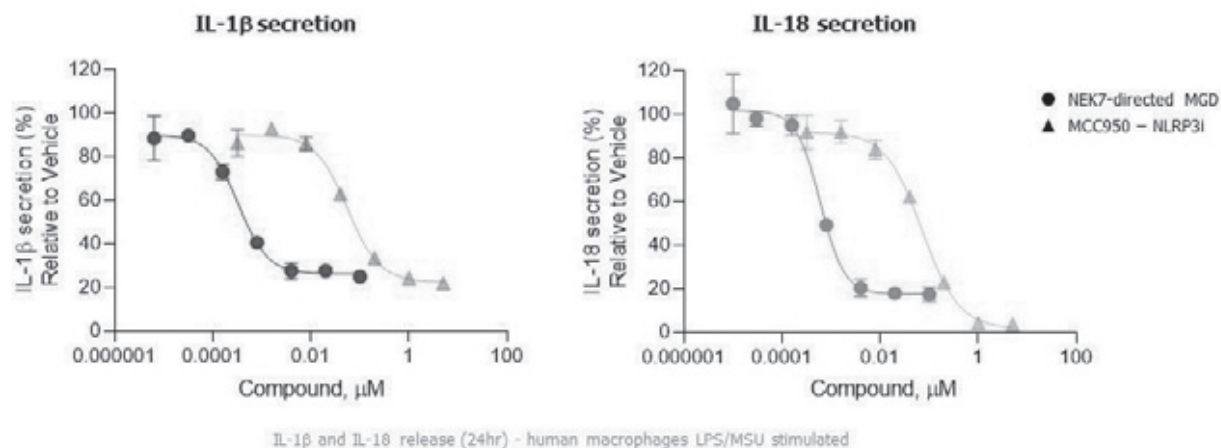


The amino acid sequence of the NEK7 degron is unique among the NEK family members, indicating the potential to identify MGDs that are highly selective for NEK7. Our lead optimization process has provided several MGDs that promote ternary complex formation and highly selective degradation of NEK7. As shown in Figure 33, right panel, U937 cells were treated with one of our MGDs for 24 hours, followed by proteomic profiling. Highly selective and profound degradation of NEK7 is evidenced by selective decrease in NEK7 protein fold-change, without significant changes in other detected proteins. Other NEK family members are highlighted on the volcano plot and confirmed not to be degraded.

*NEK7-directed MGDs show high potency modulation of the NLRP3 pathway in human monocyte-derived macrophages*

To assess the functional impact of NEK7 degradation on NLRP3 inflammasome activation, we treated human monocyte-derived macrophages, or hMDMs, with increasing concentrations of one of our NEK7-directed MGDs. We measured IL-1 $\beta$  and IL-18 secretion from hMDMs following pre-treatment with our MGD and subsequent exposure to inflammasome stimulators LPS and monosodium urate crystals or MSU. The MSU stimulus is relevant to the setting of gout, where high uric acid levels lead to accumulation of MSU crystals in joints and the subsequent pathogenic activation of NLRP3 inflammasome. As shown in Figure 34, our NEK7-directed MGD led to a dose-dependent decrease in IL-1 $\beta$  (left) and IL-18 (right) secretion. We also compared the activity of our MGD to the NLRP3 inhibitor MCC950 and, as shown in Figure 34, our MGD shows superior modulation of NLRP3 pathway-induced IL-1 $\beta$  and IL-18 secretion.

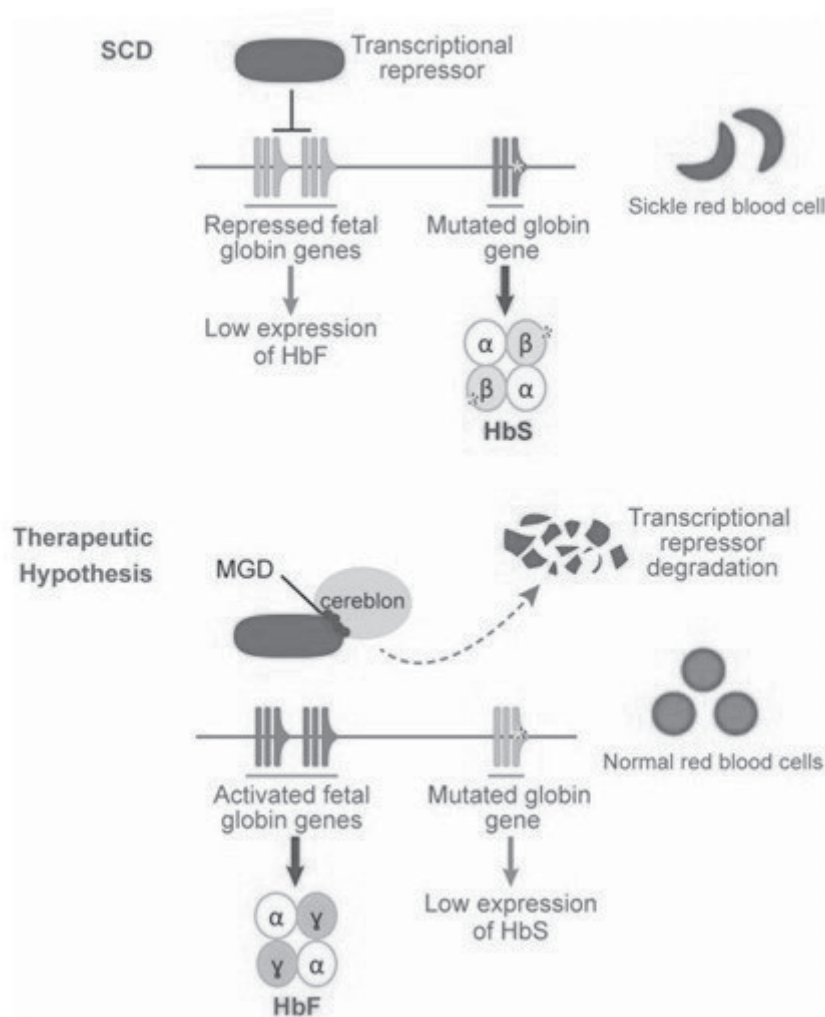
**Figure 34: NEK7-Directed MGDs Modulate NLRP3 Pathway in Human Macrophages**



### ***MGDs targeting Transcriptional Repressors for the treatment of Hemoglobinopathies (SCD and $\beta$ -Thalassemia)***

Sickle cell disease, or SCD, is caused by a mutation in a form of hemoglobin, leading to severe disease manifestations, including anemia and vaso-occlusive crises. However, in SCD patients, increasing levels of fetal hemoglobin, or HbF, are associated with fewer co-morbidities and a better prognosis. In adults, several transcription repressors prevent transcription of the HBG gene, thereby silencing HbF expression. We believe that degradation of one of these repressors to reactivate HbF expression is a promising therapeutic strategy, and it is being clinically tested by third parties to treat SCD using adoptive cell therapy. These repressors have to date been considered undruggable using small molecule therapies. We believe reactivation of HbF through MGD-mediated protein degradation could be used as a therapeutic strategy for both SCD as well as other hemoglobinopathies, such as  $\beta$ -Thalassemia, as shown in Figure 35.

**Figure 35: Zinc finger domain-containing transcriptional repressors of the fetal globin genes**



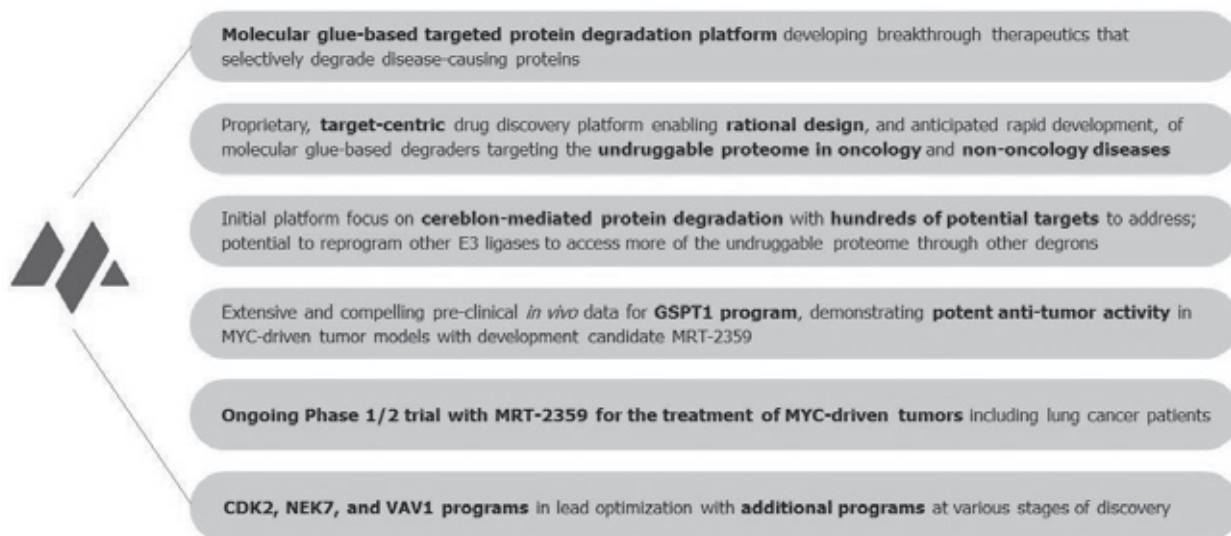
### **Current status and next steps of our discovery programs**

We are currently optimizing chemical leads that are derived from multiple series of MGD molecules in our CDK2, NEK7, VAV1 and sickle cell disease programs. Our VAV1, CDK2 and NEK7 programs are currently in lead optimization with the next anticipated milestone being selection of a development candidate and the initiation of IND-enabling studies.

### **Other programs**

We are specifically focused on developing product candidates for target proteins that have been deemed undruggable or inadequately drugged. Our QuEEN™ platform was purpose-built to support the discovery and development of drugs that degrade a wide landscape of therapeutically-relevant proteins by (i) systematically identifying therapeutically-relevant target proteins that may be amenable to molecular glue-based degradation; and (ii) rationally designing molecules that can be optimized towards high potency and selectivity, with properties that we believe to be favorable. Our early pipeline includes programs in genetically defined oncology indications, as well as inflammatory, immunologic and other disease indications. We are further engaged in the discovery of additional target proteins in other indications, including, but not limited to, neurodegenerative and other neurological diseases.

**Figure 36: Monte Rosa Therapeutics; From Serendipity to Rational Design of MGDs**



## Our services, collaboration and licenses agreements

### ***Agreements with Cancer Research Technology Limited and the Institute of Cancer Research***

Cancer Research Technology Limited or CRT and the Institute of Cancer Research or ICR jointly own certain intellectual property generated at the ICR using funding from Cancer Research UK or CRUK related to the field of protein degradation. In April 2018, we concurrently entered into a license agreement, or the License Agreement, with CRT and the ICR, and a formation and investment agreement, or the Formation and Investment Agreement with CRT and the ICR, pursuant to which we agreed to issue an aggregate of 1,132,984 common shares to CRT, the ICR and affiliated founding scientists as consideration for the rights granted under the License Agreement at a price per share of CHF 0.04 for an aggregate purchase price of CHF 40,000.

### ***Collaboration and option agreement***

In April 2018, we entered into the Collaboration and Option Agreement, with CRT, a wholly-owned subsidiary of CRUK, and the ICR, to support our early product development as we built our internal capabilities. Under the Collaboration and Option Agreement, the ICR was responsible for performing certain research and development activities through December 31, 2020, or the Collaboration Term, which included assembling a library of cereblon-binding compounds and identifying and validating new biological target proteins for drug discovery through phenotypic cell based screening. During the Collaboration Term, we paid the ICR certain amounts to cover the cost of employing eight full-time employees and certain research outsourcing costs.

Under the Collaboration and Option Agreement, we are obligated to, among other things, use commercially reasonable efforts to (i) develop one or more products covered under the Collaboration and Option Agreement for use in human clinical trials, including at least one product with an application in oncology indication, (ii) pursue regulatory authorization for each product and, where applicable, price approval in at least one major market (iii) introduce and commercialize each product in major markets where regulatory authorization and, where applicable, price approval for such product has been obtained.

Pursuant to the Collaboration and Option Agreement, we may be obligated to pay CRT certain milestone payments upon the achievement of specific clinical progression events and sales-based royalties for certain products. Whether or not we are obligated to pay such milestones and royalties will depend on whether any product is subject to the Collaboration and Option Agreement. If owed, milestone payments could total up to \$7.0 million for any first covered product we develop that is subject to the Collaboration and Option Agreement and \$3.5 million for any additional covered product we develop that is subject to the Collaboration and Option Agreement. We may also be obligated to pay CRT low-single digit royalties on net sales on a product-by-product and country-by-country basis for any covered product that is subject to the Collaboration and Option Agreement. Our obligation to pay royalties will expire upon the later of (i) the expiration of the last patent which covers such

product in such country; (ii) 10 years following the first commercial sale of such product in such country; and (iii) the expiration of any extended exclusivity period in the relevant country. We have paid \$4.8 million under the Collaboration and Option Agreement for activities that occurred during the Collaboration Term.

All intellectual property developed or discovered pursuant to the research collaboration during the Collaboration term is owned by us, subject to the ICR's and CRT's rights in and to their pre-existing intellectual property and the ICR's and CRT's research rights; provided, however, any substrate list and target deconvolution data that is generated by or on behalf of the ICR in connection with its independent research and screening activities that result in a non-degradation program may be jointly owned by CRT and the ICR under certain conditions. We are permitted to grant sub-licenses in respect of the rights granted under the Collaboration and Option Agreement, subject to certain limitations.

Even though the Collaboration Term under the Collaboration and Option Agreement expired on December 31, 2020, the term of the Collaboration and Option Agreement itself continues until it is otherwise terminated by (i) either party in the event of an uncured material breach or upon an insolvency event, (ii) mutual agreement of the parties for any reason, (iii) us in the event that CRT and/or the ICR challenges the validity of any patent made or conceived pursuant to the research collaboration or if the joint steering committee determines that the continuation of the research collaboration would be commercially unreasonable, scientifically unviable, illegal or impossible or (iv) CRT and the ICR (acting together) in the event that any person who develops, sells or manufactures tobacco or otherwise makes a majority of its profits in the tobacco business acquires more than 50% of our voting securities or if we permanently abandon all discovery, development and commercialization efforts for all products covered under the research collaboration.

### ***License agreement***

Under the License Agreement, CRT and the ICR granted us a worldwide, exclusive, fully-paid, irrevocable, perpetual, sub-licensable license to (i) CRT and the ICR's intellectual property rights in its compound library to research, develop and commercialize products that (a) contain or comprise such compounds or (b) are discovered, developed or generated using or incorporating CRT and the ICR's existing intellectual property, or Licensed Products, and (ii) CRT and the ICR's certain specified know-how and other intellectual property rights unrelated to its compound library to research, develop and commercialize products designed or intended to have a primary mechanism of action through cereblon-mediated protein degradation, or Protein Degradation Products, in each case of (i) and (ii), for the treatment, prevention and/or diagnosis of any and all diseases, disorders or conditions. CRT and the ICR also granted us a worldwide, non-exclusive, fully-paid, irrevocable, perpetual and sub-licensable license to certain of CRT and the ICR's specified non-compound intellectual property rights and know-how to research, develop and commercialize Licensed Products and Protein Degradation Products for the treatment, prevention and/or diagnosis of any and all diseases, disorders or conditions. The foregoing exclusive license is subject to CRT and the ICR's retained rights to practice certain specified licensed intellectual property rights to carry out noncommercial academic research and teaching.

In consideration for the rights granted under the License Agreement, we issued an aggregate of 1,132,984 common shares to CRT, the ICR and affiliated founding scientists pursuant to the Formation and Investment Agreement for an aggregate purchase price of CHF 40,000 and paid CRT a technology access fee equal to approximately \$42,000. The License Agreement will remain effective until terminated by written agreement between us, CRT and the ICR.

### **Competition**

The biotechnology industry is extremely competitive in the race to develop new products and the industry is characterized by a high level of innovation and strong emphasis on proprietary products and intellectual property rights. While we believe we have significant competitive advantages due to our management team's years of expertise in protein degradation, molecular glues and clinical and preclinical development of precision medicines in general, coupled with our unique scientific expertise and our growing portfolio of intellectual property rights, we currently face and will continue to face competition for our development programs from other companies that develop heterobifunctional degraders, similar molecular glue degraders or have protein degradation development platforms and their own associated intellectual property. Our competition will also include companies focused on existing and novel therapeutic modalities such as small molecule inhibitors antibodies and gene therapies. The competition is likely to come from multiple sources, including large and specialty pharmaceutical companies, biotechnology companies and academic institutions that are in the business of research, development, manufacturing and commercialization. Moreover, the existence of large numbers of patents and frequent allegations of patent infringement is typical in our industry.



Competitors in our efforts to develop MGD therapeutics for patients, include, but are not limited to, BioTheryX Therapeutics, Inc., C4 Therapeutics, Inc., Nurix Therapeutics, Inc., Kymera Therapeutics, Inc., Seed Therapeutics, Inc., Plexium Inc, Bristol-Myers Squibb, and Novartis, all of whom have reported having MGD product candidates in preclinical or clinical development. In addition, lenalidomide and pomalidomide, which are both marketed by Bristol-Myers Squibb, have been shown to function as MGDs. Further, several large pharmaceutical companies have disclosed investments in this field.

In addition to the competitors we face in developing small molecule-based protein degraders, we will also face competition in the indications we expect to pursue with our MGD programs. Many of these indications already have approved standards of care which may include existing therapeutic modalities. In order to compete effectively with these existing therapies, we will need to demonstrate that our MGDs perform favorably when compared to existing therapeutics.

## **Manufacturing**

We do not own or operate manufacturing facilities for the production of our product candidates and we currently have no plans to build our own clinical or commercial scale manufacturing capabilities. We currently contract with third-party contract manufacturing organizations, or CMOs, for the manufacture of our product candidates and we intend to continue to do so in the future. We rely on and expect to continue to engage on third-party manufacturers for the production of both drug substance and finished drug product. We currently obtain our supplies from these manufacturers on a purchase order basis and do not have long-term supply arrangements in place. Should any of these manufacturers become unavailable to us or their services to us become delayed for any reason, we believe that there are a number of potential replacements, although we may incur some delay in identifying and qualifying such replacements.

## **Intellectual property**

We are an innovation-driven company and we seek to aggressively protect the innovations, intellectual property, and proprietary technology that we generate that we consider important to our business, including by pursuing patent applications that cover our product candidates and methods of using the same, innovations around our industry leading QuEEN™ platform and our proprietary library of MGDs, as well as any other relevant innovations, inventions, and improvements that are considered potentially commercially relevant to the development of our business and to maintain our perceived competitive advantages. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position. For our product candidates, we generally intend to pursue patent protection covering compositions of matter, pharmaceutical compositions, methods of use, including combination therapies, methods of administration including dosing methods, methods for monitoring potential clinical events, compositions and methods for personalizing, monitoring, and potentially refining clinical use, including biomarkers, processes of manufacture and process intermediates, where relevant. For our QuEEN™ platform, we generally intend to pursue patent protection covering our approaches, methods, and research and development tools relevant to our degron database, our Rhapsody, tools, and our library of MGDs. We continually assess and iteratively refine our intellectual property strategies as we develop new innovations and product candidates. We currently plan to continue to invest in filing additional patent applications based on our intellectual property strategies to continue to build value in our business and/or to improve our business and potential partnering opportunities, where appropriate.

Our commercial success depends, in part, on our ability to obtain, maintain, enforce and protect our intellectual property and other proprietary rights for the technology, inventions and improvements we consider important to our business, and to defend any patents we may own or in-license in the future, prevent others from infringing any patents we may own or in-license in the future, preserve the confidentiality of our trade secrets, and operate without infringing, misappropriating or otherwise violating the valid and enforceable patents and proprietary rights of third parties.

As with other biotechnology and pharmaceutical companies, our ability to maintain and solidify our proprietary and intellectual property position for our product candidates and technologies will depend on our success in obtaining effective patent claims and enforcing those claims if granted. However, our pending provisional and Patent Cooperation Treaty, or PCT, patent applications, and any patent applications that we may in the future file or license from third parties, may not result in the issuance of patents and the validity and/or enforceability of any of our issued patents may be challenged by third parties. Further, as with other companies, the patents we may obtain do not guarantee us the right to practice our technology in relation to the commercialization of our

products. Regarding obtaining issued patents, here in the United States as well as in other jurisdictions of interest to our business, the patent positions for biopharmaceutical companies like us are generally uncertain and can involve complex legal, scientific, and factual issues. Further, the laws governing the protection of intellectual property may change over time due to the issuance of new judicial decisions or the passage of new laws, rules or regulations. In addition, the coverage claimed in a patent application can be significantly reduced before a patent is issued and its scope can be reinterpreted and challenged even after issuance. As a result, we cannot guarantee that any of our product candidates will be protected or remain protectable by valid, enforceable patents. We also cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. Any patents that we hold may be challenged, circumvented, or invalidated by third parties.

The exclusivity terms of our patents depend upon the laws of the countries in which they are obtained. In the countries in which we currently intend to file, the patent term is 20 years from the earliest date of filing of a non-provisional patent application. The term of a U.S. patent may be extended to compensate for the time required to obtain regulatory approval to sell a drug (referred to as a patent term extension) or by delays encountered during patent prosecution that are caused by the United States Patent and Trademark Office (referred to as patent term adjustment). For example, the Hatch-Waxman Act permits a patent term extension for FDA-approved new chemical entity drugs of up to five years beyond the ordinary expiration date of one patent that covers the approved drug or its use. The length of the patent term extension is related to the length of time the drug is under regulatory review and diligence during the review process. Patent term extensions in the United States cannot extend the term of a patent beyond a total of 14 years from the date of product approval and only one patent covering an approved drug or its method of use may be extended. A similar kind of patent extension, referred to as a Supplementary Protection Certificate, is available in Europe. Legal frameworks may also be available in certain other jurisdictions to extend the term of a patent. We currently intend to seek patent term extensions for our products on any of our issued patents in any jurisdiction where we have a qualifying patent and the extension is available; however, there is no guarantee that the applicable regulatory authorities, including the FDA in the United States, will agree with our assessment of whether extensions of this nature should be granted and, even if granted, the length of these extensions. Further, even if any of our patents are extended or adjusted, those patents, including the extended or adjusted portion of those patents, may be held invalid or unenforceable by a court of final jurisdiction in the United States or a foreign country.

### **Patents and Patent Applications**

As of December 31, 2022, we solely owned a patent portfolio that included twenty-eight (28) pending patent families, including fourteen pending patent application filed under the Patent Cooperation Treaty and multiple pending United States provisional patent applications. Our portfolio is being built to cover our MGDs product candidates and various uses thereof, MGDs drawn to currently undisclosed target proteins and uses thereof, and our industry-leading QuEEN™ platform, as further described below. Patent prosecution related to our portfolio is currently in the early stages and, as such, no patent examiner has yet fully scrutinized the merits of any of our pending patent applications.

### **Wholly Owned Product Candidates**

With respect to our GSPT1 program, as of December 31, 2022, our portfolio included eight pending PCT patent applications, two pending non-provisional patent application in the United States, and patent applications in Europe and Japan that cover various GSPT1-directed MGDs and uses thereof. These patent applications are drawn to composition of matter, pharmaceutical compositions, and methods of using our GSPT1-directed MGDs. We also owned one pending PCT application, that cover biomarkers related to use of our GSPT1-directed MGDs. The earliest scheduled expiration of any U.S. or foreign patent drawn to our GSPT1-directed MGDs, if such patent is issued, would be 2040, excluding any additional term for available patent term adjustment or patent term extension, and assuming timely payment of all applicable maintenance or annuity fees.

With respect to our CDK2 program, as of December 31, 2022, our portfolio included two pending PCT applications and two pending U.S. provisional patent applications that cover various CDK2-directed MGDs and uses thereof. The earliest scheduled expiration of any U.S. or foreign patents issuing from these PCT applications or U.S. provisional patent applications, if such patents are issued, would be 2042, excluding any additional term for available patent term adjustment or patent term extension.

With respect to our NEK7 program, as of December 31, 2022, our portfolio included two U.S. provisional patent applications that cover various NEK7-directed MGDs and uses thereof. The earliest scheduled expiration of any U.S. or foreign patents issuing from these U.S. provisional patent applications, if such patents are issued, would be 2042, excluding any additional term for available patent term adjustment or patent term extension.

## **QuEEN™ platform**

With respect to our QuEEN™ platform, as of December 31, 2022, our portfolio included four U.S. provisional patent applications and two pending U.S. provisional patent applications drawn to our QuEEN™ platform and uses thereof for the design, discovery, and development of MGD product candidates. The earliest scheduled expiration of any U.S. or foreign patent issuing from these U.S. provisional patent applications, if such patents are issued, would be 2042, excluding any available additional term for patent term adjustment or patent term extension.

## **Trademarks**

As of December 31, 2022, we owned various registered and unregistered trademarks in the United States, including Monte Rosa Therapeutics, our housemark logo, the name of our QuEEN™ platform, and the name of our Glueomics resource.

## **Trade Secrets and Know How**

As an innovation driven biotechnology company, we rely on trade secrets, technical know-how and continuing innovation to develop and maintain the competitive advantage relevant to our business. Under the agreements we enter into with our employees and consultants, full rights in any intellectual property are assigned to us. We also rely on confidentiality or other agreements with our employees, consultants, other advisors and business partners to protect our proprietary information. Our policy is to require third parties that receive material confidential information to enter into confidentiality or other agreements with us that contain appropriate protections for our confidential and trade secret information.

## **Government regulation**

The FDA and other regulatory authorities at federal, state and local level, as well as in foreign countries and local jurisdictions, extensively regulate among other things, the research, development, testing, manufacture, quality control, sampling, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring and post-approval reporting of drugs. We, along with our vendors, contract research organizations, or CROs, and contract manufacturers, will be required to navigate the various preclinical, clinical, manufacturing and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval of our product candidates. The process of obtaining regulatory approvals of drugs and ensuring subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources.

In the U.S., the FDA regulates drug products under the Federal Food, Drug, and Cosmetic Act, or FD&C Act, as amended, its implementing regulations and other laws. If we fail to comply with applicable FDA or other requirements at any time with respect to product development, clinical testing, approval or any other legal requirements relating to product manufacture, processing, handling, storage, quality control, safety, marketing, advertising, promotion, packaging, labeling, export, import, distribution, or sale, we may become subject to administrative or judicial sanctions or other legal consequences. These sanctions or consequences could include, among other things, the FDA's refusal to approve pending applications, issuance of clinical holds for ongoing studies, withdrawal of approvals, warning or untitled letters, product withdrawals or recalls, product seizures, relabeling or repackaging, total or partial suspensions of manufacturing or distribution, injunctions, fines, civil penalties or criminal prosecution.

The process required by the FDA before a drug may be marketed in the U.S. generally involves the following:

- completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with good laboratory practice, or GLP, requirements;
- submission to the FDA of an IND application, which must become effective before clinical trials may begin;
- approval by an IRB or independent ethics committee at each clinical trial site before each trial may be initiated;
- performance of adequate and well-controlled clinical trials in accordance with applicable IND regulations, GCP requirements and other clinical trial-related regulations, to establish the safety and efficacy of the investigational product for each proposed indication;
- submission to the FDA of a NDA;

- a determination by the FDA within 60 days of its receipt of a New Drug Application, or an NDA, to accept the filing for review;
- satisfactory completion of one or more FDA pre-approval inspections of the manufacturing facility or facilities where the drug will be produced to assess compliance with cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- potential FDA audit of the clinical trial sites that generated the data in support of the NDA;
- payment of user fees for FDA review of the NDA; and
- FDA review and approval of the NDA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug in the U.S.

### ***Preclinical studies and clinical trials for drugs***

Before testing any drug in humans, the product candidate must undergo rigorous preclinical testing. Preclinical studies include laboratory evaluations of drug chemistry, formulation and stability, as well as in vitro and animal studies to assess safety and in some cases to establish the rationale for therapeutic use. The conduct of preclinical studies is subject to federal and state regulations and requirements, including GLP requirements for safety/toxicology studies. The results of the preclinical studies, together with manufacturing information and analytical data must be submitted to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational product to humans and must become effective before clinical trials may begin. Some long-term preclinical testing may continue 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 concerns or questions about the conduct of the clinical trial, including concerns that human research patients will be exposed to unreasonable health risks, 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. Submission of an IND may result in the FDA not allowing clinical trials to commence or not allowing clinical trials to commence on the terms originally specified in the IND.

The clinical stage of development involves the administration of the product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirements that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters and criteria to be used in monitoring safety and evaluating effectiveness. Each protocol, and any subsequent amendments to the protocol must be submitted to the FDA as part of the IND. Furthermore, each clinical trial must be reviewed and approved by an IRB for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable related to the anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative, and must monitor the clinical trial until completed. The FDA, the IRB or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the patients are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may 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. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trials to public registries. Information about applicable clinical trials, including clinical trial results, must be submitted within specific timeframes for publication on the [www.clinicaltrials.gov](http://www.clinicaltrials.gov) website.

A sponsor who wishes to conduct a clinical trial outside of the U.S. may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor must submit data from the clinical trial to the FDA in support of an NDA. The FDA will accept a well-designed and well-conducted foreign clinical trial not conducted under an IND if the trial was conducted in accordance with GCP requirements, and the FDA is able to validate the data through an onsite inspection if deemed necessary.

Clinical trials to evaluate therapeutic indications to support NDAs for marketing approval are typically conducted in three sequential phases, which may overlap or be combined.



- Phase 1—Phase 1 clinical trials involve initial introduction of the investigational product into healthy human volunteers or patients with the target disease or condition. These studies are typically designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, excretion the side effects associated with increasing doses, and, if possible, to gain early evidence of effectiveness. In the case of some products for severe or life-threatening diseases, such as cancer, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- Phase 2—Phase 2 clinical trials typically involve administration of the investigational product to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks.
- Phase 3—Phase 3 clinical trials typically involve administration of the investigational product to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval and physician labeling. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of an NDA.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication and are commonly intended to generate additional safety data regarding use of the product in a clinical setting. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA. Written IND safety reports must be submitted to the FDA and the investigators fifteen days after the trial sponsor determines the information qualifies for reporting for serious and unexpected suspected adverse events, findings from other studies or animal or in vitro testing that suggest a significant risk for human volunteers and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must also notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction as soon as possible but in no case later than seven calendar days after the sponsor's initial receipt of the information.

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

### ***U.S. marketing approval for drugs***

Assuming successful completion of the required clinical testing, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. An NDA must contain proof of the drug's safety and efficacy in order to be approved. The marketing application may include both negative and ambiguous results of preclinical studies and clinical trials, as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of the FDA. FDA approval of an NDA must be obtained before a drug may be marketed in the U.S.

The FDA reviews all submitted NDAs before it accepts them for filing and may request additional information rather than accepting the NDA for filing. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt, and such decision could include a refusal to file by the FDA. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the NDA. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and



purity. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, the FDA targets ten months, from the filing date, in which to complete its initial review of a new molecular entity NDA and respond to the applicant, and six months from the filing date of a new molecular entity NDA for priority review. The FDA does not always meet its PDUFA goal dates for standard or priority NDAs, and the review process is often extended by FDA requests for additional information or clarification.

Further, under PDUFA, as amended, each NDA must be accompanied by a user fee. The FDA adjusts the PDUFA user fees on an annual basis. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA also may require submission of a Risk Evaluation and Mitigation Strategy, or REMS, program to ensure that the benefits of the drug outweigh its risks. The REMS program could include medication guides, physician communication plans, assessment plans and/or elements to assure safe use, such as restricted distribution methods, patient registries or other risk-minimization tools.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, which reviews, evaluates and provides 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.

Before approving an NDA, the FDA typically 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 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 may inspect one or more clinical trial sites to assure compliance with GCP and other requirements and the integrity of the clinical data submitted to the FDA.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter 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 in order for the FDA to reconsider the application. Even with submission of this 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 will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, depending on the specific risk(s) to be addressed it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product 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 and FDA review and approval.

### ***Orphan drug designation and exclusivity***

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the U.S., or if it affects 200,000 or more individuals in the U.S., there is no reasonable expectation that the cost of developing and making the product available in the U.S. for the disease or condition will be recovered from sales of the product. Orphan designation must be requested before submitting an NDA. After the FDA grants orphan designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process, though companies developing orphan products are eligible for certain incentives, including tax credits for qualified clinical testing and waiver of application fees.

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 a seven-year period of marketing exclusivity during which the FDA may not approve any other applications to market the same therapeutic agent for the same indication, except in limited circumstances, such as a subsequent product's showing of clinical superiority over the product with orphan exclusivity or where the original applicant cannot produce sufficient quantities of product. Competitors, however, may receive approval of different therapeutic agents for the indication for which the orphan product has exclusivity or obtain approval for the same therapeutic agent but for a different indication than that for which the orphan product has exclusivity. Orphan product exclusivity could also block the approval of one of our products for seven years if a competitor obtains approval for the same therapeutic agent for the same indication before we do, unless we are able to demonstrate that our product is clinically superior. If an orphan designated product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan exclusivity. Further, orphan drug exclusive marketing rights in the U.S. may be lost if the FDA later determines that the request for designation was materially defective or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

### ***Expedited development and review programs for drugs***

The FDA maintains several programs intended to facilitate and expedite development and review of new drugs to address unmet medical needs in the treatment of serious or life-threatening diseases or conditions. These programs include Fast Track designation, Breakthrough Therapy designation, Priority Review and Accelerated Approval, and the purpose of these programs is to either expedite the development or review of important new drugs to get them to patients earlier than under standard FDA development and review procedures.

A new drug is eligible for Fast Track designation if it is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address unmet medical needs for such disease or condition. Fast Track designation provides increased opportunities for sponsor interactions with the FDA during preclinical and clinical development, in addition to the potential for rolling review once a marketing application is filed, meaning that the agency may review portions of the marketing application before the sponsor submits the complete application, as well as Priority Review, discussed below.

In addition, a new drug may be eligible for Breakthrough Therapy designation if it is intended 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. Breakthrough Therapy designation provides all the features of Fast Track designation in addition to intensive guidance on an efficient drug development program beginning as early as Phase 1, and FDA organizational commitment to expedited development, including involvement of senior managers and experienced review staff in a cross-disciplinary review, where appropriate.

Any product submitted to the FDA for approval, including a product with Fast Track or Breakthrough Therapy designation, may also be eligible for additional FDA programs intended to expedite the review and approval process including Priority Review designation and Accelerated Approval. A product is eligible for Priority Review if it has the potential to provide a significant improvement in safety or effectiveness in the treatment, diagnosis or prevention of a serious disease or condition. Under priority review, the FDA targets reviewing an application in six months after filing compared to ten months after filing for a standard review.

Additionally, products are eligible for Accelerated Approval if they can be shown to have an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or an effect on a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality which 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. Accelerated Approval is usually contingent on a sponsor's agreement to conduct additional post-approval studies to verify and describe the product's clinical benefit and, under the Food and Drug Omnibus Reform Act of 2022, or FDORA, the FDA is now permitted to require, as appropriate, that such trials be underway prior to approval or within a specific time period after the date of approval for a product granted Accelerated Approval. Under FDORA, the FDA has increased authority for expedited procedures to withdraw approval of a drug or indication approved under Accelerated Approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product. In addition, unless otherwise informed by the FDA, the FDA generally requires, unless otherwise informed by the agency, that all advertising and promotional materials that are intended for dissemination or publication within 120 days following marketing approval be submitted to the agency for review during the pre-approval review period, and that after

120 days following marketing approval, all advertising and promotional materials must be submitted at least 30 days prior to the intended time of initial dissemination or publication.

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 the time period for FDA review or approval may not be shortened. Furthermore, Fast Track designation, Breakthrough Therapy designation, Priority Review and Accelerated Approval do not change the scientific or medical standards for approval or the quality of evidence necessary to support approval but may expedite the development or review process.

### ***Pediatric information and pediatric exclusivity***

Under the Pediatric Research Equity Act, or PREA, as amended, certain NDAs and certain supplements to an NDA must contain data 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 grant deferrals for submission of pediatric data or full or partial waivers. The FD&C Act requires that a sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within 60 days of an end-of-Phase 2 meeting or, if there is no such meeting, as early as practicable before the initiation of the Phase 3 or Phase 2/3 trial. The FDA and the sponsor must reach an agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical trials and/or other clinical development programs.

A drug can also obtain pediatric market exclusivity in the U.S. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric trial or of multiple pediatric trials in accordance with an FDA-issued "Written Request" for such trials.

### ***U.S. post-approval requirements for drugs***

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, reporting of adverse experiences with the product, complying with promotion and advertising requirements, which include restrictions on promoting products for unapproved uses or patient populations (known as "off-label use") and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available products for off-label uses, manufacturers and individuals working on behalf of manufacturers may not market or promote such uses. 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, including investigation by federal and state authorities. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use or first publication. Further, if there are any modifications to the drug, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA or NDA supplement, which may require the development of additional data or preclinical studies and clinical trials. The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-market testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, drug manufacturers and their subcontractors involved in the manufacture and distribution of approved drugs, and those supplying products, ingredients, and components of them, are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP, which impose certain procedural and documentation requirements upon us and our contract manufacturers. Failure to comply with statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning letters, suspension of manufacturing, product seizures, injunctions, civil penalties or criminal prosecution. There is also a continuing, annual prescription drug product program user fee.

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 revisions to the approved labeling to add new safety information, requirements for post-market studies or

clinical trials to assess new safety risks, or imposition of distribution or other restrictions under a REMS. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- fines, warning letters or untitled letters or holds on post-approval clinical trials;
- refusal of the FDA to approve applications or supplements to approved applications, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- injunctions or the imposition of civil or criminal penalties; and
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs or mandated modification of promotional materials and labeling and issuance of corrective information.

### ***Marketing exclusivity***

Market exclusivity provisions under the FD&C Act can delay the submission or the approval of certain marketing applications. The FD&C Act provides a five-year period of non-patent exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not approve or even accept for review an abbreviated new drug application, or ANDA, or an NDA submitted under Section 505(b)(2), or 505(b)(2) NDA, submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication. However, such an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder.

The FD&C Act alternatively provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA, if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to any preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

### ***Other regulatory matters***

Manufacturing, sales, promotion and other activities of product candidates following product approval, where applicable, or commercialization are also subject to regulation by numerous regulatory authorities in the U.S. in addition to the FDA, which may include the Centers for Medicare & Medicaid Services, or CMS, other divisions of the Department of Health and Human Services, the Department of Justice, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments and governmental agencies.

### ***Current and future healthcare reform legislation***

In the United States and in some foreign jurisdictions, there have been, and likely will continue to be, a number of legislative and regulatory changes and proposed changes intended to broaden access to healthcare, improve the quality of healthcare, and contain or lower the cost of healthcare. For example, in the United States, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or ACA, among other things, subjected products to potential competition by lower-cost products, expanded the types of entities eligible for the 340B drug discount program, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increases rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations,



established annual fees and taxes on manufacturers of certain branded prescription drugs, and created a Medicare Part D coverage gap discount program for certain Medicare Part D beneficiaries, in which manufacturers must agree to offer 50% (increased to 70% pursuant to the Bipartisan Budget Act of 2018, or BBA, effective as of January 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

There have been executive, judicial and congressional challenges to certain aspects of the ACA Act as well as efforts to repeal or replace certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021, through August 15, 2021, for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA.

Other federal health reform measures have been proposed and adopted in the U.S. since the ACA was enacted. By way of example, the Budget Control Act of 2011, among other things, included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year. This reduction went into effect in April 2013 and, due to subsequent legislative amendments, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020, through March 31, 2022. Then, a 1% payment reduction will occur beginning April 1, 2022, through June 30, 2022, and the 2% payment reduction will resume on July 1, 2022. CMS has indicated that it is delaying the processing of claims in April to allow Congress to pass legislation that would extend the suspension. In addition, the American Taxpayer Relief Act of 2012 was signed into law which, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Furthermore, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several congressional inquiries and proposed legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient assistance programs and reform government program reimbursement methodologies for drug products. At the federal level, the previous administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. On July 9, 2021, President Biden issued an executive order directing the FDA to, among other things, continue to clarify and improve the approval framework for generic drugs and identify and address any efforts to impede generic drug competition.

On August 16, 2022, the Inflation Reduction Act of 2022, or the IRA, was passed, which among other things, allows for Centers for Medicare & Medicaid Services to negotiate prices for certain single-source drugs and biologics reimbursed under Medicare Part B and Part D, beginning with select high-cost drugs in 2026. The legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for offering a price that is not equal to or less than the price negotiated under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. Further, the legislation caps Medicare beneficiaries' annual out-of-pocket drug expenses at \$2,000. The effect of IRA on our business and the healthcare industry in general is not yet known.

Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical 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. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. It is difficult to predict the future legislative landscape in healthcare and the effect on our business, results of operations, financial condition and prospects. However, we expect that additional state and federal healthcare reform measures will be adopted in the future. Further, it is possible that additional governmental action is taken in response to the COVID-19 pandemic.



### ***Third-party payor coverage and reimbursement***

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval. In the U.S. and markets in other countries, sales of any products for which we may receive regulatory marketing approval for commercial sale will depend, in part, on the availability of coverage and reimbursement from third-party payors. Third-party payors include government healthcare programs (e.g., Medicare, Medicaid), managed care providers, private health insurers, health maintenance organizations and other organizations. These third-party payors decide which medications they will pay for and will establish reimbursement levels. The availability of coverage and extent of reimbursement by governmental and other third-party payors is essential for most patients to be able to afford treatments such as targeted protein degradation therapies.

In the United States, no uniform policy exists for coverage and reimbursement for products among third-party payors. Therefore, decisions regarding the extent of coverage and amount of reimbursement to be provided can differ significantly from payor to payor. Third-party payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates, but also have their own methods and approval process apart from Medicare determinations. Factors payors consider in determining reimbursement are based on whether the product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

One third-party payor's decision to cover a particular product or service does not ensure that other payors will also provide coverage for the medical product or service. Third-party payors may limit coverage to specific products on an approved list or formulary, which may not include all FDA-approved products for a particular indication. Also, third-party payors may refuse to include a particular branded product on their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available. Our ability to successfully commercialize our product candidates 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.

Moreover, the process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate a payor will pay for the product. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to secure coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA or comparable regulatory approvals. Additionally, we may also need to provide discounts to purchasers, private health plans or government healthcare programs. Despite our best efforts, our product candidates may not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover an approved product as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, our operations and financial condition.

Finally, in some foreign countries, the proposed pricing for a product candidate must be approved before it may be lawfully marketed. The requirements governing product pricing vary widely from country to country. For example, in the European Union, or EU, pricing and reimbursement of pharmaceutical products are regulated at a national level under the individual EU Member States' social security systems. Some foreign countries provide options to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and can control the prices of medicinal products for human use. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. A country may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of

the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Even if approved for reimbursement, historically, product candidates launched in some foreign countries, such as some countries in the EU, do not follow price structures of the U.S. and prices generally tend to be significantly lower.

### ***Other healthcare laws and regulations***

Healthcare providers, physicians, and third-party payors will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our business operations and any current or future arrangements with third-party payors may expose us to broadly applicable federal and state fraud and abuse laws, as well as other healthcare laws and regulations. These laws may impact, among other things, our proposed sales, marketing, and distribution strategies. In the U.S., these laws include, among others:

- The federal Anti-Kickback Statute, or AKS, which prohibits, among other things, any person or entity from knowingly and willfully offering, soliciting, receiving or paying remuneration (a term interpreted broadly to include anything of value, including, for example, gifts, discounts and credits), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, or arranging for, an item, good, facility or service for which payment may be made under a federal healthcare program such as Medicare and Medicaid. The AKS has been interpreted to apply to arrangements between manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violations can result in significant civil monetary and criminal penalties for each violation, plus up to three times the amount of remuneration, imprisonment, and exclusion from government healthcare programs.
- Additionally, the civil False Claims Act, or FCA, prohibits knowingly presenting or causing the presentation of a false, fictitious or fraudulent claim for payment to the U.S. government. Actions under the FCA may be brought by the Attorney General or as a *qui tam* action by a private individual in the name of the government. Violations of the FCA can result in very significant monetary penalties, for each false claim and treble the amount of the government's damages. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. Further, a violation of the AKS can also form the basis for FCA liability.
- The U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes additional criminal and civil liability for 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 the payor (e.g., public or private); and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statement in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the AKS, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and its implementing regulations, including the final omnibus rule published on January 25, 2013, imposes, among other things, certain requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain, transmit, or obtain, protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, 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 attorney's fees and costs associated with pursuing federal civil actions.
- Federal transparency laws, including the federal Physician Payment Sunshine Act created under the ACA, and its implementing regulations, which requires manufacturers of certain drugs, devices, medical supplies, and biologics, among others, to track and disclose payments under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) and other transfers of value they make to U.S. physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family

members. Effective January 1, 2022, these reporting obligations were extended to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners. This information is subsequently made publicly available in a searchable format on a CMS website.

- Federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs.
- Federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.
- Analogous state law equivalents of each of the above U.S. federal laws and similar healthcare laws and regulations in the European Union and other jurisdictions, such as anti-kickback and false claims laws, which may apply to items or services reimbursed by any third-party payor, including commercial insurers or patients; state and local marketing and/or transparency laws applicable to manufacturers that may be broader in scope than the federal requirements; state laws that require the reporting of information related to drug pricing; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and pricing information; state and local laws that require the licensure and/or registration of pharmaceutical sales representatives; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; and state laws governing the privacy and security of health information and/or other health information in certain circumstances, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal, state and foreign enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. 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 civil, criminal and administrative penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, individual imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or similar settlement to resolve allegations of non-compliance with these laws, any of which could adversely affect our ability to operate our business and our financial results. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to similar actions, penalties, and sanctions. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource consuming and can divert a company's attention from the business.

### ***Privacy and data protection laws and regulations***

We may be subject to Swiss, European, US federal, state, and foreign data protection laws and regulations (i.e., laws and regulations that address privacy and data security). In the European Union, we may be subject to additional privacy restrictions. The collection and use of personal data including health information in the European Union is governed by the provisions of the General Data Protection Regulation, or GDPR as well as national data protection laws. The GDPR imposes a broad range of strict requirements on companies subject to the GDPR, such as including requirements relating to having legal bases for processing personal data relating to identifiable individuals and transferring such information outside the European Economic Area, or EEA, including to the U.S. (see below), providing details to those individuals regarding the processing of their personal data, implementing safeguards to keep personal data secure, having data processing agreements with third parties who process personal data, providing information to individuals regarding data processing activities, responding to individuals' requests to exercise their rights in respect of their personal data, obtaining consent of the individuals to whom the personal data relates, reporting security and privacy breaches involving personal data to the competent national data protection authority and affected individuals, appointing data protection officers, conducting data protection impact assessments, and record-keeping. The GDPR substantially increases the penalties to which we could be subject in the event of any non-compliance, including fines of up to €20,000,000 or 4% of total annual global revenue, whichever is greater. The GDPR increases the responsibility and liability of

pharmaceutical companies in relation to processing personal data, and companies may be required to put in place additional mechanisms to ensure compliance with the new EU data protection rules. The GDPR introduced new data protection requirements in the EU and substantial fines for breaches of the data protection rules. The GDPR may impose additional responsibility and liability in relation to personal data that we process and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. This may be onerous and adversely affect our business, financial condition, results of operations and prospects.

In addition, the United Kingdom (UK) incorporated the GDPR (as it existed on December 31, 2020 but subject to certain UK specific amendments) into UK law (referred to as the 'UK GDPR'), following its exit from the EU in 2020. The UK GDPR and the UK Data Protection Act 2018 set out the UK's data protection regime, which is independent from but aligned to the EU's data protection regime. Non-compliance with the UK GDPR may result in monetary penalties of up to £17.5 million or 4% of worldwide revenue, whichever is higher. Although the UK is regarded as a third country under the EU's GDPR, the European Commission or EC has now issued a decision recognizing the UK as providing adequate protection under the EU GDPR and, therefore, transfers of personal data originating in the EU to the UK remain unrestricted. Like the EU GDPR, the UK GDPR restricts personal data transfers outside the UK to countries not regarded by the UK as providing adequate protection. The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing.

In Switzerland, we are also subject to comprehensive data protection requirements including the Swiss Federal Act on Data Protection, or the DPA, which imposes stringent rules on the processing of personal data including health related information.

In the United States, numerous federal and state laws and regulations, including federal health information privacy laws, state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), that govern the collection, use, disclosure and protection of health-related and other personal information could apply to our operations or the operations of our collaborators. In California, for example, the California Consumer Privacy Act (CCPA) was enacted in June 2018, became effective on January 1, 2020, and became subject to enforcement by the California Attorney General's office on July 1, 2020. The CCPA broadly defines personal information, and creates new individual privacy rights and protections for California consumers. places increased privacy and security obligations on entities handling personal data of consumers or households, and provides for civil penalties for violations and a private right of action for data breaches. The CCPA requires covered companies to provide certain disclosures to consumers about its data collection, use and sharing practices, and to provide affected California residents with ways to opt-out of certain sales or transfers of personal information. While there is an exception for protected health information that is subject to HIPAA and clinical trial regulations, the CCPA may impact our business activities if we become a "Business" regulated by the scope of the CCPA.

Further, a new privacy law, the California Privacy Rights Act, or CPRA, was passed by California voters on November 3, 2020. The CPRA will create additional obligations relating to personal information that are scheduled to take effect on January 1, 2023 (with certain provisions having retroactive effect to January 1, 2022). While the legislation and proposed regulations include the CCPA and CPRA contain an exception for activities that are subject to HIPAA, we cannot yet determine the impact the CCPA, CPRA or other such future laws, regulations and standards may have on our business. A number of other states have proposed new privacy laws, some of which are similar to the above discussed recently passed laws. Such proposed legislation, if enacted, may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies. The existence of comprehensive privacy laws in different states in the country would make our compliance obligations more complex and costly and may increase the likelihood that we may be subject to enforcement actions or otherwise incur liability for noncompliance.

The uncertainty surrounding the implementation of the CCPA, recent and emerging state privacy and other similar laws, regulations and standards that may be adopted in other jurisdictions exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information. Compliance with U.S. and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Failure to comply with these laws and regulations could result in government enforcement actions (which could include civil, criminal and administrative penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects, employees and other individuals about whom we or our potential collaborators obtain personal information, as well as the providers who share this information with us, may limit our ability to collect,



use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

Many jurisdictions outside of Europe where we do business directly or through master resellers today and may seek to expand our business in the future, are also considering and/or have enacted comprehensive data protection legislation. We also continue to see jurisdictions imposing data localization laws. These and similar regulations may interfere with our intended business activities, inhibit our ability to expand into those markets, require modifications to our products or services or prohibit us from continuing to offer services in those markets without significant additional costs.

### ***Compliance with other federal and state laws or requirements; changing legal requirements***

If any products that we may develop are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, labeling, packaging, distribution, sales, promotion and other activities also are potentially subject to federal and state consumer protection and unfair competition laws, among other requirements to we may be subject.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with any of these laws or regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, exclusion from federal healthcare programs, requests for recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, relabeling or repackaging, or refusal to allow a firm to enter into supply contracts, including government contracts. Any claim or 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. Prohibitions or restrictions on marketing, sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling or packaging; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

### ***Other U.S. environmental, health and safety laws and regulations***

We may be 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. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

### ***Government regulation of drugs outside of the United States***

To market any product outside of the U.S., we would need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials,



marketing authorization or identification of an alternate regulatory pathway, manufacturing, commercial sales and distribution of our products.

Whether or not we obtain FDA approval of a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

### ***Non-clinical studies and clinical trials***

Similarly to the U.S., the various phases of non-clinical and clinical research in the European Union, or EU, are subject to significant regulatory controls.

Non-clinical studies are performed to demonstrate the safety and non-toxicity of new chemical (or biological) substances. Non-clinical studies must be conducted in compliance with the principles of good laboratory practice, or GLP, as set forth in the Directive 2004/10/EC. In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

In April 2014, the EU adopted the new Clinical Trials Regulation (EU) No 536/2014, or the Clinical Trials Regulation, which replaced the Clinical Trials Directive 2001/20/EC, or Directive, on January 31, 2022. The Clinical Trials Regulation, which is directly applicable in all EU member states (meaning no national implementing legislation in each EU member state is required), aims to simplify and streamline the approval of clinical trials in the EU, for example by providing for a streamlined application procedure via a single entry point and simplifying reporting procedures for clinical trial sponsors.

### ***Marketing authorizations***

In the EU, medicinal products can only be placed on the market after obtaining a marketing authorization, or MA. To obtain regulatory approval of an investigational medicinal product in the EU, a marketing authorization application, or MAA must be submitted. The process for doing this depends, among other things, on the nature of the medicinal product. Medicinal products must be authorized for marketing by using either the centralized authorization procedure or a national authorization procedures.

- **Centralized procedure**—If pursuing an MA for a product candidate for a therapeutic indication under the centralized procedure, following the opinion of the European Medicines Agency's, or EMA, Committee for Medicinal Products for Human Use, or CHMP, the European Commission issues a single MA valid across the EU as well as the additional Member States of the EEA. The centralized procedure is compulsory for human medicines derived from biotechnology processes, such as genetic engineering, or advanced therapy medicinal products (such as gene therapy, somatic cell therapy and tissue engineered products), products that contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, neurodegenerative disorders, diabetes, autoimmune diseases and other immune dysfunctions, viral diseases, and officially designated orphan medicinal products. For medicines that do not fall within these categories, an applicant has the option of submitting an application for a centralized MA to the EMA, as long as the medicine concerned contains a new active substance not yet authorized in the EU, is a significant therapeutic, scientific or technical innovation, or if its authorization would be in the interest of public health in the EU. Under the centralized procedure the maximum timeframe for the evaluation of an MAA by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Clock stops may extend the timeframe of evaluation of a MAA considerably beyond 210 days. Where the CHMP gives a positive opinion, the EMA provides the opinion together with supporting documentation to the European Commission, who makes the final decision to grant a marketing authorization, which is issued within 67 days of receipt of the EMA's recommendation. In exceptional cases, the CHMP might perform an accelerated review of a MAA in no more than 150 days (not including clock stops). Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for certain expedited development and review programs, such as the PRIME scheme, which provides incentives similar to the breakthrough therapy designation in the U.S. PRIME is a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Product

developers that benefit from PRIME designation can expect to be eligible for accelerated assessment, however this is not guaranteed. The benefits of a PRIME designation include the appointment of a CHMP rapporteur before submission of an MAA, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review earlier in the application process.

- National authorization procedures—There are also two other possible routes to authorize products for therapeutic indications in several EU Member States, which are available for products that fall outside the scope of the centralized procedure:
  - Decentralized procedure—Under the decentralized procedure, an applicant may apply for simultaneous authorization in more than one EU Member State for medicinal products that have not yet been authorized in any EU Member States.
  - Mutual recognition procedure—Under the mutual recognition procedure, a medicine is first authorized in one EU Member State, in accordance with the national procedures of that country. Following this, the applicant may seek additional MAs from other EU Member States in a procedure whereby the countries concerned agree to recognize the validity of the original, national MA.

MAAs have an initial duration of five years. After these five years, the authorization may be renewed for an unlimited period on the basis of a reevaluation of the risk-benefit balance.

Now that the UK (which comprises Great Britain and Northern Ireland) has left the EU, Great Britain will no longer be covered by centralized MAs (under the Northern Ireland Protocol, centralized MAs continue to be recognized in Northern Ireland). All medicinal products with a current centralized MA were automatically converted to Great Britain MAs on January 1, 2021. For a period of three years from January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, the UK medicines regulator, may rely on a decision taken by the European Commission on the approval of a new MA in the centralized procedure, in order to more quickly grant a new Great Britain MA. A separate application will, however, still be required. On January 24, 2023, the MHRA announced that a new international recognition framework will be put in place from January 1, 2024. Under this new framework, the MHRA will have regard to decisions on the approval of a marketing authorization made by the EMA and certain other regulators when considering whether to grant a UK marketing authorization. The MHRA also has the power to have regard to marketing authorizations approved in EU Member States through decentralized or mutual recognition procedures with a view to more quickly granting a marketing authorization in the UK or Great Britain.

### ***Data and market exclusivity***

In the EU, upon receiving an MA, innovative medicinal products, sometimes referred to as new chemical entities (i.e., reference products) generally qualify for eight years of data exclusivity and an additional two years of market exclusivity. If granted, the data exclusivity period prevents generic or biosimilar applicants from relying on the non-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. During the additional two-year period of market exclusivity, a generic/biosimilar MAA can be submitted, and the innovator's data may be referenced, but no generic or biosimilar product can be marketed in the EU until the expiration of the market exclusivity period. The overall ten-year period can be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU or Member State regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity.

### ***Orphan medicinal products***

The criteria for designating an “orphan medicinal product” in the EU are similar in principle to those in the U.S. In the EU a medicinal product may be designated as orphan if (i) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (ii) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) it is unlikely that the product, without the benefits derived from orphan status, would generate sufficient return in the EU to justify the investment in its development; and (iii) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of a significant benefit to those affected by that condition. The application for orphan designation must be submitted before the MAA. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon

grant of an MA, entitled to ten years of market exclusivity for the approved therapeutic indication. During this ten-year orphan market exclusivity period, no MAA shall be accepted by the EMA for the same indication in respect of a similar medicinal product. A “similar medicinal product” is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the for the same therapeutic indication. An orphan medicinal product can also obtain an additional two years of market exclusivity in the EU for pediatric studies. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The ten-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Market exclusivity may also be revoked in very select cases, such as if (i) it is established that a similar medicinal product is safer, more effective or otherwise clinically superior than the authorized product; (ii) the marketing authorization holder of the authorized product consents to such revocation; or (iii) the marketing authorization holder of the authorized product cannot supply enough orphan medicinal product.

### ***Pediatric development***

In the EU, MAAs for new medicinal products must include the results of trials conducted in the pediatric population, in compliance with a pediatric investigation plan, or PIP, agreed with the EMA's Pediatric Committee, or PDCO, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the product for which an MA is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data are not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the MA is obtained in all EU Member States and study results are included in the product information, even when negative, the product is eligible for a six-months supplementary protection certificate extension (if any is in effect at the time of approval) or, in the case of orphan medicinal products, a two-year extension of the orphan market exclusivity is granted. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

### ***Post-approval requirements***

Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the European Commission and/or the competent regulatory authorities of the Member States. The holder of an MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports, or PSURs. All new MAAs must include a risk management plan, or RMP, describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies.

The advertising and promotion of medicinal products is also subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each Member State and can differ from one country to another.

Failure to comply with EU and Member State laws that apply to the conduct of clinical trials, manufacturing approval, authorization of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti-corruption or with

other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

The aforementioned EU rules are generally applicable in the European Economic Area, or EEA, which consists of the 27 EU Member States plus Norway, Liechtenstein and Iceland.

For other countries outside of the European Union, such as countries in Latin America or Asia, the requirements governing the conduct of clinical studies, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical studies are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

Should we utilize third-party distributors, compliance with such foreign governmental regulations would generally be the responsibility of such distributors, who may be independent contractors over whom we have limited control.

### ***Brexit and the regulatory framework in the United Kingdom***

The United Kingdom formally left the European Union on January 31, 2020, and the EU and the UK have concluded a trade and cooperation agreement, or TCA, which was provisionally applicable since January 1, 2021, and has been formally applicable since May 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations. At present, Great Britain has implemented EU legislation on the marketing, promotion and sale of medicinal products through the Human Medicines Regulations 2012 (as amended) (under the Northern Ireland Protocol, the EU regulatory framework will continue to apply in Northern Ireland). Except in respect of the new EU Clinical Trials Regulation, the regulatory regime in Great Britain therefore largely aligns in many ways with current EU medicines regulations, however it is possible that these regimes will diverge more significantly in future now that Great Britain's regulatory system is independent from the EU and the TCA does not provide for mutual recognition of UK and EU pharmaceutical legislation.

### **Employees and human capital resources**

As of December 31, 2022, we had 123 full-time employees, of which 67 have M.D. or Ph.D. degrees. Within our workforce, 100 employees are engaged in research and development and 23 are engaged in business development, finance, legal, and general management and administration. 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 existing and new employees, advisors and consultants. The principal purposes of our equity incentive plans are to attract, retain and reward personnel through the granting of equity-based compensation awards in order to increase shareholder value and the success of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives.

### **Facilities**

Our corporate headquarters is located in Boston, Massachusetts, where we currently lease and occupy approximately 16,748 square feet of office space at 645 Summer Street, Boston, MA 02210. On May 5, 2022, we entered into an Agreement for Termination of Lease, or the Lease Termination Agreement, with OPG MP Parcel Owner (DE) LLC, or the Summer Street Landlord, which, subject to the Summer Street Landlord executing a lease with a new tenant, provided us with the option to terminate the existing lease agreement. On August 8, 2022, the termination condition was met. As a result, pursuant to the Lease Termination Agreement, the 645 Summer Street lease will terminate on June 1, 2023. In December 2021, we executed a lease with B9 LS Harrison & Washington LLC, or the Harrison Avenue Landlord, for approximately 63,327 square feet of office and laboratory space at 321 Harrison Avenue, Boston, Massachusetts, or the Premises, which is expected to serve as our new headquarters beginning in the second quarter of 2023. Our obligation to pay rent pursuant to the lease began on December 21, 2022. The initial term of the lease is one hundred twenty-eight (128) months following April 1, 2022. The annual base rent under the lease is \$95.00 per square foot for the first year, which is subject to scheduled annual increases of 3%, plus certain costs, operating expenses and property management fees. We have the option to extend the lease once for five (5)-years upon notice to the Harrison Avenue Landlord at least

one (1) year prior to the end of the then-current term. We also have the option to sublet the Premises on the terms and conditions set forth in the lease. We have an additional location used for office and lab space that occupies approximately 21,422 square feet located at Klybeckstrasse 191, WKL-136.3, 4057 Basel, Basel-City, Switzerland. The current term of our Basel lease expires in March 2026.

We believe that our facilities are adequate for our current needs and for the foreseeable future. To meet the future needs of our business, we may lease additional or alternate space. We believe that suitable additional or substitute space at commercially reasonable terms will be available as needed to accommodate any future expansion of our operations.

## **Legal proceedings**

From time to time, we may become involved in litigation or other legal proceedings arising in the ordinary course of business. We are not currently a party to any litigation or legal proceedings that, in the opinion of our management, are probable to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on our business, financial condition, results of operations and prospects because of defense and settlement costs, diversion of management resources and other factors.

## **Available Information**

Investors and others should note that we announce material information to our investors using our investor relations website (<https://ir.monterosatx.com/>), SEC filings, press releases, public conference calls and webcasts. We use these channels as well as social media, including LinkedIn and our Twitter (@MonteRosaRx), to communicate with the public about our company, our business, our product candidates and other matters. It is possible that the information we post on social media could be deemed to be material information. Therefore, we encourage investors, the media, and others interested in our company to review the information we post on the social media channels listed on our investor relations website. Information that is contained in and can be accessed through our website or our social media posts are not incorporated into, and does not form a part of, this Annual Report on Form 10-K.

We file Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, proxy statements and other information with the SEC. Our filings with the SEC are available on the SEC's website at [www.sec.gov](http://www.sec.gov).

We make available, free of charge, in the Investor Relations section of our website, documents we file with or furnish to the SEC, including our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, including exhibits, proxy and information statements and amendments to those reports. We make this information available as soon as reasonably practicable after we electronically file such materials with, or furnish such information to, the SEC. The other information found on our website is not part of this or any other report we file with, or furnish to, the SEC. Copies of such documents are available in print at no charge to any shareholder who makes a request. Such requests should be made to our corporate secretary at our corporate headquarters, 645 Summer Street, Boston, MA 02210.



## Item 1A. Risk Factors

*Careful consideration should be given to the following risk factors, in addition to the other information set forth in this Annual Report and in other documents that we file with the SEC, in evaluating our business. Investing in our common stock involves a high degree of risk. If any of the following risks and uncertainties actually occurs, our business, prospects, financial condition and results of operations could be materially and adversely affected. The risks described below are not intended to be exhaustive and are not the only risks that we face. New risk factors can emerge from time to time, and it is not possible to predict the impact that any factor or combination of factors may have on our business, prospects, financial condition and results of operations. Certain statements in this Annual Report are forward-looking statements. Please also see the section entitled "Special Note Regarding Forward-Looking Statements."*

### **Risks related to our financial position and capital needs**

***We are a biotechnology company with a limited operating history and have not generated any revenue to date from drug sales, and may never become profitable.***

Biopharmaceutical drug development is a highly speculative undertaking and involves a substantial degree of risk. Since our formation as Monte Rosa Therapeutics AG in 2018, our operations have been limited primarily to organizing and staffing our company, business planning, raising capital, researching and developing our Quantitative and Engineered Elimination of Neosubstrates drug discovery platform, or our QuEEN™ platform, building our proprietary library of MGDs, developing our pipeline of product candidates, building our intellectual property portfolio, undertaking preclinical and IND-enabling studies of our lead product candidates, including MRT-2359, and conducting our first clinical trial. We have never generated any revenue from drug sales. We have not obtained regulatory approvals for any of our current or future product candidates.

Typically, it takes many years to develop one new pharmaceutical drug from the time it is discovered to when it is available for treating patients. Consequently, any predictions we make about our future success or viability may not be as accurate as they could be if we had a longer operating history. In addition, as a business with a limited operating history, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors, such as the ongoing COVID-19 pandemic or the effect of sanctions imposed by the U.S. and other countries in response to the war in Ukraine. We will need to transition from a company focused on research and early-stage development to a company capable of supporting late-stage development and commercial activities. We may not be successful in such a transition.

***We have incurred significant operating losses since our inception and anticipate that we will incur continued losses for the foreseeable future.***

Since our inception, we have focused substantially all of our efforts and financial resources on developing our proprietary QuEEN™ platform, our proprietary MGD library, and our initial pipeline of product candidates. To date, we have financed our operations primarily through the issuance and sale of convertible promissory notes and our convertible preferred stock to outside investors in private equity financings. From our inception through the date hereof, we raised an aggregate of \$499.8 million of gross proceeds from such transactions. As of December 31, 2022, our cash, cash equivalents, restricted cash and marketable securities were \$268.1 million. We have incurred net losses in each year since our inception, and we had an accumulated deficit of \$230.5 million as of December 31, 2022. For the years ended December 31, 2022 and 2021, we reported net losses of \$108.5 million and \$74.0 million, respectively. Substantially all of our operating losses have resulted from costs incurred in connection with our research and initial pipeline programs and from general and administrative costs associated with our operations. We expect to continue to incur significant expenses and increasing operating losses over the next several years and for the foreseeable future. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' deficit and working capital. We expect our expenses to significantly increase in connection with our ongoing activities, as we:

- conduct our clinical trial for MRT-2359;
- continue preclinical activities for our NEK7, CDK2, VAV1 and sickle cell disease or SCD and other currently undisclosed programs;
- prepare and submit IND applications with the FDA for other current and future product candidates;
- complete preclinical studies for current or future product candidates;

- progress MGD molecules from our initial programs through lead optimization to development candidates;
- initiate and complete clinical trials for current or future product candidates;
- expand and improve the capabilities of our QuEEN™ platform;
- continue to build our proprietary library of MGDs;
- contract to manufacture our product candidates;
- advance research and development related activities to expand our product pipeline;
- seek regulatory approval for our product candidates that successfully complete clinical development;
- develop and scale up our capabilities to support our ongoing preclinical activities and future clinical trials for our product candidates and commercialization of any of our product candidates for which we may obtain marketing approval;
- maintain, expand, and protect our intellectual property portfolio;
- hire additional staff, including clinical, scientific and management personnel; and
- secure facilities to support continued growth in our research, development and commercialization efforts.

In addition, if we obtain marketing approval for our current or future product candidates, we will incur significant expenses relating to our commercialization of such via our sales, marketing, product manufacturing and distribution efforts. Because of the numerous risks and uncertainties associated with developing pharmaceutical drugs, including in light of economic slowdowns or the ongoing evolution of the COVID-19 pandemic, we are unable to predict the extent of any future losses or when we will become profitable, if at all.

Even if we achieve profitability, we may not be able to sustain or increase our 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 are very early in our development efforts. All but one of our programs are still in the preclinical stages of drug development. If we are unable to commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.***

Our ability to become profitable depends upon our ability to generate revenue. To date we have not generated any revenue from our product candidates, and we do not expect to generate any revenue from the sale of drugs in the near future. We do not expect to generate revenue from product sales unless and until we complete the development of, obtain marketing approval for, and begin to sell, one or more of our product candidates. We are also unable to predict when, if ever, we will be able to generate revenue from such product candidates due to the numerous risks and uncertainties associated with drug development, including the uncertainty of:

- our plans to submit IND applications to the FDA for our future product candidates;
- our ability to timely and successfully complete preclinical studies and clinical trials for MRT-2359 and our NEK7, CDK2, VAV1 and sickle cell disease or SCD programs, and other current or future product candidates;
- our ability to advance additional MGD molecules through lead optimization;
- our successful initiation, enrollment in and completion of clinical trials, including our ability to generate positive data from any such clinical trials;
- our ability to demonstrate, to the satisfaction of the FDA and comparable regulatory authorities the safety, efficacy, consistent manufacturing quality and acceptable risk-benefit profile of our product candidates for their intended uses;
- our ability to timely receive necessary regulatory approvals from applicable regulatory authorities, including the FDA;
- the costs associated with the development of any additional development programs we identify in-house or via collaborations or other arrangements;

- our ability to establish timely manufacturing capabilities or make arrangements with third-party manufacturers for clinical supply and commercial manufacturing;
- obtaining and maintaining patent and trade secret protection or regulatory exclusivity for our current and future product candidates;
- launching commercial sales of our product candidates, if and when approved, whether alone or in collaboration with others;
- obtaining and maintaining acceptance of our product candidates, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- obtaining and maintaining healthcare coverage and adequate reimbursement;
- the terms and timing of any additional collaboration, license or other arrangement, including the terms and timing of any payments thereunder;
- our ability to enforce and defend intellectual property rights and claims; and
- our ability maintain a continued acceptable safety profile of our product candidates following approval.

We expect to incur significant sales and marketing costs as we prepare to commercialize our current or future product candidates. Even if we initiate and successfully complete pivotal or registration-enabling clinical trials of our current or future product candidates, and our current or future product candidates are approved for commercial sale, and despite expending these costs, our current or future product candidates may not be commercially successful. We may not achieve profitability soon after generating drug sales, if ever. If we are unable to generate revenue, we will not become profitable and may be unable to continue operations without continued funding.

***As part of our ongoing business, we will need to raise substantial additional funding beyond our current capital. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, scale back or discontinue some of our product candidate development programs or future commercialization efforts.***

We are currently progressing our Phase 1/2 trial of MRT-2359 and advancing multiple discovery programs through the preclinical stages of drug development across a number of potential indications. We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we continue the research and development of, advance the preclinical and clinical activities of, and seek marketing approval for, our current or future product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Furthermore, we expect to continue to incur significant additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. However, changing circumstances may cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control. We cannot be certain that additional funding will be available on acceptable terms, or at all. Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations through a combination of public or private equity offerings, debt financings, governmental funding, collaborations, strategic partnerships and alliances or marketing, distribution or licensing arrangements with third parties. If we are unable to raise capital or generate revenue when needed or on attractive terms, we would be forced to delay, reduce or eliminate our discovery and preclinical development programs or any future commercialization efforts. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these 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.

We expect that the net proceeds from our initial public offering, or IPO, together with our existing cash and cash equivalents and marketable securities, will be sufficient to fund our operations into 2025. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. This estimate also assumes that we do not obtain any additional funding through collaborations or other strategic alliances. Our future capital requirements will depend on, and could increase significantly as a result of, many factors, including:

- the scope, prioritization and number of our research and development programs;
- the costs, timing and outcome of regulatory review of our current or future product candidates;
- the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and planned clinical trials for our current or future product candidates, including additional expenses attributable to adjusting our development plans (including any supply related matters) in response to the ongoing COVID-19 pandemic or other geopolitical events;
- our ability to establish and maintain additional collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under any additional collaboration agreements we obtain;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under future collaboration agreements, if any;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other current or future product candidates and technologies;
- the costs of securing timely manufacturing arrangements for commercial production; and
- the costs of establishing or contracting for sales and marketing capabilities if we obtain regulatory clearances to market our current or future product candidates.

Identifying potential current or future product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve drug sales. In addition, our current or future product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of drugs that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional funding to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

## **Risks related to our business and industry**

### Risks related to drug development and regulatory approval

***Our approach to the discovery and development of product candidates based on our QuEEN™ platform is novel, which makes it difficult to predict the time, cost of development and likelihood of successfully developing any product candidates.***

Our QuEEN™ platform is a relatively new technology. Our future success depends on the successful development of this novel product candidate development approach. We have not yet succeeded and may not succeed in demonstrating the efficacy and safety of any of our product candidates in clinical trials or in obtaining marketing approval thereafter. In particular, our ability to successfully target therapeutically-relevant proteins using MGDs requires the successful development of MGDs developed via our QuEEN™ platform. This is a complex process requiring a number of component parts or biological mechanisms to work in unison to achieve the desired effect. We cannot be certain that we will be able to discover MGDs by matching the right target and its degron with the ideal E3 ligase in a timely manner, or at all. We have only initiated clinical development of our lead product candidate, and there may be adverse effects from treatment with any of our current or future product candidates that we cannot predict at this time.

As a result of these factors, it is more difficult for us to predict the time and cost of product candidate development, and we cannot predict whether our approaches will result in the development and marketing approval of any product candidates. Any development problems we experience in the future related to our QuEEN™ platform or any of our discovery programs may cause significant delays or unanticipated costs or may prevent the development of a commercially viable product. Any of these factors may prevent us from completing our preclinical studies and clinical trials, or any clinical trials that we may initiate in the future or commercializing any product candidates we may develop on a timely or profitable basis, if at all.

***We may not be successful in our efforts to identify or discover additional product candidates or we may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize***

***on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.***

A key element of our strategy is to apply our QuEEN™ platform and product pipeline to address a broad array of target proteins in various therapeutic areas. The discovery activities that we are conducting may not be successful in identifying product candidates that are useful in treating oncology, inflammatory, immunologic and other diseases, and neurodegenerative or other neurologic diseases. Our discovery programs may be unsuccessful in identifying potential product candidates, or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval.

Because we have limited financial and management resources, we focus on a limited number of discovery programs and product candidates at a time. As a result, we may forego or delay pursuit of opportunities with other current or future product 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 product 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 product candidate, we may relinquish valuable rights to that product 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 such product candidate.

***Our business is dependent on the success of our lead program, and any other product candidates that we advance into the clinic. We cannot be certain that we will be able to obtain regulatory approval for, or successfully commercialize, any of our current or future product candidates.***

All of our pipeline programs other than MRT-2359 are currently in preclinical development. The preclinical studies and future clinical trials of our current or future product candidates are, and the manufacturing and marketing of our current or future product candidates will be, subject to extensive and rigorous review and regulation by numerous government authorities in the U.S. and in other countries where we intend to test or, if approved, market any of our current or future product candidates. Before obtaining regulatory approvals for the commercial sale of any of our current or future product candidates, we must demonstrate through preclinical studies and clinical trials that each product candidate is safe and effective for use in each target indication. Drug development is a long, expensive and uncertain process, and delay or failure can occur at any stage of any of our preclinical studies and clinical trials. This process can take many years and may include post-marketing studies and surveillance, which will require the expenditure of substantial resources beyond the proceeds we raised in our IPO. Of the large number of drugs in development in the U.S., only a small percentage will successfully complete the FDA regulatory approval process and will be commercialized, with similarly low rates of success for drugs in development in the European Union obtaining regulatory approval from the EMA. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development and preclinical studies and clinical trials, we cannot assure you that any of our current or future product candidates will be successfully developed or commercialized.

We are not permitted to market our current or future product candidates in the U.S. until we receive approval of an NDA from the FDA, or in the EEA, until we receive approval of a marketing authorization application, or an MAA, from the EMA, or in any other foreign countries until we receive the requisite approval from such countries. Obtaining approval of an NDA or MAA is a complex, lengthy, expensive, and uncertain process, and the FDA or EMA may delay, limit or deny approval of any of our current or future product candidates for many reasons, including, among others:

- we may not be able to demonstrate that our current or future product candidates are safe and effective in treating their target indications to the satisfaction of the FDA or applicable foreign regulatory agency;
- the results of our preclinical studies and clinical trials may not meet the level of statistical or clinical significance required by the FDA or applicable foreign regulatory agency for marketing approval;
- the FDA or applicable foreign regulatory agency may disagree with the number, design, size, conduct or implementation of our preclinical studies and clinical trials;
- the FDA or applicable foreign regulatory agency may require that we conduct additional preclinical studies and clinical trials;



- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or applicable foreign regulatory agency may not approve the formulation, labeling or specifications of any of our current or future product candidates;
- the CROs that we retain to conduct our preclinical studies and clinical trials may take actions outside of our control that materially adversely impact our preclinical studies and clinical trials;
- the FDA or applicable foreign regulatory agency may find the data from preclinical studies and clinical trials insufficient to demonstrate that our current or future product candidates' clinical and other benefits outweigh their safety risks;
- the FDA or applicable foreign regulatory agency may disagree with our interpretation of data from our preclinical studies and clinical trials;
- the FDA or applicable foreign regulatory agency may not accept data generated at our preclinical study and clinical trial sites;
- if our NDA, if and when submitted, is reviewed by an advisory committee, the FDA may have difficulties scheduling an advisory committee meeting in a timely manner or the advisory committee may recommend against approval of our application or may recommend that the FDA require, as a condition of approval, additional preclinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions;
- the FDA may require development of a Risk Evaluation and Mitigation Strategy, or REMS, as a condition of approval or post-approval;
- the FDA or the applicable foreign regulatory agency may determine that the manufacturing processes or facilities of third-party manufacturers with which we contract do not conform to applicable requirements, including current Good Manufacturing Practices, or cGMPs;
- the FDA or applicable foreign regulatory agency may be delayed in their review processes due to staffing or other constraints arising from the ongoing COVID-19 pandemic; or
- the FDA or applicable foreign regulatory agency may change its approval policies or adopt new regulations.

Any of these factors, many of which are beyond our control, could jeopardize our ability to obtain regulatory approval for and successfully market our current or future product candidates. Any such setback in our pursuit of regulatory approval would have a material adverse effect on our business and prospects.

***If we experience delays or difficulties in the initiation, enrollment and/or retention of patients in clinical trials, our regulatory submissions or receipt of necessary regulatory approvals could be delayed or prevented.***

We may not be able to initiate our planned clinical trials or continue our ongoing trial on a timely basis or at all if we are unable to recruit and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the U.S. Patient enrollment is a significant factor in the timing of clinical trials. Our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate.

Moreover, some of our clinical trials will compete with other clinical trials that are in the same therapeutic areas as our current or future product candidates, and this competition reduces the number and types of patients available to us, as some patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' current or future product candidates. Because the number of qualified clinical investigators and clinical trial sites is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites. There may be limited patient pools from which to draw for clinical studies. In addition to the rarity of some diseases, the eligibility criteria of our clinical studies will further limit the pool of available study participants as we will require that patients have specific characteristics that we can measure or to assure their disease is either severe enough or not too advanced to include them in a study.

Patient enrollment for our ongoing clinical trial and any of our future clinical trials may be affected by other factors including:

- the size and nature of the patient population;
- competition with other companies for clinical sites or patients;
- the willingness of participants to enroll in our clinical trials in our countries of interest;
- the severity of the disease under investigation;
- availability and efficacy of approved drugs for the disease under investigation;
- the eligibility criteria for the clinical trial in question as defined in the protocol;
- the availability of an appropriate screening test for the indications we are pursuing;
- the perceived risks and benefits of the product candidate under study in relation to other available therapies, including any new products that may be approved for the indications we are investigating;
- the efforts to facilitate timely enrollment in and completion of clinical trials;
- delays in or temporary suspension of the enrollment of patients in our future clinical trials due to the ongoing COVID-19 pandemic;
- ability to obtain and maintain patient consents;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- the proximity and availability of clinical trial sites for prospective patients; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion.

These factors may make it difficult for us to enroll enough patients to complete our clinical trials in a timely and cost-effective manner. Our inability to enroll 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 for our product candidates and jeopardize our ability to obtain marketing approval for the sale of our product candidates. Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining participation in our clinical trials through the treatment and any follow-up periods.

***The incidence and prevalence for target patient populations of our product candidates have not been established with precision. If the market opportunities for our product candidates are smaller than we estimate or if any approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability will be adversely affected, possibly materially.***

The precise incidence and prevalence for the indications being pursued by our current and future product candidates is currently unknown. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates. Our GSPT1 program developed a product candidate, MRT-2359, for the treatment of cancers dependent on or characterized by the expression of high levels of MYC family genes, our NEK7 program will develop a product candidate for the treatment of inflammatory diseases, our CDK2 program will develop a product candidate for the treatment of cancers such as ovarian and breast cancers, our VAV1 program will develop a product candidate for the treatment of T and B cell malignancies and autoimmune diseases, and our sickle cell disease or SCD program will develop a product candidate for the treatment of sickle cell disease and  $\beta$ -Thalassemia. The total addressable market opportunity for product candidates from these discovery programs and future product candidates will ultimately depend upon, among other things, its proven safety and efficacy, the diagnosis criteria included in the final label for each, whether our product candidates are approved for sale for these indications, acceptance by the medical community and patient access, product pricing and reimbursement. The number of patients for our product candidates in the United States and elsewhere may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our products, 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.

***Preclinical and clinical drug development is a lengthy and expensive process, with an uncertain outcome. Our preclinical and clinical programs may experience delays or may never advance, which would***

***adversely affect our ability to obtain regulatory approvals or commercialize our product candidates on a timely basis or at all, which could have an adverse effect on our business.***

In order to obtain FDA approval to market a new small molecule product, we must demonstrate the safety and efficacy of our product candidates in humans to the satisfaction of the FDA. To meet these requirements, we will have to conduct adequate and well-controlled clinical trials. Clinical testing is expensive, time-consuming and subject to uncertainty. Before we can commence clinical trials for a product candidate, we must complete extensive preclinical studies that support our planned and future INDs in the United States. Other than MRT-2359, which is being evaluated in an ongoing clinical trial, we are currently selecting lead development candidates for preclinical development. We cannot be certain of the timely completion or outcome of our preclinical studies and cannot predict if the FDA will allow our proposed clinical programs to proceed or if the outcome of our preclinical studies will ultimately support further development of our programs. We cannot be sure that we will be able to submit INDs or similar applications with respect to our other product candidates on the timelines we expect, if at all, and we cannot be sure that submission of an IND or similar applications will result in the FDA or other regulatory authorities allowing clinical trials to begin.

Conducting preclinical testing and clinical trials represents is a lengthy, time-consuming and expensive process. The length of time may vary substantially according to the type, complexity and novelty of the program, and often can be several years or more per program. Delays associated with programs for which we are directly conducting preclinical studies may cause us to incur additional operating expenses. The commencement and rate of completion of preclinical studies and clinical trials for a product candidate may be delayed by many factors, including, for example:

- inability to generate sufficient preclinical or other *in vivo* or *in vitro* data to support the initiation of clinical studies;
- timely completion of preclinical laboratory tests, animal studies and formulation studies in accordance with the FDA's good laboratory practice requirements and other applicable regulations;
- approval by an independent Institutional Review Board, or IRB, ethics committee at each clinical site before each trial may be initiated;
- delays in reaching a consensus with regulatory agencies on study design and obtaining regulatory authorization to commence clinical trials;
- delays in reaching agreement on acceptable terms with prospective CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- delays in identifying, recruiting and training suitable clinical investigators;
- delays in recruiting suitable patients to participate in our clinical trials;
- delays in manufacturing, testing, releasing, validating or importing/exporting sufficient stable quantities of our product candidates for use in clinical trials or the inability to do any of the foregoing;
- insufficient or inadequate supply or quality of product candidates or other materials necessary for use in clinical trials, or delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for clinical trials;
- imposition of a temporary or permanent clinical hold by regulatory authorities;
- developments on trials conducted by competitors for related technology that raises FDA or foreign regulatory authority concerns about risk to patients of the technology broadly, or if the FDA or a foreign regulatory authority finds that the investigational protocol or plan is deficient to meet its stated objectives;
- delays in recruiting, screening and enrolling patients and delays caused by patients withdrawing from clinical trials or failing to return for post-treatment follow-up;
- difficulty collaborating with patient groups and investigators;
- failure by our CROs, other third parties or us to adhere to clinical trial protocols;
- failure to perform clinical trials in accordance with the FDA's good clinical practice requirements, or GCPs, or applicable regulatory guidelines in other countries;

- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits, or occurrence of adverse events in a trial of the same class of agents conducted by other companies;
- changes to the clinical trial protocols;
- clinical sites dropping out of a trial;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- selection of clinical endpoints that require prolonged periods of observation or analyses of resulting data;
- the cost of clinical trials of our product candidates being greater than we anticipate;
- clinical trials of our product candidates producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or abandon development of such product candidates;
- transfer of manufacturing processes to larger-scale facilities operated by a CMO and delays or failure by our CMOs or us to make any necessary changes to such manufacturing process; and
- third parties being unwilling or unable to satisfy their contractual obligations to us.

Further, conducting clinical trials in foreign countries, as we may do for our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries. Delays in the completion of any preclinical studies or clinical trials of our product candidates will increase our costs, slow down our product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate product revenue. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Any delays to our preclinical studies or clinical trials that occur as a result could shorten any period during which we may have the exclusive right to commercialize our product candidates and our competitors may be able to bring products to market before we do, and the commercial viability of our product candidates could be significantly reduced. Any of these occurrences may harm our business, financial condition and prospects significantly.

***The results of preclinical testing and early clinical trials may not be predictive of the results of later preclinical studies and clinical trials, and the results of our current and future clinical trials may not satisfy the requirements of the FDA or other comparable regulatory authorities. If we cannot replicate the positive results from our preclinical studies of our current or future product candidates in our current or future clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize our current or future product candidates.***

We will be required to demonstrate with substantial evidence through well-controlled clinical trials that our product candidates are safe and effective before we can seek marketing approvals for their commercial sale. Positive results from our preclinical studies of our current or future product candidates, and any positive results we may obtain from our early clinical trials of our current or future product candidates, may not necessarily be predictive of the results from required subsequent preclinical studies and clinical trials. Similarly, even if we are able to complete our planned preclinical studies or any clinical trials of our current or future product candidates according to our current development timeline, the positive results from such preclinical studies and clinical trials of our current or future product candidates may not be replicated in subsequent preclinical studies or clinical trial results.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway or safety or efficacy observations made in preclinical studies and clinical trials, including previously unreported adverse events. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed

satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain approval from the FDA or a comparable foreign regulatory authority. If we fail to produce positive results in our planned preclinical studies or clinical trials of any of our current or future product candidates, the development timeline and regulatory approval and commercialization prospects for our current or future product candidates, and, correspondingly, our business and financial prospects, would be materially adversely affected. Thus, even if the results from our initial research and preclinical activities appear positive, we do not know whether subsequent clinical studies we may conduct will demonstrate adequate efficacy and safety to result in regulatory approval to market any product candidates.

***Interim, top-line and preliminary data from our preclinical studies and clinical trials that we announce or publish from time to time may change as more data become available and are subject to audit and verification procedures that could result in material changes in the final data.***

From time to time, we may publicly disclose interim, topline or preliminary data from our preclinical studies and clinical trials, which is 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. 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 interim, topline or preliminary 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 have been received and fully evaluated. Interim, topline and preliminary data also remain 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, such data should be viewed with caution until the final data are available. Adverse differences between preliminary, interim or topline data and final data could significantly harm our business prospects.

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 product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and 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, product candidate or our business. If the interim, topline or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

***If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our current or future product candidates, we will not be able to commercialize, or will be delayed in commercializing, our current or future product candidates, and our ability to generate revenue will be materially impaired.***

Our current or future product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export, are subject to comprehensive regulation by the FDA and other regulatory agencies in the U.S. and by comparable authorities in other countries. Before we can commercialize any of our current or future product candidates, we must obtain marketing approval from the regulatory authorities in the relevant jurisdictions. We have not received approval to market any of our current or future product candidates from regulatory authorities in any jurisdiction, and it is possible that none of our current product candidates, nor any product candidates we may seek to develop in the future, will ever obtain regulatory approval. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the drug manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Our current or future product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our current or future product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our drugs, may grant approval contingent on the performance of costly post-marketing clinical trials, or



may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our current or future product candidates.

If we experience delays in obtaining approval or if we fail to obtain approval of our current or future product candidates, the commercial prospects for our current or future product candidates may be harmed and our ability to generate revenues will be materially impaired.

***The current ongoing pandemic of COVID-19 and its variants, and the future outbreak of other highly infectious or contagious diseases, may materially and adversely affect our business and our financial results and could cause a disruption to the development of our product candidates.***

The COVID-19 pandemic and the emergence of new variant strains of COVID-19, including the omicron variant and subvariants, and government measures taken in response, have had a significant impact, both direct and indirect, on businesses and commerce. In response to the spread of COVID-19, we have implemented policies at our locations to mitigate the risk of exposure to COVID-19 by our personnel, including by limiting the number of staff in any given research and development laboratory or manufacturing facility, a work-from-home policy applicable to our non-laboratory based employees, such as clinical, manufacturing, finance, administrative, quality, regulatory and program managers, and a phased approach to bringing personnel back to our locations over time. As a result of the COVID-19 pandemic, we have experienced and we expect to continue to experience disruptions that could severely impact our business and preclinical studies, including:

- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines;
- interruption of, or delays in receiving, supplies of our product candidates from our CMOs, due to staffing shortages, production slowdowns or stoppages, disruptions in delivery systems and the diversion of resources to prioritize manufacturing products that are related to treating or preventing COVID-19;
- interruptions in preclinical studies due to restricted or limited operations at our laboratory facility and those of our sub-contractors;
- delays in necessary interactions with local regulators, institutional review board, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees;
- changes in local regulations as part of a response to the COVID-19 pandemic, which may require us to change the ways in which our preclinical studies are conducted, which may result in unexpected costs, or to discontinue such preclinical studies altogether; and
- limitations on employee resources that would otherwise be focused on the conduct of our preclinical studies, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people.

Health regulatory agencies globally may experience disruptions in their operations as a result of the ongoing COVID-19 pandemic. The FDA and comparable foreign regulatory agencies may have slower response times or be under-resourced and review, inspection, and other timelines may be materially delayed. Since March 2020 when foreign and domestic inspections of facilities were largely placed on hold, the FDA has been working to resume pre-pandemic levels of inspection activities, including routine surveillance, bioresearch monitoring and pre-approval inspections. Should 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. During the COVID-19 public health emergency, 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 U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. Any delay in regulatory review resulting from such disruptions could materially affect the development and study of our product candidates.

The extent to which the COVID-19 pandemic, or the future outbreak of any other highly infectious or contagious diseases, impacts our operations will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the scope, severity, and duration of the pandemic, actions taken to contain

the pandemic or mitigate its impact, and the direct and indirect economic effects of the pandemic and containment measures, among others.

***Our current or future product candidates may cause adverse or other undesirable side effects that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.***

Undesirable side effects caused by our current or future product candidates could cause us to interrupt, delay or halt preclinical studies or could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other regulatory authorities. As is the case with many treatments for cancer, inflammatory and autoimmune diseases, neurodegeneration or other diseases it is likely that there may be adverse side effects associated with the use of our product candidates. Additionally, a potential risk in any protein degradation product is that healthy proteins or proteins not targeted for degradation will be degraded or that the degradation of the targeted protein, in itself, could cause adverse events, undesirable side effects, or unexpected consequences. It is possible that healthy proteins or proteins not targeted for degradation could be degraded using our MGD molecules in any of our planned or future clinical studies. There is also the potential risk of delayed adverse events following treatment using any of our current or future product candidates.

These side effects could arise due to off-target activity, allergic reactions in trial subjects or unwanted on-target effects in the body. Results of our current or planned clinical trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of, or deny approval of, our current or future product candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Further, our current or future product candidates could cause undesirable side effects in clinical trials related to on-target toxicity. If on-target toxicity is observed, or if our current or future product candidates have characteristics that are unexpected, we may need to abandon their development or limit 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. Many compounds that initially showed promise in early-stage testing for treating cancer or other diseases have later been found to cause side effects that prevented further development of the compound.

In addition, clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients and limited duration of exposure, rare and severe side effects of our current or future product candidates may only be uncovered with a significantly larger number of patients exposed to the product candidate. In any such event, our studies could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. The side effects experienced could affect patient recruitment or the ability of enrolled subjects to complete the study or result in potential product liability claims. Moreover, if we elect, or are required, not to initiate, or to delay, suspend or terminate any future clinical trial of any of our product candidates, the commercial prospects of such product candidates may be harmed and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to develop other product candidates, and may harm our business, financial condition and prospects significantly.

In addition, if our current or future product candidates receive marketing approval and we or others identify undesirable side effects caused by such current or future product candidates after such approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may suspend, withdraw or limit approvals of such current or future product candidates, or seek an injunction against their manufacture or distribution;
- regulatory authorities may require the addition of labeling statements or warnings, such as a “boxed” warning or a contraindication;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;

- we may be required to change the way such current or future product candidates are distributed or administered, conduct additional clinical trials or change the labeling of the current or future product candidates;
- we may be required to conduct post-marketing studies or change the way the product is administered;
- regulatory authorities may require a REMS plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools;
- we may be subject to regulatory investigations and government enforcement actions;
- we may decide to remove such current or future product candidates from the market;
- we could be sued and held liable for injury caused to individuals exposed to or taking our current or future product candidates;
- we may be subject to fines, injunctions or imposition of criminal penalties; and
- our reputation may suffer.

We believe that any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidates and could substantially increase the costs of commercializing our current or future product candidates, if approved, and significantly impact our ability to successfully commercialize our current or future product candidates and generate revenues.

***We may seek and fail to obtain Breakthrough Therapy Designation or Fast Track Designation from the FDA for our current or future product candidates. Even if granted for any of our current or future product candidates, these programs may not lead to a faster development, regulatory review or approval process, and such designations do not increase the likelihood that any of our product candidates will receive marketing approval in the United States.***

We may seek a Breakthrough Therapy Designation for one or more of our current or future product candidates. A breakthrough therapy is defined as a drug that is 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 drugs 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. Product candidates designated as breakthrough therapies by the FDA may also be eligible for priority review and accelerated approval. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our current or future product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy Designation for a current or future product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our current or future product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification and rescind the designation or decide that the time period for FDA review or approval will not be shortened.

We may also seek Fast Track Designation for one or more of our current or future product candidates. If a product candidate is intended for the treatment of a serious or life-threatening condition and preclinical or clinical data demonstrate the potential to address an unmet medical need for this condition, the product sponsor may apply for Fast Track Designation. The sponsor of a product candidate with Fast Track Designation has opportunities for more frequent interactions with the applicable FDA review team during product development and, once an NDA is submitted, the product candidate may be eligible for priority review. Such product candidate may also be eligible for rolling review, where the FDA may consider reviewing sections of the NDA on a rolling basis before the complete 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. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular current or future product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation for certain current or future product candidates, such as the Fast Track

Designation we received for MRT-2359 for the treatment of patients with previously treated, metastatic NSCLC with L-MYC or N-MYC expression, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may rescind fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program. Fast Track Designation alone does not guarantee qualification for the FDA's priority review procedures.

***We may seek approval from the FDA through the use of the accelerated approval pathway. If we are unable to obtain such approval, we may be required to conduct additional preclinical studies or clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may seek to withdraw accelerated approval.***

A product may be eligible for accelerated approval if it is designed to treat a serious or life-threatening disease or condition and generally provides a meaningful advantage over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical 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. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug 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, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. Under FDORA, the FDA is permitted to require, as appropriate, that a post-approval confirmatory study or studies be underway prior to approval or within a specified time period after the date of approval for a product granted accelerated approval. FDORA also requires sponsors to send updates to the FDA every 180 days on the status of such studies, including progress toward enrollment targets, and the FDA must promptly post this information publicly. FDORA also gives the FDA increased authority to withdraw approval of a drug or biologic granted accelerated approval on an expedited basis if the sponsor fails to conduct such studies in a timely manner, send the necessary updates to the FDA, or if such post-approval studies fail to verify the drug's predicted clinical benefit. Under FDORA, the FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post-approval confirmatory study or submit timely reports to the agency on their progress. 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. There can be no assurance that the FDA would allow any of the product 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 such submission or application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. Moreover, even if we received accelerated approval, any post-approval studies required to confirm and verify clinical benefit may not show such benefit, which could lead to withdrawal of any approvals we have obtained. Receiving accelerated approval does not assure that the product's accelerated approval will eventually be converted to a traditional approval.

***We may seek Orphan Drug Designation for certain of our current or future product candidates, and we may be unsuccessful or may be unable to maintain the benefits associated with Orphan Drug Designation, including the potential for market exclusivity.***

As part of our business strategy, we may seek Orphan Drug Designation for certain indications of our current or future product candidates, and we may be unsuccessful. Regulatory authorities in some jurisdictions, including the U.S. and Europe, 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 a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the U.S., or a patient population of 200,000 or more in the U.S. where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U.S. In the U.S., 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.

Similarly, in Europe, the European Commission, upon the recommendation of the EMA's Committee for Orphan Medicinal Products, grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in the EU and for which no satisfactory method of diagnosis, prevention, or treatment has been authorized for marketing in the EU (or, if a method exists, the product would be of significant benefit to those affected by the condition). Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of life-threatening or chronically debilitating conditions, and when, without incentives, it is unlikely that sales of the product in the EU would generate sufficient return to justify the necessary investment in developing the product. In the EU, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers.

Generally, if a product with an Orphan Drug Designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same drug for the same indication for that time period. The applicable period is seven years in the U.S. and ten years in the European Union. The exclusivity period in the European Union can be reduced to six years if a drug no longer meets the criteria for Orphan Drug Designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan Drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because different therapies can be approved for the same condition and the same therapies can be approved for different conditions but used off-label. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In addition, 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. 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. While we may seek Orphan Drug Designation for applicable indications for our current and any future product candidates, we may never receive such designations. Even if we do receive such designations, there is no guarantee that we will enjoy the benefits of those designations.

***Even if we receive marketing authorization for our product candidates, we will be subject to extensive 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 product candidates.***

If the FDA or a comparable foreign regulatory authority approves any of our current or future product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the drug will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration requirements, continued compliance with cGMPs and GCPs, and applicable product tracking and tracing requirements. Any regulatory approvals that we receive for our current or future product candidates may also be subject to limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the drug. Later discovery of previously unknown problems with a drug, 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 result in, among other things:

- restrictions on the marketing or manufacturing of our product candidates, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- manufacturing delays and supply disruptions where regulatory inspections identify observations of noncompliance during remediation;
- revisions to the labeling, including limitation on approved uses or the addition of warnings, contraindications, or other safety information, including boxed warnings;
- imposition of a REMS, which may include distribution or use restrictions;



- requirements to conduct additional post-market clinical trials to assess the safety of the product;
- fines, warning or untitled letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of approvals;
- product seizure or detention, or refusal to permit the import or export of drugs; and
- injunctions or the imposition of civil or criminal penalties.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.

The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our current or future product candidates. We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. 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.

***Even if we receive marketing approval for our current or future product candidates in the U.S., we may never receive regulatory approval to market our current or future product candidates outside of the U.S.***

We plan to seek regulatory approval of our current or future product candidates outside of the U.S. Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction.

For example, even if the FDA grants marketing approval of a product candidate, we may not obtain approvals in other jurisdictions, and comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion and reimbursement of the product candidate in those countries. However, a failure or delay in obtaining marketing approval in one jurisdiction may have a negative effect on the regulatory approval process in others. Approval procedures vary among countries and can involve additional product candidate testing and administrative review periods different from those in the United States. The time required to obtain approvals in other countries might differ substantially from that required to obtain FDA approval. The marketing approval processes in other countries generally implicate all of the risks detailed above regarding FDA approval in the U.S. as well as other risks. In particular, in many countries outside of the U.S., products must receive pricing and reimbursement approval before the product can be commercialized. Obtaining this approval can result in substantial delays in bringing products to market in such countries.

Obtaining foreign regulatory approvals and establishing and maintaining compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we or any future collaborator fail to comply with regulatory requirements in international markets or fail to receive applicable marketing approvals, it would reduce the size of our potential market, which could have a material adverse impact on our business, results of operations and prospects.

***If we 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. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste products. 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. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

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, this insurance may not provide adequate

coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development and production efforts, which could harm our business, prospects, financial condition or results of operations.

***Our future growth may depend, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties that could materially adversely affect our business.***

We are not permitted to market or promote any of our current or future product candidates before we receive regulatory approval from the applicable regulatory authority in that foreign market, and we may never receive such regulatory approval for any of our current or future product candidates. To obtain separate regulatory approval in many other countries we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy. Such requirements govern, among other things, clinical trials and commercial sales, and pricing and distribution of our current or future product candidates, and we cannot predict success in these jurisdictions. If we obtain approval of our current or future product candidates and ultimately commercialize our current or future product candidates in foreign markets, we would be subject to additional risks and uncertainties, including:

- differing regulatory requirements in foreign countries, such that obtaining regulatory approvals outside of the U.S. may take longer and be more costly than obtaining approval in the U.S.;
- our customers' ability to obtain reimbursement for our current or future product candidates in foreign markets;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- longer lead times for shipping;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries;
- the existence of additional potentially relevant third-party intellectual property rights;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the U.S.;
- potential liability under the Foreign Corrupt Practices Act of 1977 or comparable foreign regulations;
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

Foreign sales of our current or future product candidates could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs.

***Changes in funding or disruptions at the FDA, the SEC and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, 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 and accept the payment of user fees, and statutory, regulatory and policy changes and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the FDA have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those 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 slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, in recent years, including for 35 days beginning on December 22, 2018, the U.S. government shut down several times and certain regulatory agencies, such as the FDA and the SEC, had to furlough critical employees and stop critical activities.

If a prolonged government shutdown occurs, or if global health concerns prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews or other regulatory activities, 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. Further, in our operations as a public company, future government shutdowns or delays could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

***We may in the future conduct clinical trials for current or future product candidates outside the U.S., and the FDA and comparable foreign regulatory authorities may not accept data from such trials.***

We may in the future choose to conduct one or more clinical trials outside the U.S., including in Europe. The acceptance of study data from clinical trials conducted outside the U.S. or another jurisdiction by the FDA or comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the U.S., the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. In addition, even where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the U.S. or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which could be costly and time-consuming, and which may result in current or future product candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction.

***We are subject to certain U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations. We can face serious consequences for violations.***

Among other matters, U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations, which we collectively refer to as Trade Laws, prohibit companies and their employees, agents, clinical research organizations, legal counsel, accountants, consultants, contractors, and other partners from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of Trade Laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other

consequences. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations.

***Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.***

In some countries, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product candidates. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after coverage and reimbursement have been obtained. Reference pricing used by various countries and parallel distribution or arbitrage between low-priced and high-priced countries, can further reduce prices. 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 product candidate to other available therapies, which is time-consuming and costly. If coverage and reimbursement of our product candidates are unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

## **Risks related to commercialization**

***Even if we receive marketing approval for our current or future product candidates, our current or future product candidates may not achieve broad market acceptance, which would limit the revenue that we generate from their sales.***

The commercial success of our current or future product candidates, if approved by the FDA or other applicable regulatory authorities, will depend upon the awareness and acceptance of our current or future product candidates among the medical community, including physicians, patients and healthcare payors. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant revenue and we may not become profitable. Market acceptance of our current or future product candidates, if approved, will depend on a number of factors, including, among others:

- the efficacy of our current or future product candidates as demonstrated in clinical trials, and, if required by any applicable regulatory authority in connection with the approval for the applicable indications, to provide patients with incremental health benefits, as compared with other available medicines;
- the timing of market introduction of the product candidates and potential advantages to alternative treatments;
- limitations or warnings contained in the labeling approved for our current or future product candidates by the FDA or other applicable regulatory authorities;
- the clinical indications for which our current or future product candidates are approved;
- availability of alternative treatments already approved or expected to be commercially launched in the near future;
- the potential and perceived advantages of our current or future product candidates over current treatment options or alternative treatments, including future alternative treatments;
- the willingness of the target patient population to try new therapies or treatment methods and of physicians to prescribe these therapies or methods;
- the need to dose such product candidates in combination with other therapeutic agents, and related costs;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments;
- pricing and cost effectiveness;
- the effectiveness of our sales and marketing strategies;
- our ability to increase awareness of our current or future product candidates;
- our ability to obtain sufficient third-party coverage or reimbursement; or
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage.

If our current or future product candidates are approved but do not achieve an adequate level of acceptance by patients, physicians and payors, we may not generate sufficient revenue from our current or future product candidates to become or remain profitable. Before granting reimbursement approval, healthcare payors may require us to demonstrate that our current or future product candidates, in addition to treating these target indications, also provide incremental health benefits to patients. Our efforts to educate the medical community, patient organizations and third-party payors about the benefits of our current or future product candidates may require significant resources and may never be successful.

***If we are unable to establish sales, marketing and distribution capabilities for any product candidate that may receive regulatory approval, we may not be successful in commercializing those product candidates if and when they are approved.***

We do not have sales or marketing infrastructure. To achieve commercial success for any product candidate for which we may obtain marketing approval, we will need to establish a sales and marketing organization. In the future, we expect to build a focused sales and marketing infrastructure to market some of our product candidates in the United States, if and when they are approved. There are risks involved with establishing our own sales, marketing and distribution 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 product 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. This may 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 market our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians in order to educate physicians about our product candidates, once approved;
- 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.

If we are unable to establish our own sales, marketing and distribution capabilities and are forced to enter into arrangements with, and rely on, third parties to perform these services, our revenue and our profitability, if any, are likely to be lower than if we had developed such capabilities ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

***The market opportunities for any current or future product 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 product 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 product 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 product candidates in both oncology and non-oncology indications may be limited, if and when approved. Even if we obtain significant market share for any product 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.



***We face substantial competition, which may result in others discovering, developing or commercializing drugs before or more successfully than we do.***

The development and commercialization of new drugs is highly competitive. We face and will continue to face competition from third parties that use protein degradation, antibody therapy, inhibitory nucleic acid, gene editing or gene therapy development platforms and from companies focused on more traditional therapeutic modalities, such as small molecule inhibitors. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization of new drugs.

We are aware of several biotechnology companies focused on developing MGD therapeutics for patients, including but not limited to, BioTheryX Therapeutics, Inc., C4 Therapeutics, Inc., Nurix Therapeutics, Inc., Kymera Therapeutics, Inc., Seed Therapeutics, Inc., Plexium Inc., Bristol-Myers Squibb, and Novartis, all of which are currently in development. In addition, lenalidomide and pomalidomide, which are both marketed by Bristol-Myers Squibb, are believed to function as MGDs. Further, several large pharmaceutical companies have disclosed investments in this field.

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

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any drugs that we or our collaborators may develop. 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 or our collaborators are able to enter the market. The key competitive factors affecting the success of all of our current or future product 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.

***Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any current or future product candidates that we may develop.***

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

- decreased demand for any current or future product candidates that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any current or future product candidates that we may develop.

We do not yet maintain product liability insurance, and we anticipate that we will need to increase our insurance coverage when we begin clinical trials and if we successfully commercialize any product candidate. Insurance coverage is increasingly expensive. We may not be able to maintain product liability insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

***Even if we are able to commercialize any current or future product candidates, such drugs may become subject to unfavorable pricing regulations or third-party coverage and reimbursement policies, which would harm our business.***

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval. In the U.S. and in other countries, sales of any products for which we may receive regulatory marketing approval for commercial sale will depend, in part, on the availability of coverage and reimbursement from third-party payors. Third-party payors include government healthcare programs (e.g., Medicare and Medicaid), managed care providers, private health insurers, health maintenance organizations and other organizations. These third-party payors decide which medications they will pay for and establish reimbursement levels. The availability of coverage and extent of reimbursement by governmental and other third-party payors is essential for most patients to be able to afford treatments such as targeted protein degradation therapies.

In the United States, no uniform policy exists for coverage and reimbursement for products among third-party payors. Therefore, decisions regarding the extent of coverage and amount of reimbursement to be provided can differ significantly from payor to payor. Third-party payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates, but also have their own methods and approval process apart from Medicare determinations. Factors payors consider in determining reimbursement are based on whether the product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

One third-party payor's decision to cover a particular product or service does not ensure that other payors will also provide coverage for the medical product or service. Third-party payors may limit coverage to specific products on an approved list or formulary, which may not include all FDA-approved products for a particular indication. Also, third-party payors may refuse to include a particular branded product on their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available. We cannot be sure that coverage will be available for any product candidate that we commercialize.

Moreover, the process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate a payor will pay for the product. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. If coverage is available, but reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

Further, third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to secure coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA or comparable regulatory approvals. Additionally, we may also need to provide discounts to purchasers, private health plans or government healthcare programs. Despite our best efforts, our product candidates may not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover an approved product as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, our operations and financial condition.

Finally, in some foreign countries, the proposed pricing for a product candidate must be approved before it may be lawfully marketed. The requirements governing product pricing vary widely from country to country. For example, in the European Union, or EU, pricing and reimbursement of pharmaceutical products are regulated at a national level under the individual EU Member States' social security systems. Some foreign countries provide options to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and can control the prices and reimbursement levels of medicinal products for human use. Some

jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. A country may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Even if approved for reimbursement, historically, product candidates launched in some foreign countries, such as some countries in the EU, do not follow price structures of the U.S. and prices generally tend to be significantly lower.

***Current and future healthcare legislative reform measures may have a material adverse effect on our business and results of operations.***

In the United States and in some foreign jurisdictions, there have been, and likely will continue to be, a number of legislative and regulatory changes and proposed changes intended to broaden access to healthcare, improve the quality of healthcare, and contain or lower the cost of healthcare. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the ACA, was passed, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the U.S. pharmaceutical industry. The ACA, among other things, subjected drug products to potential competition by lower-cost biosimilars, expanded the types of entities eligible for the 340B drug discount program, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (increased to 70% pursuant to the Bipartisan Budget Act of 2018, or BBA, effective as of January 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

Since its enactment, there have been judicial, Congressional and executive challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021, through August 15, 2021, for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures of the Biden administration or other efforts, if any, to challenge, repeal or replace the ACA will impact our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013, and, due to subsequent legislative amendments, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. Then, a 1% payment reduction will occur beginning April 1, 2022, through June 30, 2022, and the 2% payment reduction will resume on July 1, 2022. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several 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.

Furthermore, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several congressional inquiries and proposed legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient assistance programs and reform government program reimbursement methodologies for pharmaceutical and biological products. At the federal level, the previous administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. On July 9, 2021, President Biden issued an executive order affirming the administration's policy to (i) support legislative reforms that would lower the prices of prescription drug and

biologics, including by allowing Medicare to negotiate drug prices, by imposing inflation caps, and, by supporting the development and market entry of lower-cost generic drugs and biosimilars; and (ii) support the enactment of a public health insurance option. Among other things, the Executive Order also directs HHS to provide a report on actions to combat excessive pricing of prescription drugs, enhance the domestic drug supply chain, reduce the price that the Federal government pays for drugs, and address price gouging in the industry; and directs the FDA to work with states and Indian Tribes that propose to develop section 804 Importation Programs in accordance with the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, and the FDA's implementing regulations. FDA released such implementing regulations on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. On September 25, 2020, CMS stated drugs imported by states under this rule will not be eligible for federal rebates under Section 1927 of the Social Security Act and manufacturers would not report these drugs for "best price" or Average Manufacturer Price purposes. Since these drugs are not considered covered outpatient drugs, CMS further stated it will not publish a National Average Drug Acquisition Cost for these drugs. If implemented, importation of drugs from Canada may materially and adversely affect the price we receive for any of our product candidates.

On November 20, 2020, CMS issued an Interim Final Rule implementing the Most Favored Nation, or MFN, Model under which Medicare Part B reimbursement rates would have been calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. However, on December 29, 2021, CMS rescinded the Most Favored Nations rule.

Additionally, on December 2, 2020, HHS published a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to court order, the removal and addition of the aforementioned safe harbors were delayed and recent legislation imposed a moratorium on implementation of the rule until January 1, 2026. The IRA further delayed implementation of this rule to January 1, 2032.

In August 2022, the IRA was signed into law. The IRA includes several provisions that will impact our business to varying degrees, including provisions that create a \$2,000 out-of-pocket cap for Medicare Part D beneficiaries, impose new manufacturer financial liability on all drugs in Medicare Part D, allow the U.S. government to negotiate Medicare Part B and Part D pricing for certain high-cost drugs and biologics without generic or biosimilar competition, require companies to pay rebates to Medicare for drug prices that increase faster than inflation, and delay the rebate rule that would require pass through of pharmacy benefit manager rebates to beneficiaries. The effect of IRA on our business and the healthcare industry in general is not yet known.

Further, on December 31, 2020, CMS published a new rule, effective January 1, 2023, requiring manufacturers to ensure the full value of co-pay assistance is passed on to the patient or these dollars will count toward the Average Manufacturer Price and Best Price calculation of the drug. On May 17, 2022, the U.S. District Court for the District of Columbia granted the Pharmaceutical Research and Manufacturers of America's or PhRMA motion for summary judgment invalidating the accumulator adjustment rule.

Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical 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. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. It is difficult to predict the future legislative landscape in healthcare and the effect on our business, results of operations, financial condition and prospects. However, we expect that additional state and federal healthcare reform measures will be adopted in the future. Further, it is possible that additional governmental action is taken in response to the COVID-19 pandemic.

At the state level, individual states are increasingly aggressive in passing legislation and implementing 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. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other



health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our current or future product candidates or additional pricing pressures. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States. 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 product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

***Our relationships with customers, health care providers, physicians, and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm and diminished future profits and earnings.***

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any current or future product candidates for which we obtain marketing approval. Our business operations and any current or future arrangements with third-party payors and customers may expose us to broadly applicable federal and state laws relating to fraud and abuse, as well as other healthcare laws and regulations. These laws may impact, among other things, the business or financial arrangements and relationships through which we market, sell and distribute any current or future product candidates for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include, among others:

- the laws and regulations described within the “Governmental Regulation” section of this Form 10-K; and
- analogous state law equivalents of each of the above U.S. federal laws, such as state anti-kickback and false claims laws, which may apply to items or services reimbursed by any third-party payor, including commercial insurers or patients; state and local marketing and/or transparency laws applicable to manufacturers that may be broader in scope than the federal requirements; state laws that require the reporting of information related to drug pricing; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and pricing information; state and local laws that require the licensure and/or registration of pharmaceutical sales representatives; state laws that require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; and state laws governing the privacy and security of health information and/or other health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

It is possible that governmental authorities will conclude that our business practices, including our arrangements with certain physicians, some of whom are compensated in the form of stock or stock options for services provided to us, do 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 to be 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 civil, criminal and administrative penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or similar settlement to resolve allegations of non-compliance with these laws, any of which could adversely affect our ability to operate our business and our financial results. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to similar actions, penalties, and sanctions.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to physicians is generally governed by the national anti-bribery laws of EU Member States, and the U.K. Bribery Act 2010 in the U.K. Infringement of these laws could result in substantial fines and imprisonment. Payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician’s employer, his or her competent professional organization and/or the regulatory authorities of the individual EU



Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

## **Risks related to our dependence on third parties**

***We currently rely, and plan to rely on in the future, on third parties to conduct and support our preclinical studies, and we expect to rely on third parties to conduct our clinical trials for our current and future product candidates. If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain marketing approval for or commercialize our current and potential future product candidates and our business could be substantially harmed.***

We utilize and depend upon independent investigators and collaborators, such as medical institutions, CROs, CMOs and strategic partners to help conduct our preclinical studies.

We do not have the ability to independently conduct clinical trials. We expect to rely on medical institutions, clinical investigators, contract laboratories, and other third parties, including collaboration partners, to conduct or otherwise support clinical trials for our current or future product candidates. We expect to rely heavily on these parties for execution of clinical trials for our product candidates and control only certain aspects of their activities. Nevertheless, we will be responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on CROs will not relieve us of our regulatory responsibilities.

We and any third parties that we contract with are required to comply with regulations and requirements, including GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development, for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate, and that the trial patients are adequately informed of the potential risks of participating in clinical trials and their rights are protected. These regulations are enforced by the FDA, the Competent Authorities of the Member States of the EEA and comparable foreign regulatory authorities for any drugs in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we or the third parties we contract with fail to comply with applicable GCP requirements, 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 clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our future clinical trials will comply with GCP requirements. In addition, our clinical trials must be conducted with current or future product candidates produced under cGMP regulations and will require a large number of study subjects. Our failure or the failure of third parties that we may contract with to comply with these regulations or to recruit a sufficient number of subjects may require us to repeat some aspects of a specific, or an entire, clinical trial, which would delay the marketing approval process and could also subject us to enforcement action. We also are required to register certain ongoing clinical trials and provide certain information, including information relating to the trial's protocol, on a government-sponsored database, ClinicalTrials.gov, within specific timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Although we intend to design the clinical trials for our current or future product candidates, or be involved in the design when other parties sponsor the trials, we anticipate that third parties will conduct all of our clinical trials. As a result, many important aspects of our clinical development, including their conduct, timing and response to the ongoing COVID-19 pandemic, will be outside of our direct control. Our reliance on third parties to conduct our ongoing clinical trial and future clinical trials will also result in less direct control over the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff, and we cannot control whether or not they will devote sufficient time and resources to our product candidates. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues; and

- form relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our clinical trials and may subject us to unexpected cost increases that are beyond our control. If our CROs do not perform clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development, marketing approval and commercialization of our current or future product candidates may be delayed, we may not be able to obtain marketing approval and commercialize our current or future product candidates, or our development programs may be materially and irreversibly harmed. If we are unable to rely on clinical data collected by our CROs, we could be required to repeat, extend the duration of, or increase the size of any clinical trials we conduct and this could significantly delay commercialization and require significantly greater expenditures.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs on commercially reasonable terms, or at all. If our CROs 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 are compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, any clinical trials such CROs are associated with may be extended, delayed or terminated, and we may not be able to obtain marketing approval for or successfully commercialize our current or future product candidates. As a result, we believe that our financial results and the commercial prospects for our current or future product candidates in the subject indication would be harmed, our costs could increase and our ability to generate revenue could be delayed.

***The third parties upon whom we rely on for the supply of drug product and starting materials used in our product candidates are limited in number, and the loss of any of these suppliers, or their noncompliance with regulatory requirements or our quality standards, could significantly harm our business.***

The drug substance and drug product in our product candidates are supplied to us from a small number of suppliers, and in some cases sole source suppliers. Our ability to successfully develop our current or future product candidates, and to ultimately supply our commercial drugs in quantities sufficient to meet the market demand, depends in part on our ability to obtain the drug product and drug substance for these drugs in accordance with regulatory requirements and in sufficient quantities for commercialization and clinical testing.

The facilities used by our contract manufacturers to manufacture our product candidates will be identified in, and subject to inspections that will be conducted after we submit, any marketing application to the FDA or other comparable foreign regulatory authorities. We may not control the manufacturing process of, and may be completely dependent on, our contract manufacturing partners for compliance with cGMP requirements and any other regulatory requirements of the FDA or other regulatory authorities for the manufacture of our product candidates. Beyond periodic audits, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve our marketing applications identifying these facilities for the manufacture of our product candidates or if it withdraws any approval in the future, we may need to find alternative manufacturing facilities, which would require that we incur significant additional costs and materially adversely affect our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Similarly, if any third-party manufacturers on which we will rely fail to manufacture quantities of our product candidates at quality levels necessary to meet regulatory requirements and at a scale sufficient to meet anticipated demand at a cost that allows us to achieve profitability, our business, financial condition and prospects could be materially and adversely affected.

Further, we do not currently have arrangements in place for a redundant or second-source supply of all drug product or drug substance in the event any of our current suppliers of such drug product and drug substance cease their operations for any reason. Any delays in the delivery of our drug substance, drug product or starting materials could have an adverse effect and potentially harm our business.

For all of our current or future product candidates, we intend to identify and qualify additional manufacturers to provide drug product and drug substance prior to submission of an NDA to the FDA and/or an MAA to the EMA. We are not certain, however, that our single-source and dual source suppliers will be able to meet our demand for their products, either because of the nature of our agreements with those suppliers, our limited experience with those suppliers or our relative importance as a customer to those suppliers. It may be difficult for us to assess their ability to timely meet our demand in the future based on past performance. While our suppliers have generally met our demand for their products on a timely basis in the past, they may subordinate our needs in the future to their other customers.

Establishing additional or replacement suppliers for the drug product and drug substance used in our current or future product candidates, if required, may not be accomplished quickly. In some cases, the technical skills required to manufacture our products or product candidates may be unique or proprietary to the original supplier and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. If we are able to find a replacement supplier, such replacement supplier would need to be qualified and may require additional regulatory approval, which could result in further delay. In addition, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials.

While we seek to maintain adequate inventory of the drug product and drug substance used in our current or future product candidates, any interruption or delay in the supply of components or materials, or our inability to obtain drug product and drug substance from alternate sources at acceptable prices in a timely manner, could impede, delay, limit or prevent our development efforts, which could harm our business, results of operations, financial condition and prospects.

In addition, some of our suppliers are located outside of the United States. We currently have a supplier based in Ukraine which supplies us with services and materials related to the ongoing expansion of our library of MGDs. Although we have reduced the work done by this supplier, continued Ukrainian geopolitical developments, including military activities related to Russia's invasion of Ukraine, could adversely affect the ability for such supplier to meet our ongoing demand. We also have a supplier based in China which supplies us with services and materials to support the ongoing expansion of our library of MGDs and materials for use in the pre-clinical and clinical development of our product candidates, including for MRT-2359, and recent changes in U.S.-China trade policies, and a number of other economic and geopolitical factors both in China and abroad could affect the ability for such supplier to meet our ongoing demand. Disruptions in our suppliers ability to meet our ongoing demand could have an adverse effect on our business and could have a material adverse effect on our business, financial condition, results of operations or prospects.

***Our success is dependent on our executive management team's ability to successfully pursue business development, strategic partnerships and investment opportunities as our company matures. We may also form or seek strategic alliances or acquisitions or enter into additional collaboration and licensing arrangements in the future, and we may not realize the benefits of such collaborations, alliances, acquisitions or licensing arrangements.***

We may in the future form or seek strategic alliances or acquisitions, create joint ventures, or enter into additional collaboration and licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to our current product candidates and any future product candidates that we may develop. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business.

In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or acquisition or other alternative arrangements for our current or future product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view our current or future product candidates as having the requisite potential to demonstrate safety, potency, purity and efficacy and obtain marketing approval.

Further, collaborations involving our technologies or current or future product candidates are subject to numerous risks, which may include the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to a collaboration;
- collaborators may not pursue development and commercialization of our current or future product candidates or may elect not to continue or renew development or commercialization of our current or future product candidates based on clinical trial results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;

- collaborators may delay clinical trials, provide insufficient funding for a clinical trial, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our current or future product candidates;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to their marketing and distribution;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that cause the delay or termination of the research, development or commercialization of our current or future product candidates, or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable current or future product candidates;
- collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to commercialize such intellectual property; and
- collaborators may not pay milestones and royalties due to the company in a timely manner.

As a result, we may not be able to realize the benefits of our existing collaboration and licensing arrangements or any future strategic partnerships or acquisitions, collaborations or license arrangements we may enter into if we are unable to successfully integrate them with our existing operations and company culture, which could delay our timelines or otherwise adversely affect our business. We also cannot be certain that, following a strategic transaction, license, collaboration or other business development partnership, we will achieve the revenue or specific net income that justifies such transaction. Any delays in entering into new collaborations or strategic partnership agreements related to our current or future product candidates could delay the development and commercialization of our current or future product candidates in certain geographies or for certain indications, which would harm our business prospects, financial condition and results of operations.

***Manufacturing our current or future product candidates is complex and we may encounter difficulties in production. If we encounter such difficulties, our ability to provide supply of our current or future product candidates for our preclinical studies and clinical trials or for commercial purposes could be delayed or stopped.***

The process of manufacturing of our current or future product candidates is complex and highly regulated. We do not have our own manufacturing facilities or personnel and currently rely, and expect to continue to rely, on third parties for the manufacture of our current or future product candidates. These third-party manufacturing providers may not be able to provide adequate or timely resources or capacity to meet our needs and may incorporate their own proprietary processes into our product candidate manufacturing processes. We have limited control and oversight of a third party's proprietary process, and a third party may elect to modify its process without our consent or knowledge. These modifications could negatively impact our manufacturing, including product loss or failure that requires additional manufacturing runs or a change in manufacturer, either of which could significantly increase the cost of and significantly delay the manufacture of our current or future product candidates.

As our current or future product candidates progress through preclinical studies and clinical trials towards potential approval and commercialization, it is expected that various aspects of the manufacturing process will be altered in an effort to optimize processes and results. Such changes may require amendments to be made to regulatory applications which may further delay the timeframes under which modified manufacturing processes can be used for any of our current or future product candidates and additional bridging studies or trials may be required and may not be successful. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials. Any such delay could have a material adverse impact on our business, results of operations and prospects.

***Our manufacturing process needs to comply with FDA regulations relating to the quality and reliability of such processes. Any failure to comply with relevant regulations could result in delays in or termination of our preclinical and future clinical programs and suspension or withdrawal of any regulatory approvals.***



In order to commercially produce our products either at our own facility or at a third party's facility, we will need to comply with the FDA's cGMP regulations and guidelines. We may encounter difficulties in achieving quality control and quality assurance and may experience shortages in qualified personnel. We and our third-party manufacturers are subject to inspections by the FDA and comparable foreign regulatory authorities to confirm compliance with applicable regulatory requirements. Any failure to follow cGMP or other regulatory requirements or delay, interruption or other issues that arise in the manufacture, fill-finish, packaging, or storage of our product candidates as a result of a failure of our facilities or the facilities or operations of third parties to comply with regulatory requirements or pass any regulatory authority inspection could significantly impair our ability to develop and commercialize our current or future product candidates, including leading to significant delays in the availability of our product candidates for our future clinical trials or the termination of or suspension of a future clinical trial, or the delay or prevention of a filing or approval of marketing applications for our current or future product candidates. Significant non-compliance could also result in the imposition of sanctions, including warning or untitled letters, fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals for our current or future product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could damage our reputation and our business.

***If our third-party manufacturers use hazardous and biological materials in a manner that causes injury or violates applicable law, we may be liable for damages.***

Our research and development activities involve the controlled use of potentially hazardous substances, including chemical materials, by our third-party manufacturers. Our manufacturers are subject to federal, state and local laws and regulations in the U.S. governing the use, manufacture, storage, handling and disposal of medical and hazardous materials. Although we believe that our manufacturers' procedures for using, handling, storing and disposing of these materials comply with legally prescribed standards, we cannot completely eliminate the risk of contamination or injury resulting from medical or hazardous materials. As a result of any such contamination or injury, we may incur liability or local, city, state or federal authorities may curtail the use of these materials and interrupt our business operations. In the event of an accident, we could be held liable for damages or penalized with fines, and the liability could exceed our resources. We do not have any insurance for liabilities arising from medical or hazardous materials. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development and production efforts, which could harm our business, prospects, financial condition or results of operations.

## **Risks related to intellectual property**

***If we are unable to obtain and maintain patent and other intellectual property protection for our technology and product candidates or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and drugs similar or identical to ours, and our ability to successfully commercialize our technology and drugs may be impaired, and we may not be able to compete effectively in our market.***

We rely upon a combination of patents, trademarks, trade secret protection and confidentiality agreements to protect the intellectual property related to our products and technologies and to prevent third parties from copying and surpassing our achievements, thus eroding our competitive position in our market. Our commercial success depends in part on our ability to obtain and maintain patent or other intellectual property protection in the U.S. and other countries for our current or future product candidates and our core technologies, including our proprietary QuEEN™ platform, our GSPT1 program, including our product candidate named MRT-2359, NEK7, CDK2, VAV1 and sickle cell disease or SCD programs, which are our four most advanced preclinical stage pipeline programs, as well as our proprietary compound library and other know-how. We seek to protect our proprietary and intellectual property position by, among other methods, filing patent applications in the U.S. and abroad related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business.

As of December 31, 2022, we owned patent applications related to our QuEEN™ platform, our CDK2 program, our NEK7 program, and our GSPT1 program, including GSPT1-directed MGDs, biomarkers related to these compounds. We currently do not own any issued patents. Further, patent prosecution related to our pending patent applications is in the early stages and, as such, no patent examiner has yet fully scrutinized the merits of any of our pending patent applications.

As of December 31, 2022, our patent portfolio covering GSPT1-directed MGDs and uses thereof included ten patent families, our patent portfolio related to our QuEEN™ platform included six patent families, our patent portfolio related to our CDK2 program included four patent families, and our patent portfolio related to our NEK7



program included two patent families. Patent term adjustments, supplementary protection certificate filings, or patent term extensions could result in later expiration dates in various countries, while terminal disclaimers could result in earlier expiration dates in the U.S.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As such, we cannot guarantee that our pending and future patent applications will result in patents being issued or that issued patents will afford sufficient protection of our product candidates or their intended uses against competitors, nor can there be any assurance that the patents issued will not be infringed, designed around, invalidated by third parties, or effectively prevent others from commercializing competitive technologies, products or product candidates.

The degree of patent protection we require to successfully commercialize our current or future product candidates may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep any competitive advantage. We cannot provide any assurances that any of our pending patent applications that mature into issued patents will include claims with a scope sufficient to protect our QuEEN™ platform and our current or future product candidates. In addition, if the breadth or strength of protection provided by our patent applications or any patents we may own or in-license is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Other parties have developed technologies that may be related or competitive to our own, and such parties may have filed or may file patent applications, or may have acquired or may acquire patents, claiming inventions that may overlap or conflict with those claimed in our own patent applications or issued patents, with respect to either the same compounds, methods, formulations or other subject matter, in either case that we may rely upon to dominate our patent position in the market. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until at least 18 months after the earliest priority date of the patent filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in patents we may own or in-license patents or pending patent applications, or that we were the first to file for patent protection of such inventions. In addition, the USPTO might require that the term of a patent issuing from a pending patent application be disclaimed and limited to the term of another patent that is commonly owned or names a common inventor. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights cannot be predicted with any certainty.

In addition, the patent prosecution 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. Further, with respect to certain pending patent applications covering our current or future product candidates or technologies, prosecution has yet to commence and as such, no patent examiner has scrutinized the merits of such pending patent applications. Patent prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the relevant patent office(s) may be significantly narrowed by the time they issue, if they ever do. It is also possible that we will fail to identify 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 technology that we license from or to third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

Even if we acquire patent protection that we expect should enable us to establish and/or maintain a competitive advantage, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the U.S. and abroad. We may become involved in opposition, derivation, reexamination, *inter partes* review, or post-grant review proceedings challenging our patent rights or the patent rights of others from whom we may in the future obtain licenses to such rights, in the U.S. Patent and Trademark Office, or USPTO, the European Patent Office, or EPO, or the relevant patent authorities in other countries. In addition, we may be subject to third-party submissions to the USPTO, the EPO, or elsewhere, that may reduce the scope or preclude the granting of claims from our pending patent applications. Competitors may challenge our issued patents or may file patent applications before we do.

Competitors may also claim that we are infringing their patents and that we therefore cannot practice our technology as claimed under our patents or patent applications. Competitors may also contest our patents by arguing before an administrative patent authority or judge that the invention was not patent-eligible, was not

novel, was obvious, and/or lacked inventive steps, and/or that the patent application failed to meet relevant requirements relating to description, basis, enablement, and/or support; in litigation, a competitor could assert that our patents are not valid or are unenforceable for a number of reasons. If a court or administrative patent authority agrees, we would lose our protection of those challenged patents.

An adverse determination in any such submission or proceeding may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and drugs, without payment to us, or could limit the duration of the patent protection covering our technology and current or future product candidates. Such challenges may also result in our inability to manufacture or commercialize our current or future product candidates without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Even if they are unchallenged, our issued patents and our pending patent applications, if issued, may not provide us with any meaningful protection or prevent competitors from designing around our patent claims to circumvent patents we may own or in-license by developing similar or alternative technologies or drugs in a non-infringing manner. For example, a third party may develop a competitive drug or product that provides benefits similar to one or more of our current or future product candidates but that has a different composition or otherwise falls outside the scope of our patent protection. If the patent protection provided by the patents and patent applications we hold or pursue with respect to our current or future product candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our current or future product candidates could be negatively affected, which would harm our business.

***Obtaining and maintaining our patent protection, including patent term, depends on compliance with various procedural, document submission, deadlines, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated if we miss a filing deadline for patent protection on these inventions or otherwise fail to comply with these requirements.***

The USPTO and foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and after issuance of any patent. In addition, periodic maintenance fees, renewal fees, annuity fees and/or various other government fees are required to be paid periodically. While an inadvertent lapse, including due to the effect of the COVID-19 pandemic on us or our maintenance vendors, can in some cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance 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. Noncompliance events that could result in abandonment or lapse of a patent 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. In such an event, our competitors might be able to enter the market with similar or identical products or platforms, which could have a material adverse effect on our business prospects and financial condition.

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

Patents have a limited lifespan. In the U.S., and most other jurisdictions in which we have undertaken patent filings, the natural expiration of a patent is generally twenty years after it is filed, assuming all maintenance fees are paid. Various extensions may be available, on a jurisdiction-by-jurisdiction basis; however, the life of a patent, and thus the protection it affords, is limited. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, patents we may own or in-license may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing drugs similar or identical to our current or future product candidates, including generic versions of such drugs.

Depending upon the timing, duration and specifics of FDA marketing approval of our current or future product candidates, one or more of the U.S. patents we own or license may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to 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. Different laws govern the extension of patents on approved pharmaceutical products in Europe and other jurisdictions. However, we may not be granted a patent extension because of, for example, failing to exercise due diligence

during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. For example, we may not be granted an extension in the U.S. if all of our patents covering an approved product expire more than fourteen years from the date of NDA approval for a product covered by those patents. 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 ability to generate revenues could be materially adversely affected.

***If our trademarks and trade names for our products or company name are not adequately protected in one or more countries where we intend to market our products, we may delay the launch of product brand names, use different trademarks or tradenames in different countries, or face other potentially adverse consequences to building our product brand recognition.***

We use and will continue to use registered and/or unregistered trademarks or trade names to brand and market ourselves and our products. Our trademarks or trade names may be challenged, infringed, diluted, circumvented or declared generic or determined to be infringing on other marks. We intend to rely on both registration and common law protection for our trademarks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. During the trademark registration process, we may receive Office Actions from the USPTO or from comparable agencies in foreign jurisdictions objecting to the registration of our trademark. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and/or to seek the cancellation of registered trademarks. Opposition or cancellation proceedings may be filed against our trademark applications or registrations, and our trademark applications or registrations may not survive such proceedings. In addition, there could be potential trade name or trademark infringement claims brought by owners of other trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long run, if we are unable to obtain a registered trademark or establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

Additionally, we may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names.

***If we are unable to adequately protect and enforce our trade secrets, our business and competitive position would be harmed.***

In addition to the protection afforded by patents we may own or in-license, we seek to rely on trade secret protection, confidentiality agreements, and license agreements to protect proprietary know-how that may not be patentable, processes for which patents are difficult to enforce and any other elements of our product discovery and development processes that involve proprietary know-how, information, or technology that may not be covered by patents. Although we require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information, or technology to enter into non-disclosure and confidentiality agreements, trade secrets can be difficult to protect and we have limited control over the protection of trade secrets used by our collaborators and suppliers. We cannot be certain that we have or will obtain these agreements in all circumstances and we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary information.

Moreover, any of these parties might breach the agreements and intentionally or inadvertently disclose our trade secret information and we may not be able to obtain adequate remedies for such breaches. In addition, competitors may otherwise gain access (such as through a cybersecurity breach) to our trade secrets or independently develop substantially equivalent information and techniques. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. If we choose to go to court to stop a third party from using any of our trade secrets, we may incur substantial costs. These lawsuits may consume our time and other resources even if we are successful. Furthermore, the laws of some foreign countries do not protect proprietary rights and trade secrets to the same extent or in the same manner as the laws of the U.S. We may need to share our proprietary information, including trade secrets, with future business partners, collaborators, contractors and others located in countries at heightened risk of theft of trade secrets, including through direct intrusion by private parties or foreign actors, and those affiliated with or controlled by state actors. As a result, we may encounter significant problems in protecting

and defending our intellectual property both in the U.S. and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, financial condition, results of operations and future prospects.

***We may initiate, become a defendant in, or otherwise become party to lawsuits to protect or enforce our intellectual property rights, which could be expensive, time-consuming and unsuccessful.***

Competitors may infringe or otherwise violate any patents or other intellectual property we may own or in-license. In addition, any patents we may own or in-license also may become involved in inventorship, priority, validity or unenforceability disputes. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. Any such claims could provoke these parties to assert counterclaims against us, including claims alleging that we infringe their patents or other intellectual property rights. In patent litigation in the U.S. and in some other jurisdictions, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld material information from the USPTO or the applicable foreign counterpart, or made a misleading statement, during prosecution. A litigant or the USPTO itself could challenge our patents on this basis even if we believe that we have conducted our patent prosecution in accordance with the duty of candor and in good faith. The outcome following such a challenge is unpredictable. Moreover, with respect to challenges to the validity of our patents, there might be invalidating prior art, of which we and the patent examiner were unaware during prosecution.

We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. In addition, in an infringement proceeding, a court may decide that one or more of any patents we may own or in-license is not valid or is unenforceable or that the other party's use of our technology that may be patented falls under the safe harbor to patent infringement under 35 U.S.C. §271(e)(1). There is also the risk that, even if the validity of these patents is upheld, the court may refuse to stop the other party from using the technology at issue on the grounds that any patents we may own or in-license do not cover the technology in question or that such third party's activities do not infringe our patent applications or any patents we may own or in-license. An adverse result in any litigation or defense proceedings could put one or more of any patents we may own or in-license at risk of being invalidated, held unenforceable, or interpreted narrowly and could put our patent applications at risk of not issuing. Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, patient support or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. 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. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

We may be required to protect our patents through procedures created to attack the validity of a patent at the USPTO. Post-grant proceedings, including post-grant review, *inter partes* review and derivation proceedings, provoked by third parties or brought by the USPTO may be necessary to determine the validity or priority of inventions with respect to our patent applications or any patents we may own or in-license. These proceedings are expensive and an unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. In addition to potential USPTO post-grant proceedings, we may become a party to patent opposition proceedings in the EPO, or similar proceedings in other foreign patent offices or courts where our patents may be challenged. The costs of these proceedings could be substantial, and may result in a loss of scope of some claims or a loss of the entire patent. An unfavorable result in a post-grant challenge proceeding may result in the loss of our right to exclude others from practicing one or more of our inventions in the relevant country or jurisdiction, which could have a material adverse effect on our business. Litigation or post-grant proceedings within patent offices may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees.

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 this



type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. 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.

We may not be able to detect infringement against any patents we may own or in-license. Even if we detect infringement by a third party of any patents we may own or in-license, we may choose not to pursue litigation against or settlement with the third party. If we later sue such third party for patent infringement, the third party may have certain legal defenses available to it, which otherwise would not be available except for the delay between when the infringement was first detected and when the suit was brought. Such legal defenses may make it impossible for us to enforce any patents we may own or in-license against such third party.

Intellectual property litigation and administrative patent office patent validity challenges in one or more countries could cause us to spend substantial resources and distract our personnel from their normal responsibilities. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace, including compromising our ability to raise the funds necessary to continue our preclinical studies and future clinical trials, continue our discovery programs, license necessary technology from third parties, or enter into development collaborations that would help us commercialize our current or future product candidates, if approved.

In addition, if our product candidates are found to infringe the intellectual property rights of third parties, these third parties may assert infringement claims against our licensees and other parties with whom we have business relationships, and we may be required to indemnify those parties for any damages they suffer as a result of these claims. The claims may require us to initiate or defend protracted and costly litigation on behalf of licensees and other parties regardless of the merits of these claims. If any of these claims succeed, we may be forced to pay damages on behalf of those parties or may be required to obtain licenses for the products they use.

Any of the foregoing events would harm our business, financial condition, results of operations and prospects.

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

We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. Inventorship disputes may arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our product candidates or as a result of questions regarding co-ownership of potential joint inventions. Litigation may be necessary to resolve these and other claims challenging inventorship and/or ownership. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. 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.

Our current and future licensors may have relied on third-party consultants or collaborators or on funds from third parties, such as the U.S. government, such that our licensors are not the sole and exclusive owners of the patents we in-licensed. If other third parties have ownership rights or other rights to our in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

In the case of employees, we enter into agreements providing that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. Although we require all of our employees to assign their inventions 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. 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. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects.



***Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain. Defending against such law suits will be costly and time consuming, and an unfavorable outcome in that litigation would have a material adverse effect on our business.***

The intellectual property landscape relevant to our products and programs is crowded, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business. Our commercial success depends upon our ability to develop, manufacture, market and sell our current and future product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the valid and enforceable intellectual property rights of third parties. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including derivation, interference, reexamination, *inter partes* review and post grant review proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We or any of our current or future licensors or strategic partners may be party to, exposed to, or threatened with, future adversarial proceedings or litigation by third parties having patent or other intellectual property rights alleging that our current or future product candidates and/or proprietary technologies infringe, misappropriate or otherwise violate their intellectual property rights. We cannot assure you that our current or future product candidates, the QuEEN™ platform, and other technologies that we have developed, are developing or may develop in the future do not or will not infringe, misappropriate or otherwise violate existing or future patents or other intellectual property rights owned by third parties.

While certain activities related to development and preclinical and clinical testing of our current or future product candidates may be subject to safe harbor of patent infringement under 35 U.S.C. §271(e)(1), upon receiving FDA approval for such candidates we or any of our future licensors or strategic partners may immediately become party to, exposed to, or threatened with, future adversarial proceedings or litigation by third parties having patent or other intellectual property rights alleging that such product candidates infringe, misappropriate or otherwise violate their intellectual property rights. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our current or future product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our current or future product candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of drugs, products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our current or future product candidates, technologies or methods.

If a third party claims that we infringe, misappropriate or otherwise violate its intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement, misappropriation and other intellectual property claims which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business and may impact our reputation;
- substantial damages for infringement, misappropriation or other violations, which we may have to pay if a court decides that the product candidate or technology at issue infringes, misappropriates or violates the third party's rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees;
- a court prohibiting us from developing, manufacturing, marketing or selling our current or future product candidates, or from using our proprietary technologies, including our QuEEN™ platform, unless the third-party licenses its product rights to us, which it is not required to do on commercially reasonable terms or at all;
- if a license is available from a third party, we may have to pay substantial royalties, upfront fees and other amounts, and/or grant cross-licenses to intellectual property rights for our products, or the license to us may be non-exclusive, which would permit third parties to use the same intellectual property to compete with us;
- redesigning our current or future product candidates or processes so they do not infringe, misappropriate or violate third-party intellectual property rights, which may not be possible or may require substantial monetary expenditures and time; and

- 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.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. The occurrence of any of the foregoing could have a material adverse effect on our business, financial condition, results of operations or prospects.

Third parties may assert that we are employing their proprietary technology without authorization. Patents issued in the U.S. by law enjoy a presumption of validity that can be rebutted in U.S. courts only with evidence that is “clear and convincing,” a heightened standard of proof. There may be issued third-party patents of which we are currently unaware with claims to compositions, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our current or future product candidates. Patent applications can take many years to issue. In addition, because some patent applications in the U.S. may be maintained in secrecy until the patents are issued, patent applications in the U.S. and many foreign jurisdictions are typically not published until 18 months after their earliest priority filing date, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications covering our current or future product candidates or technology. If any such patent applications issue as patents, and if such patents have priority over our patent applications or patents we may own or in-license, we may be required to obtain rights to such patents owned by third parties which may not be available on commercially reasonable terms or at all, or may only be available on a non-exclusive basis. There may be currently pending third-party patent applications which may later result in issued patents that our current or future product candidates may infringe. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our current or future product candidates or other technologies, could be found to be infringed by our current or future product candidates or other technologies. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Moreover, we may fail to identify relevant patents or incorrectly conclude that a patent is invalid, not enforceable, exhausted, or not infringed by our activities. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of our current or future product candidates, molecules used in or formed during the manufacturing process, or any final product itself, the holders of any such patents may be able to block our ability to commercialize the product candidate unless we obtained a license under the applicable patents, or until such patents expire or they are finally determined to be held invalid or unenforceable. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy or patient selection methods, the holders of any such patent may be able to block our ability to develop and commercialize the product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms or at all. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, or at all, our ability to commercialize our current or future product candidates or the QuEEN™ platform may be impaired or delayed, which could in turn significantly harm our business. Even if we obtain a license, it may be nonexclusive, thereby giving our competitors access to the same technologies licensed to us.

In addition, parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our current or future product candidates. Defense of these claims, regardless of their merit, could involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement, misappropriation or other violation against us, we may have to pay substantial damages, including treble damages and attorneys’ fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need or may choose to obtain licenses from third parties to advance our research or allow commercialization of our current or future product candidates, which licenses may not be available on commercially reasonable terms, or at all. In that event, we would be unable to further develop and commercialize our current or future product candidates or technologies, which could harm our business significantly.

***We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information or alleged trade secrets of third parties or competitors or are in breach of non-competition or non-solicitation agreements with our competitors or their former employers.***

As is common in the biotechnology and pharmaceutical industries, we employ individuals and engage the services of consultants who previously worked for other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending and 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 we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's former employer. We may also be subject to claims that patents and applications we have filed to protect inventions of our employees, consultants and advisors, even those related to one or more of our current or future product candidates, the QuEEN™ platform, or other technologies, are rightfully owned by their former or concurrent 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 or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities.

***We will not obtain patent or other intellectual property protection for any current or future product candidates in all jurisdictions throughout the world, and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.***

We may not be able to pursue patent coverage of our current or future product candidates, the QuEEN™ platform, or other technologies in all countries. Filing, prosecuting and defending patents on current or future product candidates, the QuEEN™ platform, and other technologies in all countries throughout the world would be prohibitively expensive, and intellectual property rights in some countries outside the U.S. can be less extensive than those in the U.S. 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 U.S. Consequently, we may not be able to prevent third parties from infringing on our inventions in all countries outside the U.S., or from selling or importing products made using our inventions in and into the U.S. or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but where enforcement is not as strong as that in the U.S. These products may compete with our current or future product candidates and in jurisdictions where we do not have any issued patents our patent applications or other intellectual property rights may not be effective or sufficient to prevent them from competing. Much of our patent portfolio is at the very early stage. We will need to decide whether and in which jurisdictions to pursue protection for the various inventions in our portfolio prior to applicable deadlines.

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, trade secrets and other intellectual property protection, particularly those relating to pharmaceutical products, which could make it difficult for us to stop the infringement of any patents we may own or in-license or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce any rights we may have in our patent applications or any patents we may own or in-license in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put any patents we may own or in-license 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.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we are forced to grant a license to third parties with respect to any patents we may own or license that are relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected.

***We may not obtain or grant licenses or sublicenses to intellectual property rights in all markets on equally or sufficiently favorable terms with third parties.***

It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties. The licensing of third-party intellectual property rights is a competitive area, and more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. More established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to license such technology, or if we are forced to license such technology on unfavorable terms, our business could be materially harmed. If we are unable to obtain a necessary license, we may be unable to develop or commercialize the affected current or future product candidates, which could materially harm our business, and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties or other forms of compensation. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. Any of the foregoing could harm our competitive position, business, financial condition, results of operations and prospects.

Further, our licensors may retain certain rights under their agreements with us, including the right to use the underlying technology for noncommercial academic and research use, to publish general scientific findings from research related to the technology, and to make customary scientific and scholarly disclosures of information relating to the technology. It is difficult to monitor whether our licensors limit their use of the technology to these uses, and we could incur substantial expenses to enforce our rights to our licensed technology in the event of misuse. In addition, the United States federal government retains certain rights in inventions produced with its financial assistance under the Patent and Trademark Law Amendments Act, or the Bayh-Dole Act. The federal government retains a “nonexclusive, nontransferable, irrevocable, paid-up license” for its own benefit. The Bayh-Dole Act also provides federal agencies with “march-in rights.” March-in rights allow the government, in specified circumstances, to require the contractor or successors in title to the patent to grant a “nonexclusive, partially exclusive, or exclusive license” to a “responsible applicant or applicants.” If the patent owner refuses to do so, the government may grant the license itself. If, in the future, we co-own or license in technology which is critical to our business that is developed in whole or in part with federal funds subject to the Bayh-Dole Act, our ability to enforce or otherwise exploit patents covering such technology may be adversely affected.

***If we fail to comply with our obligations in our current or any future agreements under which we may license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.***

We are dependent on patents, know-how and proprietary technology, both our own and in-licensed from collaborators. We may in the future enter into more license agreements with third parties under which we receive rights to intellectual property that are important to our business. Our commercial success depends upon our ability to develop, manufacture, market and sell our current or future product candidates and use our and our licensors’ proprietary technologies without infringing the proprietary rights of third parties. Our success will also depend in part on the ability of our licensors to obtain, maintain and enforce patent protection for our licensed intellectual property, in particular, those patents to which we have secured exclusive rights. Our licensors may not successfully prosecute the patent applications to which we are licensed. Even if patents are issued in respect of these patent applications, our licensors may fail to maintain these patents, may determine not to pursue litigation against other companies that are infringing these patents, or may pursue such litigation less aggressively than we would. Without protection for the intellectual property we license, other companies might be able to offer substantially identical products for sale, which could adversely affect our competitive business position and harm our business prospects. Further, we may have limited control over these activities or any other intellectual property that may be in-licensed. For example, we cannot be certain that such activities by licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. We may have limited control over the manner in which our licensors initiate an infringement proceeding against a third-party infringer of the intellectual property rights, or defend certain of the intellectual property that is licensed to us. It is possible that the licensors’ infringement proceeding or defense activities may be less vigorous than had we conducted them ourselves. In the event our licensors fail to adequately pursue and maintain patent protection for patents and applications they control, and to timely cede



control of such prosecution to us, our competitors might be able to enter the market, which would have a material adverse effect on our business.

In addition, our current and future intellectual property license agreements may require us various development, regulatory and/or commercial diligence obligations, payment of milestones and/or royalties and other obligations. If we fail to comply with our obligations under these agreements (including as a result of COVID-19 impacting our operations), we use the licensed intellectual property in an unauthorized manner or we are subject to bankruptcy-related proceedings, the terms of the licenses may be materially modified, such as by rendering currently exclusive licenses non-exclusive, or it may give our licensors the right to terminate their respective agreement with us. Any termination of these licenses, or if the underlying patents fail to provide the intended exclusivity, could result in the loss of significant rights and could harm our ability to commercialize our current or future product candidates, the QuEEN™ platform, or other technologies, competitors or other third parties would have the freedom to seek regulatory approval of, and to market, products identical to ours, and we may be required to cease our development and commercialization of certain of our current or future product candidates. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Disputes may also arise between us and our current or future licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe, misappropriate or otherwise violate intellectual property rights 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 current or future product candidates, and what activities satisfy those diligence obligations;
- our right to transfer or assign the license;
- the priority of invention of any patented technology; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our current or future licensors and us and our partners.

In addition, the agreements under which we may license intellectual property or technology from third parties are likely to be complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Moreover, if disputes over intellectual property that we may license prevent or impair our ability to maintain current or future licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected current or future product candidates or technologies, which could have a material adverse effect on our business, financial conditions, results of operations and prospects.

***Changes in patent law in the U.S. and in foreign jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.***

Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming that other requirements for patentability are met, prior to March 16, 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. On March 16, 2013, under the Leahy-Smith America Invents Act, or the America Invents Act, enacted in September 2011, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. A third party that files a patent application in the USPTO on or after March 16, 2013, but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a



period of time after filing or until issuance, we cannot be certain that we or our licensors were the first to either (i) file any patent application related to our product candidates or (ii) invent any of the inventions claimed in our or our licensor's patents or patent applications.

The America Invents Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned or in-licensed patent applications and the enforcement or defense of our owned or in-licensed issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, the patent positions of companies in the development and commercialization of biopharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future 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 have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

***We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent, which might subject us to infringement claims or adversely affect our ability to develop and market our current or future product candidates.***

We cannot guarantee that any of our or our licensors' patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending patent application in the U.S. and abroad that is relevant to or necessary for the commercialization of our current or future product candidates in any jurisdiction. For example, U.S. patent applications filed before November 29, 2000, and certain U.S. patent applications filed after that date that will not be filed outside the U.S. remain confidential until patents issue. As mentioned above, patent applications in the U.S. and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our current or future product candidates could have been filed by third parties without our knowledge. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our current or future product candidates or the use of our current or future product candidates. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our current or future product candidates. We may incorrectly determine that our current or future product candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the U.S. or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our current or future product candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our current or future product candidates.

If we fail to identify and correctly interpret relevant patents, we may be subject to infringement claims. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we fail in any such dispute, in addition to being forced to pay damages, which may be significant, we may be temporarily or permanently prohibited from commercializing any of our current or future product candidates or technologies that are held to be infringing. We might, if possible, also be forced to redesign current or future product candidates so that we no longer infringe the third-party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business and could adversely affect our business, financial condition, results of operations and prospects.

***Intellectual property rights do not guarantee commercial success of current or future product candidates or other business activities. Numerous factors may limit any potential competitive advantage provided by our intellectual property rights.***

The degree of future protection afforded by our intellectual property rights, whether owned or in-licensed, is uncertain because intellectual property rights have limitations, and may not adequately protect our business, provide a barrier to entry against our competitors or potential competitors, or permit us to maintain our competitive advantage. Moreover, if a third party has intellectual property rights that cover the practice of our technology, we may not be able to fully exercise or extract value from our intellectual property rights. The following examples are illustrative:

- patent applications that we own or may in-license may not lead to issued patents;
- patents, should they issue, that we may own or in-license, may not provide us with any competitive advantages, may be narrowed in scope, or may be challenged and held invalid or unenforceable;
- others may be able to develop and/or practice technology, including compounds that are similar to the chemical compositions of our current or future product candidates, that is similar to our technology or aspects of our technology but that is not covered by the claims of any patents we may own or in-license, should any patents issue;
- third parties may compete with us in jurisdictions where we do not pursue and obtain patent protection;
- we, or our future licensors or collaborators, might not have been the first to make the inventions covered by a patent application that we own or may in-license;
- we, or our future licensors or collaborators, might not have been the first to file patent applications covering a particular invention;
- others may independently develop similar or alternative technologies without infringing, misappropriating or otherwise violating our intellectual property rights;
- our competitors might conduct research and development activities in the U.S. 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 may then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not be able to obtain and/or maintain necessary licenses on reasonable terms or at all;
- third parties may assert an ownership interest in our intellectual property and, if successful, such disputes may preclude us from exercising exclusive rights, or any rights at all, over that intellectual property;
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such trade secrets or know-how;
- we may not be able to maintain the confidentiality of our trade secrets or other proprietary information;
- we may not develop or in-license additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business, financial condition, results of operations and prospects.

## **Risks related to employee matters and managing growth**

***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 research and development, clinical and business development expertise of Markus Warmuth, M.D., our Chief Executive Officer, Owen Wallace, Ph.D., our Chief Scientific Officer, John Castle, Ph.D., our Chief Data Scientist, Sharon Townson, our Chief Technology Officer, Filip Janku, our Chief Medical Officer, Ajim Tamboli, our Chief Financial Officer, Jullian Jones, our Chief Business Officer, Philip Nickson, our General Counsel, and Jennifer Champoux, our Chief People and Operations Officer, as well as the other principal members of our management and scientific teams. Although we have entered into employment letter agreements with our executive officers, each of them may terminate their employment with us at any time.

We do not maintain “key person” insurance for any of our executives or other employees. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and 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.

Recruiting and retaining qualified scientific, clinical, 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 employees could impede the achievement of our research, 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 drugs. 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. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel. In addition, in order to induce employees to continue their employment with us, we have provided equity awards that vest over time and the value to our employees of such equity awards may be significantly affected by movements in our stock price that are beyond our control and may be at any time insufficient to counteract more lucrative offers from other companies. If we are unable to continue to attract and retain high quality personnel, the rate and success at which we can develop and commercialize product candidates will be limited.

***We will need to develop and expand our company, and we may encounter difficulties in managing this development and expansion, which could disrupt our operations.***

As of December 31, 2022, we had 123 full-time employees. We expect to increase our number of employees and the scope of our operations, including the areas of data sciences, platform biology and chemistry, drug discovery, clinical development, finance, business development, and legal. To manage our anticipated development and expansion, 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. Our management may need to divert a disproportionate amount of its attention away from its day-to-day activities and devote a substantial amount of time to managing these development activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of our current or future product candidates. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our current or future product candidates, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future development and expansion of our company.

***We have offices in multiple countries and we may further expand in the future, which presents challenges in managing our business operations.***

We are headquartered in Boston, Massachusetts and have offices in Basel, Switzerland. Conducting our business in multiple countries subjects us to a variety of risks and complexities that may materially and adversely affect our business, results of operations, financial condition and growth prospects, including, among other things:

- the increased complexity and costs inherent in managing international operations;
- diverse regulatory, financial and legal requirements, and any future changes to such requirements, in one or more countries where we are located or do business;
- country-specific tax, labor and employment laws and regulations;
- challenges inherent in efficiently managing employees in diverse geographies, including the need to adapt systems, policies, benefits and compliance programs to differing labor and other regulations;
- liabilities for activities of, or related to, our international operations or product candidates;

- changes in currency rates; and
- regulations relating to data security and the unauthorized use of, or access to, commercial and personal information.

We continue to expand our operations, and our corporate structure and tax structure is complex. In connection with our current and future potential partnerships, we are actively engaged in developing and applying technologies and intellectual property with a view toward commercialization of products globally, often with commercialization partners. In connection with those activities, we already have and will likely continue to engage in complex cross-border and global transactions involving our technology, intellectual property and other assets, between us and other entities such as partners and licensees, and between us and our subsidiaries. Such cross-border and global arrangements are both difficult to manage and can potentially give rise to complexities in areas such as tax treatment, particularly since we are subject to multiple tax regimes and different tax authorities can also take different views from each other, even as regards the same cross-border transaction or arrangement. There can be no assurance that we will effectively manage this increased complexity without experiencing operating inefficiencies, control deficiencies or tax liabilities. Significant management time and effort is required to effectively manage the increased complexity of our company, and our failure to successfully do so could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

***We may be unable to adequately protect our information systems from cyberattacks, which could result in the disclosure of confidential or proprietary information, including personal data, damage our reputation, and subject us to significant financial and legal exposure.***

We rely on information technology systems that we or our third-party providers operate to process, transmit and store electronic information in our day-to-day operations. In connection with our product discovery efforts, we may collect and use a variety of personal data, such as name, mailing address, email addresses, phone number and clinical trial information. A successful cyberattack could result in the theft or destruction of intellectual property, data or other misappropriation of assets, or otherwise compromise our confidential or proprietary information and disrupt our operations. Cyberattacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyberattacks could include wrongful conduct by hostile foreign governments, industrial espionage, wire fraud and other forms of cyber fraud, the deployment of harmful malware, denial-of-service, social engineering fraud or other means to threaten data security, confidentiality, integrity and availability. A successful cyberattack could cause serious negative consequences for us, including, without limitation, the disruption of operations, the misappropriation of confidential business information, including financial information, trade secrets, financial loss and the disclosure of corporate strategic plans. Although we devote resources to protect our information systems, we realize that cyberattacks are a threat, and there can be no assurance that our efforts will prevent information security breaches that would result in business, legal, financial or reputational harm to us, or would have a material adverse effect on our results of operations and financial condition. In addition, although we carry cyber insurance, in the event of a material security incident, such coverage may not be sufficient to cover all losses. Any failure to prevent or mitigate security breaches or improper access to, use of, or disclosure of our clinical data or patients' personal data could result in significant liability under Swiss national data protection laws, U.S. state (e.g., state breach notification laws), and/or federal (e.g., HIPAA, as amended by HITECH) laws, and laws of foreign jurisdictions (e.g., the EU General Data Protection Regulation, or GDPR) and may cause a material adverse impact to our reputation, affect our ability to use collected data, conduct new studies and potentially disrupt our business.

We rely on our third-party providers to implement effective security measures and identify and correct for any such failures, deficiencies or breaches. We also rely on our employees and consultants to safeguard their security credentials and follow our policies and procedures regarding use and access of computers and other devices that may contain our sensitive information. If we or our third-party providers fail to maintain or protect our information technology systems and data integrity effectively or fail to anticipate, plan for or manage significant disruptions to our information technology systems, we or our third-party providers could have difficulty preventing, detecting and controlling such cyber-attacks and any such attacks could result in losses described above, as well as disputes with physicians, patients and our partners, regulatory sanctions or penalties, increases in operating expenses, expenses or lost revenues or other adverse consequences, any of which could have a material adverse effect on our business, results of operations, financial condition, prospects and cash flows. Any failure by such third parties to prevent or mitigate security breaches or improper access to or disclosure of such information could have similarly adverse consequences for us. If we are unable to prevent or mitigate the impact of such security or data privacy breaches, we could be exposed to litigation and governmental investigations, which could lead to a potential disruption to our business.



***Our employees, principal investigators, CROs and consultants may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading laws.***

We are exposed to the risk that our employees, principal investigators, CROs and consultants may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violate the regulations of the FDA and other regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities; healthcare fraud and abuse laws and regulations in the U.S. and abroad; or laws that require the reporting of financial information or data accurately. In particular, sales, marketing, patient support and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Other activities subject to these laws include the improper use of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but 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 comply with these laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. 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 civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Because of the breadth of these laws and the narrowness of the statutory exceptions and 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 criminal, civil and administrative sanctions including monetary penalties, damages, fines, disgorgement, individual imprisonment, reputational harm, exclusion from participation in government 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 and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

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. 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.

## **Risks related to our common stock**

***The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock.***

Our stock price is likely to 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, purchasers of our common stock could incur substantial losses. The market price for our common stock may be influenced by many factors, including:

- the success of competitive drugs or technologies;



- results of preclinical studies and clinical trials of our current or future product candidates or those of our competitors;
- unanticipated safety concerns related to the use of any of our product candidates;
- regulatory or legal developments in the U.S. and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our current or future product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional current or future product candidates or drugs;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- product liability claims or other litigation;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this “Risk factors” section.

The stock market in general, and the Nasdaq Global Select Market and biopharmaceutical 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 recently in connection with the ongoing COVID-19 pandemic, which has 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 and other adverse effects or developments relating to geopolitical events or the ongoing COVID-19 pandemic, 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.

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

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of private and public equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. We do not currently have any committed external source of funds. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, our stockholders’ ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that materially adversely affect their rights as a common stockholder. Debt financing, if available, would increase our fixed payment obligations and 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 additional collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our intellectual property, future revenue streams, discovery programs or current or future product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, scale back or discontinue the development and commercialization of one or more of our product candidates, delay our pursuit of potential in-licenses or acquisitions or grant rights to develop and market current or future product candidates that we would otherwise prefer to develop and market ourselves.

***If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.***

The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us or our business. We do not currently have and may never obtain research coverage by industry or financial analysts. If no or few analysts commence coverage of us, the trading price of our stock would likely decrease. In the event we do have research analyst coverage, we will not have any control over the analysts or the content and opinions included in their reports. Additionally, if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

***We incur increased costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives.***

As a public company, we incur significant legal, accounting and other expenses. We are subject to the reporting requirements of the Exchange Act, which require, among other things, that we file with the SEC annual, quarterly and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act of 2002, as amended, or Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and The Nasdaq Stock Market LLC to implement provisions of the Sarbanes-Oxley Act, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, in July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas, such as “say on pay” and proxy access. Emerging growth companies may implement many of these requirements over a longer period and up to five years from the completion of an initial public offering. We intend to take advantage of these extended transition periods, but cannot guarantee that we will not be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

The rules and regulations applicable to public companies substantially increase our legal and financial compliance costs and make some activities more time-consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. The increased costs will decrease our net income or increase our net loss and may require us to reduce costs in other areas of our business or increase the prices of our products or services. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

***Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control, which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management.***

Our fourth amended and restated certificate of incorporation and our second amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of stockholders be called only by the board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors;

- a requirement of approval of not less than two-thirds of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval and which preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, or DGCL, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These antitakeover provisions and other provisions in our fourth amended and restated certificate of incorporation and amended and restated bylaws could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors and could also delay or impede a merger, tender offer or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

***Our amended and restated bylaws designate specific courts as the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit stockholders' ability to obtain a favorable judicial forum for disputes with us.***

Pursuant to our amended and restated bylaws, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware is the sole and exclusive forum for any state law claims for (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of or based on a breach of a fiduciary duty owed by any director, officer or other employee of ours to us or our stockholders; (iii) any action asserting a claim pursuant to any provision of the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws; or (iv) any action asserting a claim governed by the internal affairs doctrine, or the Delaware Forum Provision. The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act or the Exchange Act. Our amended and restated bylaws further provide that unless we consent in writing to the selection of an alternative forum, the United States District Court for the District of Massachusetts shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, or the Federal Forum Provision. In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock is deemed to have notice of and consented to the Delaware Forum Provision and the Federal Forum Provision; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

We recognize that the Delaware Forum Provision and the Federal Forum Provision in our amended and restated bylaws may impose additional litigation costs on stockholders in pursuing any such claims, particularly if the stockholders do not reside in or near the State of Delaware or the Commonwealth of Massachusetts, as applicable. Additionally, the forum selection clauses in our amended and restated bylaws may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage the filing of lawsuits against us and our directors, officers and employees, even though an action, if successful, might benefit our stockholders. In addition, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court are "facially valid" under Delaware law, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert that the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware and the United States District Court for the District of Massachusetts may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

***Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.***

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the market price of our common stock could decline. Based upon the number of shares of common stock, on an as-converted basis, outstanding as of March 10, 2023, we have outstanding a total of 49,359,033 shares of common stock.

In addition, 12,264,830 shares of common stock that are either subject to outstanding options or reserved for future issuance under our equity incentive plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

***We are an emerging growth company and a smaller reporting company, and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies and smaller reporting companies will make our common stock less attractive to investors.***

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act, or JOBS Act, enacted in April 2012. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company for up to five years following the year in which we completed our IPO, although circumstances could cause us to lose that status earlier. We will remain an emerging growth company until the earlier of (i) the last day of the fiscal year (a) following the fifth anniversary of the closing of our IPO, (b) in which we have total annual gross revenue of at least \$1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which requires the market value of our common stock that is held by non-affiliates to exceed \$700 million as of the prior June 30th, and (ii) the date on which we have issued more than \$1 billion in non-convertible debt during the prior three-year period.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to not “opt out” of this exemption from complying with new or revised accounting standards and, therefore, we will adopt new or revised accounting standards at the time private companies adopt the new or revised accounting standard and will do so 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.

Even after we no longer qualify as an emerging growth company, we may still qualify as a “smaller reporting company,” which would allow us to continue to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may 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.

***Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be the sole source of gain for our stockholders.***

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

***We are at risk of securities class action litigation.***

Historically, 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 biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years. If we were to be sued, it could result in substantial costs and a diversion of management’s attention and resources, which could harm our business.

***If our estimates or judgments relating to our critical accounting policies are based on assumptions that change or prove to be incorrect, our operating results could fall below our publicly announced guidance or the expectations of securities analysts and investors, resulting in a decline in the market price of our common stock.***

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in our consolidated financial statements and accompanying notes. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets, liabilities, equity, revenue and expenses that are not readily apparent from other sources. If our



assumptions change or if actual circumstances differ from our assumptions, our operating results may be adversely affected and could fall below our publicly announced guidance or the expectations of securities analysts and investors, resulting in a decline in the market price of our common stock.

## General risk factors

***Our executive officers, directors, principal stockholders and their affiliates exercise significant influence over our company, which will limit our stockholders' ability to influence corporate matters and could delay or prevent a change in corporate control.***

The holdings of our executive officers, directors, principal stockholders and their affiliates represents beneficial ownership, in the aggregate, of approximately 30.6% of our outstanding common stock. In addition, six of our directors, including our chief executive officer, are affiliated with our principal stockholders. As a result, these stockholders, if they act together, are able to influence our management and affairs and the outcome of matters submitted to our stockholders for approval, including the election of directors and any merger, consolidation or sale of all or substantially all of our assets. These stockholders may have interests with respect to their common stock that are different from our other stockholders. The concentration of voting power among these stockholders may have an adverse effect on the price of our common stock. In addition, this concentration of ownership might adversely affect the market price of our common stock by:

- delaying, deferring or preventing a change of control of us;
- impeding a merger, consolidation, takeover or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

***Adverse developments affecting the financial services industry, such as actual events or concerns involving liquidity, defaults or non-performance by financial institutions or transactional counterparties, could adversely affect our current and projected business operations and its financial condition and results of operations.***

Actual events involving limited liquidity, defaults, non-performance or other adverse developments that affect financial institutions, transactional counterparties or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market-wide liquidity problems. For example, on March 10, 2023, Silicon Valley Bank, or SVB, was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation, or the FDIC, as receiver. Similarly, on March 12, 2023, Signature Bank and Silvergate Capital Corp. were each swept into receivership. Although a statement by the Department of the Treasury, the Federal Reserve and the FDIC indicated that all depositors of SVB would have access to all of their money after only one business day of closure, including funds held in uninsured deposit accounts, borrowers under credit agreements, letters of credit and certain other financial instruments with SVB, Signature Bank or any other financial institution that is placed into receivership by the FDIC may be unable to access undrawn amounts thereunder. If any of our counterparties to any such instruments were to be placed into receivership, we may be unable to access such funds. In addition, if any parties with whom we conduct business are unable to access funds pursuant to such instruments or lending arrangements with such a financial institution, such parties' ability to pay their obligations to us or to enter into new commercial arrangements requiring additional payments to us could be adversely affected. In this regard, counterparties to SVB credit agreements and arrangements, and third parties such as beneficiaries of letters of credit (among others), may experience direct impacts from the closure of SVB and uncertainty remains over liquidity concerns in the broader financial services industry. Similar impacts have occurred in the past, such as during the 2008-2010 financial crisis. At the time of the closure, we had cash totaling about 2% of our total cash, cash equivalents, and marketable securities held in operating accounts and money market accounts at SVB. We received full access to this cash on March 13, 2023.

Inflation and rapid increases in interest rates have led to a decline in the trading value of previously issued government securities with interest rates below current market interest rates. Although the U.S. Department of Treasury, FDIC and Federal Reserve Board have announced a program to provide up to \$25 billion of loans to financial institutions secured by certain of such government securities held by financial institutions to mitigate the risk of potential losses on the sale of such instruments, widespread demands for customer withdrawals or other liquidity needs of financial institutions for immediately liquidity may exceed the capacity of such program. There is no guarantee that the U.S. Department of Treasury, FDIC and Federal Reserve Board will provide access to



uninsured funds in the future in the event of the closure of other banks or financial institutions, or that they would do so in a timely fashion.

Although we assess our banking relationships as we believe necessary or appropriate, our access to funding sources and other credit arrangements in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that affect us, the financial institutions with which we have arrangements directly, or the financial services industry or economy in general. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry. These factors could involve financial institutions or financial services industry companies with which we have financial or business relationships, but could also include factors involving financial markets or the financial services industry generally.

The results of events or concerns that involve one or more of these factors could include a variety of material and adverse impacts on our current and projected business operations and our financial condition and results of operations. These could include, but may not be limited to, the following:

- Delayed access to deposits or other financial assets or the uninsured loss of deposits or other financial assets;
- Loss of access to revolving existing credit facilities or other working capital sources and/or the inability to refund, roll over or extend the maturity of, or enter into new credit facilities or other working capital resources;
- Potential or actual breach of contractual obligations that require us to maintain letters or credit or other credit support arrangements; or
- Termination of cash management arrangements and/or delays in accessing or actual loss of funds subject to cash management arrangements.

In addition, investor concerns regarding the U.S. or international financial systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any decline in available funding or access to our cash and liquidity resources could, among other risks, adversely impact our ability to meet our operating expenses, financial obligations or fulfill our other obligations, result in breaches of our financial and/or contractual obligations or result in violations of federal or state wage and hour laws. Any of these impacts, or any other impacts resulting from the factors described above or other related or similar factors not described above, could have material adverse impacts on our liquidity and our current and/or projected business operations and financial condition and results of operations.

In addition, any further deterioration in the macroeconomic economy or financial services industry could lead to losses or defaults by parties with whom we conduct business, which in turn, could have a material adverse effect on our current and/or projected business operations and results of operations and financial condition. For example, a party with whom we conduct business may fail to make payments when due, default under their agreements with us, become insolvent or declare bankruptcy. Any bankruptcy or insolvency, or the failure to make payments when due, of any counterparty of ours, or the loss of any significant relationships, could result in material losses to us and may material adverse impacts on our business.

***If we fail to establish and maintain proper and effective internal control over financial reporting, our operating results and our ability to operate our business could be harmed.***

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. 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 controls and procedures for compliance with Section 404 of the Sarbanes-Oxley Act, which will require annual management assessment of the effectiveness of our internal control over financial reporting.

Implementing any appropriate changes to our internal controls may distract our officers and employees, entail substantial costs to modify our existing processes, and take significant time to complete. These changes may not,

however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase our operating costs and harm our business. In addition, investors' perceptions that our internal controls are inadequate or that we are unable to produce accurate financial statements on a timely basis may harm our stock price and make it more difficult for us to effectively market and sell any of our present or future product candidates that may receive regulatory approval.

***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.

***We or the third parties upon whom we depend may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.***

Natural disasters could severely disrupt our operations and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities on which we rely, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business. For example, following Hurricane Maria, shortages in production and delays in a number of medical supplies produced in Puerto Rico resulted, and any similar interruption due to a natural disaster affecting us or any of our third-party manufacturers could materially delay our operations.

***Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.***

As widely reported, global credit and financial markets have experienced extreme volatility and disruptions in the past several years, declines in consumer confidence, concerns about declines in economic growth, increases in the rate of inflation and uncertainty about economic stability, including most recently in connection with actions undertaken by the U.S. Federal Reserve Board to address inflation, the military conflict in Ukraine, the continuing effects of the COVID-19 pandemic and supply chain disruptions. There can be no assurance that further volatility 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 or continued unpredictable and unstable market conditions. If the current equity and credit markets continue to be volatile it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. Furthermore, our stock price may decline due in part to the volatility of the stock market and a general economic downturn.

Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay, scale back or discontinue the development and commercialization of one or more of our product candidates or delay our pursuit of potential in-licenses or acquisitions. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive these difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget.

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

Our operations, and those of our contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics, pandemics 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 product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption.

***Our internal computer systems, or those of our third-party CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our current or future product candidates' development programs.***

Despite the implementation of security measures, our internal computer systems and those of our third-party CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such system failure, accident, or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of data from preclinical studies or clinical trials for our current or future product candidates 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 results in a loss of or damage to our data or applications, other data or applications relating to our technology or current or future product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our current or future product candidates could be delayed.

***Our ability to utilize our net operating loss carryforwards and certain other tax attributes to offset future taxable income may be subject to certain limitations.***

As of December 31, 2022, we had federal and state net operating loss carryforwards of \$3.9 million and \$5.8 million, respectively, which begin to expire in various amounts in 2039 (other than federal net operating loss carryforwards arising in taxable years beginning after December 31, 2019, which are not subject to expiration). As of December 31, 2022, we had foreign net operating loss carryforwards of \$191.1 million that expire in 2026. As of December 31, 2022, we also had federal and state research and development tax credit carryforwards of \$1.1 million and \$0.6 million, respectively, which begin to expire in 2039. These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities. In addition, in general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change net operating losses or tax credits, or NOLs or credits, to offset future taxable income or taxes. For these purposes, an ownership change generally occurs where the aggregate stock ownership of one or more stockholders or groups of stockholders who owns at least 5% of a corporation's stock increases its ownership by more than 50 percentage points over its lowest ownership percentage within a specified testing period.

Our existing NOLs or credits may be subject to limitations arising from previous ownership changes, and our ability to utilize NOLs or credits could be further limited by Sections 382 and 383 of the Code. In addition, future changes in our stock ownership, many of which are outside of our control, could result in an ownership change under Sections 382 and 383 of the Code. Our NOLs or credits may also be impaired under state law. Accordingly, we may not be able to utilize a material portion of our NOLs or credits.

Furthermore, our ability to utilize our NOLs or credits is conditioned upon our attaining profitability and generating U. S. federal and state taxable income. As described above under "Risk factors—Risks related to our financial position and capital needs," we have incurred significant net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future; and therefore, we do not know whether or when we will generate the U.S. federal or state taxable income necessary to utilize our NOL or credit carryforwards that are subject to limitation by Sections 382 and 383 of the Code.

***Changes in tax law may adversely affect us or our investors.***

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service, or IRS, and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many changes have been made and changes are likely to continue to occur in the future.

It cannot be predicted whether, when, in what form, or with what effective dates, new tax laws may be enacted, or regulations and rulings may be enacted, promulgated or issued under existing or new tax laws, which could result

in an increase in our or our shareholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law or in the interpretation thereof.

## Item 1B. Unresolved Staff Comments

Not applicable.

## Item 2. Properties

Our principal offices occupy approximately 16,748 square feet of leased office space in Boston, Massachusetts. The current term of our Boston lease expires in June 2023.

As noted above, in December 2021, we executed a lease with the Harrison Avenue Landlord for approximately 63,327 square feet of office and laboratory space at 321 Harrison Avenue, Boston, Massachusetts, which is expected to serve as our new headquarters beginning in the second quarter of 2023. Our obligation to pay rent pursuant to the lease began on December 21, 2022. The initial term of the lease is one hundred twenty-eight (128) months following April 1, 2022. The annual base rent under the lease is \$95.00 per square foot for the first year, which is subject to scheduled annual increases of 3%, plus certain costs, operating expenses and property management fees. We have the option to extend the lease once for five (5)-years upon notice to the Landlord at least one (1) year prior to the end of the then-current term. We also have the option to sublet the Premises on the terms and conditions set forth in the lease.

We have an additional location used for office and lab space that occupies approximately 21,422 square feet located in Basel-City, Switzerland. The current term of our Basel lease expires in March 2026.

We believe that our facilities are adequate for our current needs and for the foreseeable future. To meet the future needs of our business, we may lease additional or alternate space. We believe that suitable additional or substitute space at commercially reasonable terms will be available as needed to accommodate any future expansion of our operations.

## Item 3. Legal Proceedings

From time to time, we may become subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Although the results of litigation and claims cannot be predicted with certainty, as of March 16, 2023, we do not believe we are party to any claim or litigation the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

## 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 Select Market on June 24, 2021, under the symbol "GLUE". Prior to that time, there was no public market for our common stock.

#### Holders of record

As of March 10, 2023, we had approximately 20 holders of record for our common stock. Certain shares are held in "street" name and accordingly, the number of beneficial owners of such shares is not known or included in the foregoing number. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

#### Dividends

We have never declared or paid cash dividends on our capital stock. We anticipate that we will retain all available funds and any future earnings, if any, for use in the operation of our business and do not anticipate paying cash dividends in the foreseeable future.

#### Stock performance graph

We are a smaller reporting company, as defined by Rule 12b-2 of the Exchange act, and are not required to provide a performance graph.

#### Recent sales of unregistered equity securities

None.

#### Use of proceeds from initial public offering

On June 28, 2021, we completed the IPO of our common stock pursuant to which we issued and sold 11,700,000 shares of our common stock at a public offering price of \$19.00 per share. On July 23, 2021, the underwriters exercised their option to purchase additional shares in full and we issued 1,755,000 shares of our common stock at the price of \$19.00 per share.

The offer and sale of all of the shares of our common stock in our IPO were registered under the Securities Act pursuant to a registration statement on Form S-1, as amended (File No. 333- 256773), which was declared effective by the SEC on June 23, 2021. J.P. Morgan Securities LLC, Cowen and Company, LLC, Piper Sandler & Co. and Guggenheim Securities, LLC acted as underwriters for the IPO.

We received aggregate gross proceeds from our IPO of \$255.6 million, or aggregate net proceeds of \$234.6 million after deducting underwriting discounts and commissions and other offering costs. None of the underwriting discounts and commissions or offering expenses were incurred or paid, directly or indirectly, to any of our directors or officers or their associates or to persons owning 10% or more of our common stock or to any of our affiliates.

There has been no material change in our planned use of the net proceeds from the IPO as described in our final prospectus dated June 25, 2021.

#### Issuer purchaser of equity securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report.

## Item 6. [Reserved]

## 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 included elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve risks and uncertainties, including those described in the section titled "Special Note Regarding Forward Looking Statements." Our actual results and the timing of selected events could differ materially from those discussed below. Factors that could cause or contribute to such differences include, but are not limited to, those identified below and those set forth under the section titled "Risk Factors" included elsewhere in this Annual Report.*

### Overview

We are a biotechnology company developing a portfolio of novel and proprietary MGDs. MGDs are small molecule drugs that employ the body's natural protein destruction mechanisms to selectively degrade therapeutically relevant proteins. MGDs work by inducing the engagement of defined surfaces identified on target proteins by an E3 ligase, such as cereblon. We have developed a proprietary and industry-leading protein degradation platform, called QuEEN™, to enable our unique, target-centric, MGD discovery and development and our rational design of MGD products. We believe our small molecule MGDs may give us significant advantages over existing therapeutic modalities, including other protein degradation approaches. We prioritize our product development on therapeutic targets backed by strong biological and genetic rationale with the goal of discovering and developing novel medicines.

Monte Rosa Therapeutics AG, a Swiss operating company, was incorporated under the laws of Switzerland in April 2018. Monte Rosa Therapeutics, Inc. was incorporated in Delaware in November 2019. In 2020, Monte Rosa Therapeutics, Inc. and Monte Rosa Therapeutics AG, entities under common control since the incorporation of Monte Rosa Therapeutics, Inc., consummated a contribution and exchange agreement, or the Contribution and Exchange, whereby Monte Rosa Therapeutics, Inc. acquired the net assets and shareholdings of Monte Rosa Therapeutics AG via a one-for-one exchange of equity between Monte Rosa Therapeutics, Inc. and the shareholders of Monte Rosa Therapeutics AG in a common control reorganization. We are headquartered in Boston, Massachusetts with research operations in both Boston and Basel, Switzerland. To date, we have been financed primarily through the issuance of convertible promissory notes, convertible preferred stock, and common stock.

### Liquidity

To date, we have financed our operations primarily through the issuance and sale of convertible promissory notes and our convertible preferred stock to outside investors in private equity financings, our initial public offering and at-the-market offerings. From our inception through the date hereof, we raised an aggregate of \$499.8 million of gross proceeds from such transactions. Since inception, we have had significant operating losses. Our primary use of cash is to fund operating expenses, which consist primarily of research and development expenditures and, to a lesser extent, general and administrative expenditures. Our net loss was \$108.5 million and \$74.0 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of \$230.5 million and \$268.1 million of cash, cash equivalents, restricted cash, and marketable securities.

### Business effects of COVID-19

The COVID-19 pandemic has presented a substantial public health and economic challenge around the world and has affected, and may continue to affect our employees, patients, communities and business operations, as well as the U.S. economy and financial markets. To date, our financial conditions and operations have not been significantly impacted by the COVID-19 pandemic; however, the full extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations, liquidity and financial condition will depend on future developments, which are highly uncertain and cannot be accurately predicted, including new information that may develop concerning COVID-19, the emergence of new variants and subvariants and the actions taken to contain it or treat its impact and the economic impact on local, regional, national and international markets.

For additional information on the various risks posed by the COVID-19 pandemic, please read the section entitled "Risk Factors" in this Annual Report.

## **Components of operating results**

### ***Research and development expenses***

Our research and development expenses include:

- expenses incurred under agreements with consultants, third-party service providers that conduct research and development activities on our behalf;
- personnel costs, which include salaries, benefits, pension and stock-based compensation;
- laboratory and vendor expenses related to the execution of preclinical and clinical studies;
- laboratory supplies and materials used for internal research and development activities; and
- facilities and equipment costs.

Most of our research and development expenses have been related to the development of our QuEEN™ platform and advancement of our GSPT1 program, advancement of our disclosed and undisclosed programs including for CDK2, NEK7, VAV1, and multiple sickle cell disease, or SCD targets. We have not reported program costs since our inception because we have not historically tracked or recorded our research and development expenses on a program-by-program basis. We use our personnel and infrastructure resources across the breadth of our research and development activities, which are directed toward identifying and developing product candidates.

We expense all research and development costs in the periods in which they are incurred. Costs for certain research and development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and third-party service providers.

We expect our research and development expenses to increase substantially for the foreseeable future as we continue to invest in research and development activities related to developing our product candidates, including investments in manufacturing, as we advance our programs and conduct clinical trials. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming, and the successful development of our product candidates is highly uncertain. As a result, we are unable to determine the duration and completion costs of our research and development projects, the costs of related clinical development costs or when and to what extent we will generate revenue from the commercialization and sale of any of our product candidates.

### ***General and administrative expenses***

Our general and administrative expenses consist primarily of personnel costs and other expenses for outside professional services, including legal fees relating to patent and corporate matters, professional fees for accounting, auditing, tax and administrative consulting services, insurance costs and other operating costs. We expect our general and administrative expenses to increase over the next several years to support our continued research and development activities, manufacturing activities, and the potential commercialization of our product candidates and development of commercial infrastructure. We also anticipate our general and administrative costs will increase and with respect to the hiring of additional personnel, fees to outside consultants, lawyers and accountants, and increased costs associated with being a public company, such as expenses related to services associated with maintaining compliance with Nasdaq listing rules and SEC reporting requirements, insurance and investor relations costs.

### ***Non-operating income and (expense)***

Our non-operating income and (expense) includes (i) interest earned on our investments, including principally U.S. government-backed money-market funds; (ii) gains and losses on transactions of our Swiss subsidiary denominated in currencies other than the U.S. Dollar; (iii) proceeds from the sale of lab equipment; and (iv) changes in the fair value of our preferred stock tranche obligations.

## Results of operations for the years ended December 31, 2022 and 2021

The following sets forth our results of operations:

(in thousands)	Year ended December 31,		Dollar change
	2022	2021	
Operating expenses:			
Research and development	\$ 85,061	\$ 57,155	\$ 27,906
General and administrative	27,323	15,727	11,596
Total operating expenses	112,384	72,882	39,502
Loss from operations	(112,384)	(72,882)	(39,502)
Other income (expense)	3,883	(1,076)	4,959
Net loss	\$ (108,501)	\$ (73,958)	\$ (34,543)

### Research and development expenses

Research and development expenses were comprised of:

(in thousands)	Year ended December 31,		Dollar change
	2022	2021	
External research and development services	\$ 35,374	\$ 26,222	\$ 9,152
Personnel costs	27,386	18,254	9,132
Laboratory and related expenses	7,433	6,032	1,401
Facility costs and other expenses	14,868	6,647	8,221
Research and development expenses	\$ 85,061	\$ 57,155	\$ 27,906

As of December 31, 2022, and December 31, 2021, respectively, we had 100 and 73 employees engaged in research and development activities in our facilities in the U.S. and Switzerland.

Most of our research and development expenses have been related to the development of our QuEEN™ platform, advancement of our GSPT1 program, including IND-enabling work for MRT-2359, and the advancement of our disclosed and undisclosed programs, including for CDK2, NEK7, VAV1, multiple SCD targets, and other discovery efforts. The increase for the year ended December 31, 2022, as compared to 2021 was primarily due to the expansion of research and development activities in the United States and Switzerland including increased headcount and facilities as well as corresponding increases in laboratory related expenses. Research and development expenses included non-cash stock-based compensation of \$6.1 million and \$2.6 million for the years end December 31, 2022, and 2021, respectively.

### General and administrative expenses

General and administrative expenses to support our business activities were comprised of:

(in thousands)	Year ended December 31,		Dollar change
	2022	2021	
Personnel costs	\$ 15,387	\$ 9,484	\$ 5,903
Professional services	4,467	2,761	1,706
Facility costs and other expenses	7,469	3,482	3,987
General and administrative expenses	\$ 27,323	\$ 15,727	\$ 11,596

As of December 31, 2022, and December 31, 2021, respectively, we had 23 and 20 employees engaged in general and administrative activities principally in our U.S. facility. Personnel and professional service costs increased in the year ended December 31, 2022, as compared to 2021 as a result of increased headcount and expenses in support of our growth and operations as a public company. General and administrative expenses included non-cash stock-based compensation of \$5.6 million and \$2.6 million for the years end December 31, 2022, and 2021, respectively.



## Other expenses, net

Other income (expense), net was comprised of:

(in thousands)	Year ended December 31,	
	2022	2021
Interest income, net	\$ 3,764	\$ 46
Foreign currency exchange gain (loss), net	10	(162)
Gain on disposal of fixed assets	109	—
Changes in fair value of preferred stock tranche obligations, net	—	(960)
Other income (expense)	\$ 3,883	\$ (1,076)

The increase in interest and other income for the year ended December 31, 2022, is principally attributable to interest income on marketable securities purchased in 2022.

Foreign exchange gains on transactions of our Swiss subsidiary denominated in currency other than the U.S. dollar increased in the year ended December 31, 2022, as to compared to the year ended December 31, 2021, principally due to the strengthening of the U.S Dollar with respect to, principally, the Swiss Franc.

## Liquidity and capital resources

### Overview

Due to our significant research and development expenditures, we have generated operating losses since our inception. We have funded our operations primarily through the sale of convertible preferred stock and common stock.

In July 2022, we entered into a sales agreement, or the Sales Agreement, with Jefferies LLC, or Jefferies, pursuant to which we may offer and sell shares of our common stock having aggregate gross proceeds of up to \$100 million from time to time in at-the-market offerings through Jefferies as sales agent. During the year ended December 31, 2022, we sold 2,482,008 shares of our common stock resulting in net proceeds of \$19.7 million.

As of December 31, 2022, we had cash, cash equivalents, restricted cash, and marketable securities, of \$268.1 million and an accumulated deficit of \$230.5 million. We believe that our cash, cash equivalents, restricted cash, and marketable securities will be sufficient to fund our planned operations for at least one year past the issuance date of these financial statements.

### Cash flows

The following table summarizes our cash flows for the periods indicated:

(in thousands)	Year ended December 31,	
	2022	2021
Net cash (used in) provided by:		
Operating activities	\$ (92,466)	\$ (59,363)
Investing activities	(219,219)	(9,653)
Financing activities	20,466	377,562
Net (decrease) increase in cash, cash equivalents and restricted cash	\$ (291,219)	\$ 308,546

### Operating activities

During the year ended December 31, 2022, net cash used in operating activities of \$92.5 million was attributable to our net loss of \$108.5 million and a \$2.1 million net change in our operating assets and liabilities, off-set by \$18.2 million in non-cash charges. Non-cash charges primarily include stock-based compensation expense of \$11.7 million, depreciation expense of \$3.7 million, and non-cash lease expense of \$4.8 million.

During the year ended December 31, 2021, net cash used in operating activities of \$59.4 million was attributable to our net loss of \$74.0 million off-set by a \$6.3 million net change in our operating assets and liabilities and \$8.3 million in non-cash charges. Non-cash charges include stock-based compensation expense of \$5.2 million, depreciation expense of \$2.1 million, and changes in the fair value of our preferred stock tranche obligation of \$1.0 million.

### *Investing activities*

Cash used in investing activities of \$219.2 million during the year ended December 31, 2022, was primarily attributable to purchases of marketable securities of \$384.4 million and purchases of property and equipment of \$12.9 million, off-set by proceeds from the maturity of marketable securities of \$178.0 million.

For the year ended December 31, 2021, our investing activities consisted of purchases of property and equipment of \$9.7 million.

### *Financing activities*

Net cash provided by financing activities for the year ended December 31, 2022, amounted to \$20.5 million principally attributable to the sale of 2,482,008 shares of common stock sold in an at-the-market offering pursuant to the Sales Agreement for aggregate net proceeds \$19.7 million after deducting underwriters discounts and commissions and other offering costs, proceeds from the exercise of stock options of \$0.4 million, and proceeds from the issuance of shares under our employee stock purchase plan of \$0.3 million.

Net cash provided by financing activities for the year ended December 31, 2021, amounted to \$377.6 million comprised principally of aggregate net proceeds upon the issuance of our Series B and Series C convertible preferred stock in February and March 2021, respectively, and the issuance of common stock in our IPO in June 2021.

### *Funding requirements*

Any product candidates we may develop may never achieve commercialization and we anticipate that we will continue to incur losses for the foreseeable future. We expect that our research and development expenses, general and administrative expenses, and capital expenditures will continue to increase. As a result, until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings or other capital sources, including potentially collaborations, licenses and other similar arrangements. Our primary uses of capital are, and we expect will continue to be, compensation and related expenses, third-party clinical research, manufacturing and development services, costs relating to the build-out of our headquarters, laboratories and manufacturing facility, license payments or milestone obligations that may arise, laboratory and related supplies, clinical costs, manufacturing costs, legal and other regulatory expenses and general overhead costs.

Based upon our current operating plan, we believe that the existing cash, cash equivalents, restricted cash, and marketable securities of \$268.1 million, will enable us to fund our operating expenses and capital expenditure requirements for at least the next twelve months. We base this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect.

We will continue to require additional financing to advance our current product candidates through clinical development, to develop, acquire or in-license other potential product candidates and to fund operations for the foreseeable future. We will continue to seek funds through equity offerings, debt financings or other capital sources, including potential collaborations, licenses and other similar arrangements. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. If we do raise additional capital through public or private equity offerings, the ownership interest of our existing stockholders, will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Any failure to raise capital as and when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies. If we are unable to raise capital, we will need to delay, reduce or terminate planned activities to reduce costs.

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

- the scope, progress, results and costs of researching, developing and manufacturing our current product candidates or any future product candidates, and conducting preclinical studies and clinical trials;
- the timing of, and the costs involved in, obtaining regulatory approvals or clearances for our lead product candidates or any future product candidates;
- the number and characteristics of any additional product candidates we develop or acquire;

- the cost of manufacturing our lead product candidate or any future product candidates and any products we successfully commercialize, including costs associated with building-out our manufacturing capabilities;
- our ability to establish and maintain strategic collaborations, licensing or other arrangements and the financial terms of any such agreements that we may enter;
- the expenses needed to attract and retain skilled personnel;
- the costs associated with being a public company;
- the timing, receipt and amount of sales of any future approved or cleared products, if any; and
- the impact of global economic and political developments, the COVID-19 pandemic and the corresponding responses of businesses and governments.

Further, our operating plans may change, and we may need additional funds to meet operational needs and capital requirements for clinical trials and other research and development activities. We currently have no credit facility or committed sources of capital. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated product development programs.

## **Critical accounting policies and significant judgments and estimates**

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles, or GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

### ***Research and development expense and accruals***

We record research and development expenses to operations as incurred. Research and development expenses represent costs incurred by us for development of our technology platform and the discovery and development of our product candidates and include: employee-related expenses, including salaries, benefits and non-cash stock-based compensation expense; external research and development expenses incurred under arrangements with third parties, including preclinical testing organizations, non-profit institutions and consultants; and other expenses, which include direct and allocated expenses for laboratory, facilities and other costs.

As part of the process of preparing financial statements, we are required to estimate and accrue expenses. We estimate costs of research and development activities conducted by service providers. Payments made prior to the receipt of goods or services to be used in research and development are deferred and recognized as expense in the period in which the related goods are received or services are rendered. If the costs have been prepaid, this expense reduces the prepaid expenses in the balance sheet, and if not yet invoiced, the costs are included in accrued expenses in the balance sheet. We classify such prepaid assets as current or non-current assets based on our estimates of the timing of when the goods or services will be realized or consumed. These costs are a significant component of our research and development expenses.

We estimate these costs based on factors such as estimates of the work completed and budget provided and in accordance with agreements established third-party service providers. We estimate the amount of work completed through discussions with internal personnel and external service providers as to the progress or stage of completion of the services and the agreed-upon fee to be paid for such services. We make significant judgments and estimates in determining the accrued expense balance in each reporting period. As actual costs become known, we adjust our estimates. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed may vary from our estimates and could result in us reporting amounts that are too high or too low in any particular period. Our

accrued expenses are dependent, in part, upon the receipt of timely and accurate reporting from external third-party service providers. Amounts ultimately incurred in relation to amounts accrued for these services at a reporting date may be substantially higher or lower than our estimates.

We have and may continue to enter into license agreements to access and utilize certain technology. We evaluate if the license agreement is an acquisition of an asset or a business. To date none of our license agreements have been considered to be an acquisition of a business. For asset acquisitions, the upfront payments to acquire such licenses, as well as any future milestone payments made before product approval, are immediately recognized as research and development expense when due, provided there is no alternative future use of the rights in other research and development projects.

### ***Stock-based compensation***

We account for stock-based compensation by measuring and recognizing compensation expense for all share-based awards made to employees and directors based on estimated grant-date fair values. We use the straight-line method to allocate compensation cost to reporting periods over the requisite service period, which is generally the vesting period, and estimate the fair value of share-based awards to employees and directors using the Black-Scholes option-pricing valuation model. The Black-Scholes model requires the input of subjective assumptions, including fair value of common stock, expected term, expected volatility, risk-free interest rate and expected dividends, which are described in greater detail below.

**Fair Value of Common Stock**—Prior to the IPO, as there was no public market for our common stock, the board of directors determined the fair value of our common stock by taking into consideration, among other things, timely valuations of our common stock prepared by an unrelated third-party valuation firm in accordance with the guidance provided by the American Institute of Certified Public Accountants Practice Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation. Given the absence of a public trading market for our common stock prior to our IPO, our board of directors exercised reasonable judgment and considered a number of objective and subjective factors to determine the best estimate of the fair value of our common stock, including our stage of development; progress of our research and development efforts; the rights, preferences and privileges of our convertible preferred stock relative to those of our common stock; equity market conditions affecting comparable public companies and the lack of marketability of our common stock. Since the completion of our IPO, the fair value of each share of common stock underlying stock option grants is based on the closing price of our common stock on the Nasdaq Global Select Market as reported on the date of grant.

**Expected Term**—The expected term of the options represents the average period the stock options are expected to remain outstanding. As we do not have sufficient historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior, the expected term of options granted is derived from the average midpoint between the weighted average vesting and the contractual term, also known as the simplified method.

**Expected Volatility**— Since we have only recently become a public company and have only a limited trading history for our common stock, the expected volatility was estimated based on the average historical volatilities of common stock of comparable publicly traded entities over a period equal to the expected term of the stock option grants. We selected companies with comparable characteristics, including enterprise value, risk profiles, position within the industry, and, where applicable, with historical share price information sufficient to meet the expected life of our stock-based awards. We will continue to apply this process until enough historical information regarding the volatility of our own stock price becomes available.

**Risk-Free Interest Rate**—The risk-free interest rate is based on the yield of zero-coupon U.S. Treasury notes as of the grant date with maturities commensurate with the expected term of the awards.

**Expected Dividends**—The expected dividends assumption is based on our expectation of not paying dividends in the foreseeable future; therefore, we used an expected dividend yield of zero.

### **Recently issued and adopted accounting pronouncements**

Refer to Note 2, “Summary of Significant Accounting Policies,” in the accompanying notes to our consolidated financial statements appearing elsewhere in this Annual Report for a discussion of recent accounting pronouncements.

## **Contractual obligations and commitments**

### ***License agreement***

In April 2018, we entered into separate license, collaboration, and investment agreements with CRT and the ICR for the purpose of development in the field of cereblon-mediated protein degradation. Pursuant to the License Agreement, CRT and the ICR granted us certain exclusive and non-exclusive, worldwide, and sublicensable licenses under CRT's and the ICR's intellectual property rights in the field of cereblon mediated protein degradation to discover, research, develop, have developed, use, keep, make, have made, market, import, offer for sale, and sell products in the field of cereblon-mediated protein degradation.

In consideration for the rights granted under the License Agreement, we issued an aggregate of 1,132,984 common shares to CRT, the ICR and affiliated founding scientists pursuant to the Formation and Investment Agreement for an aggregate purchase price of CHF 40,000 and paid CRT an immaterial technology access fee. The License Agreement will remain effective until terminated by written agreement between us, CRT and the ICR.

Under the Collaboration Agreement, we may be obligated to make certain milestone payments for achieving specific clinical progression events for certain products, solely to the extent such products are subject to the Collaboration Agreement. If owed, these milestones would aggregate up to \$7 million for any covered first product candidate and \$3.5 million for any subsequent product candidate. In addition, the Company may be obligated to pay low single-digit royalties on net sales for any covered product on a country by country basis until the later of (a) the date when the manufacture, use, offer for sale, sale or importation of such product is no longer covered by a valid claim in the country of sale, use or manufacture; (b) ten years from the first commercial sale of such product in the relevant country; and (c) the expiry of any extended exclusivity period granted with respect to an orphan drug designation, pediatric designation or other exclusivity in the relevant country. See the section entitled "Business—Our services, collaboration and licenses agreements" elsewhere in this Annual Report as well as Note 8 to our annual consolidated financial statements appearing elsewhere in this Annual Report for a description of our collaboration and license agreements.



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

Not applicable.

## **Item 8. Financial Statements and Supplementary Data**

The financial information required by Item 8 is located beginning on page F-1 of this Annual Report.

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

None.

### Item 9A. Controls and Procedures

#### Limitations on effectiveness of controls and procedures

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints, and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

#### Evaluation of disclosure controls and procedures

Our management, with the participation of our principal executive officer and principal financial officer, evaluated, as of December 31, 2022, the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act). Based on the evaluation, our principal executive officer and principal financial officer concluded that, as of December 31, 2022, our disclosure controls and procedures as of such date are effective at the reasonable assurance level.

#### Management's annual report on internal control over financial reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) under the Exchange Act. 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, 2022, our internal control over financial reporting was effective.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm due to a transition period established by rules of the SEC for "emerging growth companies".

#### Changes in Internal Control over Financial Reporting

Material weaknesses, previously disclosed in the Annual Report on Form 10-K for the period ending December 31, 2021, and the subsequently filed Form 10-Qs, have been remediated as of December 31, 2022. There were no other changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2022, 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

Not applicable.

## **PART III**

### **Item 10. Directors, Executive Officers and Corporate Governance**

Information required by this Item 10 will be set forth in the “Proposal No. 1 – Election of Class II Directors” and “Corporate Governance” sections of our definitive proxy statement relating to our 2023 annual meeting of shareholders, or the Proxy Statement, which will be filed with the Securities and Exchange Commission within 120 days after the end of the year covered by this Annual Report.

### **Item 11. Executive Compensation**

Information required by this Item 11 will be set forth in the “Corporate Governance” section of the Proxy Statement, which will be filed with the Securities and Exchange Commission within 120 days after the end of the year covered by this Annual Report.

### **Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters**

Information required by this Item 12 will be set forth in the “Principal Stockholders” section of the Proxy Statement, which will be filed with the Securities and Exchange Commission within 120 days after the end of the year covered by this Annual Report.

### **Item 13. Certain Relationships and Related Transactions, and Director Independence**

Information required by this Item 13 will be set forth in the “Corporate Governance” and “Certain Relationships and Related Party Transactions” sections of the Proxy Statement, which will be filed with the Securities and Exchange Commission within 120 days after the end of the year covered by this Annual Report.

### **Item 14. Principal Accounting Fees and Services**

Our independent public accounting firm is Deloitte & Touche LLP, Boston, Massachusetts, PCAOB Auditor ID No. 34. Information required by this Item 14 will be set forth in our Proxy Statement, which will be filed with the Securities and Exchange Commission within 120 days after the end of the year covered by this Annual Report.

## 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	Fourth Amended and Restated Certificate of Incorporation of Registrant, as currently in effect (incorporated by reference to Exhibit 3.1 of the Registrant's Current Report on Form 8-K (File No. 001-40522) filed on June 28, 2021)
3.2	Amended and Restated By-laws of the Registrant, as currently in effect (incorporated by reference to Exhibit 3.2 of the Registrant's Current Report on Form 8-K (File No. 001-40522)) filed on June 28, 2021)
4.1	Form of Specimen Common Stock Certificate (incorporated by reference to Exhibit 4.2 of the Registrant's Registration Statement on Form S-1, as amended (File No. 333-256773) filed on June 28, 2021)
4.2	Description of the Registrant's Securities registered pursuant to Section 12 of the Securities Exchange Act of 1934, as amended (incorporated by reference to Exhibit 4.2 of the Registrant's Annual Report on Form 10-K filed March 29, 2022)
10.1#	2020 Stock Option and Grant Plan, as amended, and forms of award agreements thereunder (Incorporated by reference to Exhibit 10.1 to the registrant's Registration Statement on Form S-1, as amended (File No. 333-256773) filed on June 4, 2021)
10.2#	2021 Stock Option and Incentive Plan and forms of award agreements thereunder (incorporated by reference to Exhibit 99.2 of the Registrant's Registration Statement on Form S-8 (File No. 333-257406) filed on June 25, 2021)
10.3#	2021 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.3 of the Registrant's Registration Statement on Form S-1 (File No. 333-256773) filed on June 28, 2021)
10.4#	Senior Executive Cash Incentive Bonus Plan (Incorporated by reference to Exhibit 10.4 to the registrant's Registration Statement on Form S-1, as amended (File No. 333-256773) filed on June 4, 2021)
10.5#	Form of Officer Indemnification Agreement (Incorporated by reference to Exhibit 10.5 to the registrant's Registration Statement on Form S-1, as amended (File No. 333-256773) filed on June 4, 2021)
10.6#	Form of Director Indemnification Agreement (Incorporated by reference to Exhibit 10.6 to the registrant's Registration Statement on Form S-1, as amended (File No. 333-256773) filed on June 4, 2021)
10.7#	Employment Agreement between the Registrant and Markus Warmuth, effective as of June 28, 2021 (incorporated by reference to Exhibit 10.7 of the Registrant's Registration Statement on Form S-1, as amended (File No. 333-256773) filed on June 21, 2021)
10.8#	Employment Agreement between the Registrant and Ajim Tamboli, effective as of June 28, 2021 (incorporated by reference to Exhibit 10.8 of the Registrant's Registration Statement on Form S-1, as amended (File No. 333-256773) filed on June 21, 2021)
10.9#	Employment Agreement between the Registrant and Owen Wallace, effective as of June 28, 2021 (incorporated by reference to Exhibit 10.9 of the Registrant's Registration Statement on Form S-1, as amended (File No. 333-256773) filed on June 21, 2021)
10.10#	Employment Agreement between the Registrant and Filip Janku, effective as of June 28, 2021 (incorporated by reference to Exhibit 10.12 of the Registrant's Registration Statement on Form S-1, as amended (File No. 333-256773) filed on June 21, 2021)
10.11†	License Agreement, dated as of April 10, 2018, among Cancer Research Technology Limited, The Institute of Cancer Research: Royal Cancer Hospital and Monte Rosa Therapeutics AG

	(incorporated by reference to Exhibit 10.17 of the Registrant's Registration Statement on Form S-1, as amended (File No. 333-256773) filed on June 4, 2021)
10.12†	Collaboration and Option Agreement, among Cancer Research Technology Limited, The Institute of Cancer Research: Royal Cancer Hospital and Monte Rosa Therapeutics AG, as amended (incorporated by reference to Exhibit 10.18 of the Registrant's Registration Statement on Form S-1, as amended (File No. 333-256773) filed on June 4, 2021)
10.13	Lease Agreement, dated September 23, 2020, between OPG MP Parcel Owner (DE) LLC and the Company (incorporated by reference to Exhibit 10.19 of the Registrant's Registration Statement on Form S-1, as amended (File No. 333-256773) filed on June 4, 2021)
10.14	Lease Agreement between the Registrant and B9 LS Harrison & Washington LLC, dated December 14, 2021 (incorporated by reference by reference to Exhibit 10.20 of the Registrant's Annual Report on Form 10-K filed March 29, 2022)
10.15#	Employment Agreement between the Registrant and Jullian Jones, effective as of June 28, 2021, as amended by the First Amendment to Employment Agreement, effective as of December 1, 2021 (incorporated by reference by reference to Exhibit 10.21 of the Registrant's Annual Report on Form 10-K filed March 29, 2022)
10.16#	Amended and Restated Employment Agreement between the Registrant and Philip Nickson, effective as of March 1, 2022 (incorporated by reference to Exhibit 10.22 of the Registrant's Annual Report on Form 10-K filed March 29, 2022)
10.17	Agreement for Termination of Lease, by and between the Registrant and OPG MP Parcel Owner (DE) LLC, dated May 5, 2022 (incorporated by reference to Exhibit 10.2 of the Registrant's Quarterly Report on Form 10-Q filed on May 11, 2022)
21.1*	List of Subsidiaries of the Registrant
23.1*	Consent of Deloitte & Touche LLP, independent registered public accounting firm
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 and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
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 Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

\* Filed herewith.

\*\* Deemed to be furnished with this Annual Report on Form 10-K and will not be deemed to be “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, except to the extent that the registrant specifically incorporates it by reference.

# Management compensatory plan, contract, or arrangement

† Portions of this exhibit (indicated by asterisks) will be omitted in accordance with the rules of the SEC.

## Item 16. Form 10-K Summary

Not applicable.



## 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.

Company Name

Date: March 16, 2023

By: /s/ Markus Warmuth  
**Markus Warmuth**  
**President and Chief Executive Officer**

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

<u>Name</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Markus Warmuth</u> <b>Markus Warmuth, M.D.</b>	President, Chief Executive Officer and Director (Principal Executive Officer)	March 16, 2023
<u>/s/ Ajim Tamboli</u> <b>Ajim Tamboli, CFA.</b>	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	March 16, 2023
<u>/s/ Alexander Mayweg</u> <b>Alexander Mayweg</b>	Director	March 16, 2023
<u>/s/ Ali Behbahani</u> <b>Ali Behbahani</b>	Director	March 16, 2023
<u>/s/ Kimberly L. Blackwell</u> <b>Kimberly L. Blackwell</b>	Director	March 16, 2023
<u>/s/ Andrew Schiff</u> <b>Andrew Schiff</b>	Director	March 16, 2023
<u>/s/ Chandra P. Leo</u> <b>Chandra P. Leo</b>	Director	March 16, 2023
<u>/s/ Christine Siu</u> <b>Christine Siu</b>	Director	March 16, 2023

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## **Audited consolidated financial statements**

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## **REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

To the stockholders and the Board of Directors of Monte Rosa Therapeutics, Inc.

### **Opinion on the Financial Statements**

We have audited the accompanying consolidated balance sheets of Monte Rosa Therapeutics, Inc. and subsidiaries (the "Company") as of December 31, 2022 and 2021, the related consolidated statements of operations and comprehensive income (loss), convertible preferred stock and stockholders' equity (deficit), and cash flows, for each of the two years in the period ended December 31, 2022, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2022, in conformity with accounting principles generally accepted in the United States of America.

### **Change in Accounting Principle**

As discussed in Note 2 to the financial statements, effective January 1, 2022, the Company adopted FASB Accounting Standards Codification Topic 842, *Leases*, using the modified retrospective approach.

### **Basis for Opinion**

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's 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 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 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 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 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 financial statements. We believe that our audits provide a reasonable basis for our opinion.

*/s/ Deloitte & Touche LLP*

Boston, Massachusetts  
March 16, 2023

We have served as the Company's auditor since 2021.

# Monte Rosa Therapeutics, Inc.

## Consolidated balance sheets

(in thousands, except share and per share amounts)	December 31,	
	2022	2021
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 54,912	\$ 346,071
Marketable securities	207,914	—
Other receivables	7,656	—
Prepaid expenses and other current assets	4,444	2,595
Current restricted cash	960	—
Total current assets	275,886	348,666
Property and equipment, net	27,075	12,325
Operating lease right-of-use assets	34,832	—
Restricted cash, net of current	4,318	5,338
Other long-term assets	278	—
Total assets	\$ 342,389	\$ 366,329
<b>Liabilities and stockholders' equity</b>		
Current liabilities:		
Accounts payable	\$ 7,862	\$ 6,558
Accrued expenses and other current liabilities	14,580	10,080
Current portion of operating lease liability	3,127	—
Total current liabilities	25,569	16,638
Defined benefit plan liability	1,533	2,176
Operating lease liability	43,874	—
Total liabilities	70,976	18,814
<b>Commitments and contingencies</b>		
<b>Stockholders' equity</b>		
Preferred stock, \$0.0001 par value, 10,000,000 shares authorized, no shares issued and outstanding	—	—
Common stock, \$0.0001 par value; 500,000,000 shares authorized, 49,445,802 shares issued and 49,323,531 shares outstanding as of December 31, 2022; and 500,000,000 shares authorized, 46,794,295 shares issued and 46,535,966 shares outstanding as of December 31, 2021	5	5
Additional paid-in capital	503,696	471,566
Accumulated other comprehensive loss	(1,752)	(2,021)
Accumulated deficit	(230,536)	(122,035)
Total stockholders' equity	271,413	347,515
Total liabilities and stockholders' equity	\$ 342,389	\$ 366,329

See accompanying notes to the consolidated financial statements.

# Monte Rosa Therapeutics, Inc.

## Consolidated statements of operations and comprehensive income (loss)

(in thousands, except share and per share amounts)	Year ended December 31,	
	2022	2021
Operating expenses:		
Research and development	\$ 85,061	\$ 57,155
General and administrative	27,323	15,727
Total operating expenses	112,384	72,882
Loss from operations	(112,384)	(72,882)
Other income (expense):		
Interest income, net	3,764	46
Foreign currency exchange gain (loss), net	10	(162)
Gain on disposal of fixed assets	109	—
Changes in fair value of preferred stock tranche obligations, net	—	(960)
Total other income (expense)	3,883	(1,076)
Net loss	\$ (108,501)	\$ (73,958)
Net loss per share attributable to common stockholders—basic and diluted	\$ (2.30)	\$ (2.96)
Weighted-average number of shares outstanding used in computing net loss per common share—basic and diluted	47,227,370	25,000,124
Comprehensive loss:		
Net loss	\$ (108,501)	\$ (73,958)
Other comprehensive gain (loss):		
Provision for pension benefit obligation	718	(965)
Unrealized loss on available-for-sale securities	(449)	—
Comprehensive loss	\$ (108,232)	\$ (74,923)

See accompanying notes to the consolidated financial statements.

# Monte Rosa Therapeutics, Inc.

## Consolidated statements of convertible preferred stock and stockholders' equity (deficit)

	Convertible preferred stock			Common stock			Additional paid-in capital	Accumulated other comprehensive loss	Accumulated deficit	Total stockholders' equity (deficit)
	Shares	Amount	Shares	Amount	1	\$	404	\$	(48,077)	\$
(in thousands, except share amounts)										
Balance—January 1, 2021	53,631,514	\$ 67,764	1,685,534	\$ —	—	—	—	—	—	(48,728)
Issuance of Series B convertible preferred stock, net of issuance costs of \$68	24,000,000	68,571	—	—	—	—	—	—	—	—
Issuance of Series C convertible preferred stock, net of issuance costs of \$163	32,054,521	94,837	—	—	—	—	—	—	—	—
Conversion of convertible preferred stock into common stock	(109,686,035)	(231,172)	31,068,102	3	231,170	—	—	—	—	231,173
Issuance of common stock in connection with initial public offering, net of issuance costs of \$21,001	—	—	13,455,000	1	234,644	—	—	—	—	234,645
Restricted common stock vesting	—	—	236,949	—	—	—	—	—	—	—
Exercise of common stock options	—	—	90,381	—	148	—	—	—	—	148
Stock-based compensation expense	—	—	—	—	5,200	—	—	—	—	5,200
Provision for pension benefit obligation	—	—	—	—	—	—	—	(965)	—	(965)
Net Loss	—	—	—	—	—	—	—	(73,958)	—	(73,958)
Balance—December 31, 2021	—	\$ —	46,535,966	\$ —	5	\$ 471,566	\$ (2,021)	\$ (122,035)	\$ —	347,515
Restricted common stock vesting	—	—	136,058	—	—	—	—	—	—	—
Exercise of common stock options	—	—	117,552	—	439	—	—	—	—	439
Stock-based compensation expense	—	—	—	—	11,664	—	—	—	—	11,664
Provision for pension benefit obligation	—	—	—	—	—	—	—	718	—	718
Issuance of common stock, net of issuance costs of \$984	—	—	2,482,008	—	19,691	—	—	—	—	19,691
Unrealized loss on available-for-sale securities	—	—	—	—	—	—	—	(449)	—	(449)
Issuance of shares under employee stock purchase plan	—	—	51,947	—	336	—	—	—	—	336
Net Loss	—	—	—	—	—	—	—	—	(108,501)	(108,501)
Balance—December 31, 2022	—	\$ —	49,323,531	\$ —	5	\$ 503,696	\$ (1,752)	\$ (230,536)	\$ —	271,413

See accompanying notes to the consolidated financial statements.



# Monte Rosa Therapeutics, Inc.

## Consolidated statements of cash flows

(in thousands)	Year ended December 31,	
	2022	2021
Cash flows from operating activities:		
Net loss	\$ (108,501)	\$ (73,958)
Adjustments to reconcile net loss to net cash used in operating activities		
Stock-based compensation expense	11,664	5,200
Depreciation	3,745	2,132
Noncash lease expense	4,814	—
Net accretion of discounts/premiums on marketable securities	(1,945)	—
Changes in fair value of preferred stock tranche obligations	—	960
(Gain) loss on disposal of property and equipment	(109)	17
Changes in operating assets and liabilities		
Other receivables	(187)	—
Prepaid expenses and other current assets	(2,127)	(704)
Accounts payable	(744)	(706)
Accrued expenses and other current liabilities	1,031	6,587
Defined benefit plan liability	74	1,109
Right-of-use assets and operating lease liabilities	(181)	—
Net cash used in operating activities	\$ (92,466)	\$ (59,363)
Cash flows from investing activities:		
Purchases of property and equipment	(12,911)	(9,732)
Proceeds from sale of property and equipment	109	79
Purchases of marketable securities	(384,417)	—
Proceeds from maturities of marketable securities	178,000	—
Net cash used in investing activities	\$ (219,219)	\$ (9,653)
Cash flows from financing activities:		
Proceeds from issuance of convertible preferred stock	—	143,000
Payment of convertible preferred stock issuance costs	—	(231)
Proceeds from initial public offering, net of underwriting discount of \$17,895	—	237,750
Issuance of common stock, net of underwriting discount of \$620	20,055	—
Payment of initial public offering issuance costs	—	(3,106)
Payment of common stock issuance costs	(364)	—
Proceeds from exercise of employee stock options	439	149
Proceeds from employee stock purchase plan	336	—
Net cash provided by financing activities	\$ 20,466	\$ 377,562
Net (decrease) increase in cash, cash equivalents and restricted cash	\$ (291,219)	\$ 308,546
Cash, cash equivalents and restricted cash—beginning of period	351,409	42,863
Cash, cash equivalents and restricted cash—end of period	\$ 60,190	\$ 351,409
Reconciliation of cash, cash equivalents and restricted cash		
Cash and cash equivalents	\$ 54,912	\$ 346,071
Restricted cash	5,278	5,338
Total cash, cash equivalents and restricted cash	\$ 60,190	\$ 351,409
Supplemental disclosure of noncash items		
Conversion of convertible preferred stock into common stock	\$ —	\$ 231,172
Settlement of preferred stock tranche obligation	\$ —	\$ 20,640
Reduction of right-of-use assets for lease incentives receivable	\$ 7,469	\$ —
Purchases of property and equipment in accounts payable and accrued expenses	\$ 6,240	\$ 656

See accompanying notes to the consolidated financial statements.

# Monte Rosa Therapeutics, Inc.

## Notes to the consolidated financial statements

### 1. Description of business and liquidity

#### ***Business***

Monte Rosa Therapeutics, Inc. is a biotechnology company developing a portfolio of novel small molecule precision medicines that employ the body's natural mechanisms to selectively degrade therapeutically-relevant proteins. As used in these consolidated financial statements, unless the context otherwise requires, references to the Company or Monte Rosa refer to Monte Rosa Therapeutics, Inc. and its wholly owned subsidiaries Monte Rosa Therapeutics AG and Monte Rosa Therapeutics Securities Corp. Monte Rosa Therapeutics AG, a Swiss operating company, was incorporated under the laws of Switzerland in April 2018. Monte Rosa Therapeutics, Inc. was incorporated in Delaware in November 2019. The Company is headquartered in Boston, Massachusetts with research operations in both Boston and Basel, Switzerland.

#### ***Risks and uncertainties***

The Company is subject to risks common to companies in the biotechnology industry including, but not limited to, the successful discovery and development of its product candidates, new technological innovations, protection of proprietary technology, dependence on key personnel, compliance with government regulations and the need to obtain additional financing.

#### ***Liquidity considerations***

Since inception, the Company has devoted substantially all its efforts to business planning, research and development, recruiting management and technical staff, and raising capital and has financed its operations primarily through the issuance of convertible preferred shares and public offerings of the Company's common stock.

The Company's continued discovery and development of its product candidates will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities. Even if product development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

As of December 31, 2022, the Company had an accumulated deficit of \$230.5 million. The Company has incurred losses and negative cash flows from operations since inception, including net losses of \$108.5 million and \$74.0 million for the years ended December 31, 2022, and 2021, respectively. The Company expects that its operating losses and negative cash flows will continue for the foreseeable future as the Company continues to develop its product candidates. The Company currently expects that its cash, cash equivalents and marketable securities of \$262.8 million as of December 31, 2022, will be sufficient to fund operating expenses and capital requirements for at least 12 months from the date the consolidated financial statements are issued. However, additional funding will be necessary to fund future discovery research, pre-clinical and clinical activities. The Company will seek additional funding through public financings, debt financings, collaboration agreements, strategic alliances and licensing arrangements. Although it has been successful in raising capital in the past, there is no assurance that the Company will be successful in obtaining such additional financing on terms acceptable to it, if at all, and the Company may not be able to enter into collaborations or other arrangements. If the Company is unable to obtain funding, it could be forced to delay, reduce or eliminate its research and development programs, product portfolio expansion or commercialization efforts, which could adversely affect the Company's business prospects, even the ability to continue operations.

### 2. Summary of significant accounting policies

#### ***Basis of presentation***

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America, or GAAP, and are stated in U.S. dollars. Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification and Accounting Standards Updates, or ASUs, of the Financial Accounting Standards Board, or FASB. All intercompany balances and transactions have been eliminated in combination or consolidation.

### ***Use of estimates***

The preparation of the consolidated financial statements in conformity with GAAP requires the Company to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosures of contingent assets and liabilities at the date of the financial statements and reported amounts of expenses during the reporting periods. Actual results could differ from those estimates. On an ongoing basis, the Company evaluates its estimates, including those related to accrued research and development expenses, other long-lived assets, pension benefit obligation, stock-based compensation and the valuation of deferred tax assets. The Company bases its estimates using historical experience, Company forecasts and future plans, current economic conditions, and information from third-party professionals that management believes to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities and recorded amounts of expenses that are not readily apparent from other sources and adjusts those estimates and assumptions when facts and circumstances dictate.

### ***Currency and currency translation***

The consolidated financial statements are presented in U.S. dollars, the Company's reporting currency. The functional currency of the Company's wholly owned subsidiary, Monte Rosa Therapeutics AG, is the U.S. dollar. Adjustments that arise from exchange rate changes on transactions denominated in a currency other than the functional currency are included in foreign currency exchange gain (loss), net in the consolidated statements of operations.

### ***Cash, cash equivalents and restricted cash***

The Company considers all highly liquid investments with original maturities at the date of purchase of three months or less to be cash equivalents. Cash and cash equivalents are stated at fair value and may include money market funds, U.S. Treasury and U.S. government-sponsored agency securities, corporate debt, commercial paper and certificates of deposit. The Company's cash equivalents at December 31, 2022 and 2021 consist of bank demand deposits and money market fund investments.

The Company had restricted cash of \$5.3 million as of December 31, 2022, and 2021, primarily related to security deposits on its leases for offices in Boston, Massachusetts and Basel, Switzerland.

### ***Marketable securities***

Investments in marketable securities are classified as available-for-sale. Available-for-sale securities are measured and reported at fair value using quoted prices in active markets for similar securities. Unrealized gains and losses on available-for-sale securities are reported as a separate component of stockholders' equity. Premiums or discounts from par value are amortized to investment income over the life of the underlying investment. All of the Company's available-for-sale securities are available to the Company for use in current operations. As a result, the Company classified all of these securities as current assets even though the stated maturity of some individual securities may be one year or more beyond the balance sheet date.

The cost of securities sold is determined on a specific identification basis, and realized gains and losses are included in other income (expense) within the consolidated statements of operations and comprehensive loss. If any adjustment is required to reflect a decline in the value of the investment that the Company considers to be "other than temporary", the Company recognizes a charge to the consolidated statement of operations and comprehensive loss. No such adjustments were necessary during the periods presented.

### ***Concentrations of credit risk and off-balance sheet risk***

Financial instruments that potentially subject the Company to a concentration of credit risk consist primarily of cash and cash equivalents. The Company has invested in cash and cash equivalents at December 31, 2022 and 2021, held in a financial institution that management believes is creditworthy. These deposits may exceed federally insured limits. The Company has not experienced any losses historically in these accounts and believes it is not exposed to significant credit risk in its cash and cash equivalents. The Company has no significant off-balance sheet concentrations of credit risk, such as foreign currency exchange contracts, option contracts, or other hedging arrangements.

### ***Fair value of financial instruments***

Assets and liabilities recorded at fair value on a recurring basis in the balance sheets are categorized based upon the level of judgment associated with the inputs used to measure their fair values. Fair value is defined as the exchange price that would be received for an asset or an exit price that would be paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market

participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

Level 1—Observable inputs such as unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date.

Level 2—Inputs (other than quoted prices included in Level 1) that are either directly or indirectly observable for the asset or liability. These include quoted prices for similar assets or liabilities in active markets and quoted prices for identical or similar assets or liabilities in markets that are not active.

Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

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 instrument.

### ***Property and equipment***

Property and equipment are stated at cost, subject to adjustments for impairments, less accumulated depreciation. Purchased assets that are not yet in service are classified as construction-in-process and no depreciation expense is recorded. Depreciation is calculated using the straight-line method over the estimated useful life of the asset as follows:

<b>Asset</b>	<b>Estimated useful life</b>
Laboratory equipment	Five years
Computer hardware	Three years
Furniture and fixtures	Five Years
Leasehold Improvements	Shorter of useful life or remaining lease term

Maintenance and repairs that do not improve or extend the life of the respective asset are expensed as incurred. Upon disposal of an asset, the related cost and accumulated depreciation are removed from the accounts and any resulting gain or loss is included in the results of operations. Leasehold improvements are amortized over the shorter of the useful life or remaining term of the lease.

### ***Impairment of long-lived assets***

The Company evaluates whether current facts or circumstances indicate that the carrying values of its long-lived assets may not be recoverable. If such facts or circumstances are determined to exist, an estimate of the undiscounted future cash flows of these assets is compared to the carrying value the assets to determine whether impairment exists. If the assets are determined to be impaired, the loss is measured based on the difference between the fair value and carrying value of the assets. No material impairment losses were recorded during the periods presented.

### ***Research and development expenses***

Research and development costs are expensed as incurred. The Company's research and development expenses consist primarily of costs incurred for the research and development of its product candidates and include expenses incurred under agreements with consultants to conduct preclinical and clinical studies, costs to acquire supplies for preclinical and clinical studies, salaries and related personnel costs, including stock-based compensation, depreciation and other allocated facility-related and overhead expenses.

### ***Accrued research and development costs***

The Company records accruals for estimated costs of discovery research activities, preclinical, and clinical studies. A portion of the Company's research and development activities are conducted by third-party service providers. The financial terms of these contracts are subject to negotiation, which vary by contract and may result in payments that do not match the periods over which materials or services are provided. The Company accrues the costs incurred under the agreements based on an estimate of actual work completed in accordance with the agreements. In the event the Company makes advance payments for goods or services that will be used or rendered for future research and development activities, the payments are deferred and capitalized as a prepaid

expense and recognized as expense as the goods are received or the related services are rendered. Such payments are evaluated for current or long-term classification based on when they are expected to be realized. If the Company does not identify costs that have begun to be incurred or if the Company underestimates or overestimates the level of services performed or the costs of these services, actual expenses could differ from the Company's estimates.

### ***Preferred stock tranche obligations***

Included in the terms of the Series A and Series B Preferred Stock Purchase Agreements were certain rights, or Tranche Rights, granted to the investors who purchased the Series A and Series B Preferred. The Series A Tranche Rights gave the investor the option to purchase up to an aggregate of 15,000,000 additional shares of Series A Preferred at \$1.00 per share. The Series B Tranche Rights gave investors the option to purchase up to an aggregate of 24,000,000 shares of Series B Preferred at \$2.00 per share. The Company concluded that both the Series A and the Series B Tranche Rights met the definition of a freestanding financial instrument, as the Series A and Series B Tranche Rights were legally detachable and separately exercisable from the Series A and Series B Preferred. At initial recognition, the Company recorded these Series A and Series B Tranche Rights as a liability on the balance sheets at its estimated fair value. The Series A and Series B Preferred Stock Tranche Obligations are subject to remeasurement at each balance sheet date, with changes in fair value recognized in changes in fair value of Preferred Stock Tranche Obligations on the Company's consolidated statements of operations and comprehensive loss. Immediately prior to consummation of our IPO in June 2021, all outstanding shares of the Company's Series A, Series A-2, Series B and Series C convertible preferred stock were converted into 31,068,102 shares of common stock. As such, there was no value recorded for preferred stock tranche obligations on the consolidated balance sheets as of December 31, 2022 and 2021.

### ***Stock-based compensation***

Stock-based compensation expense related to stock options granted to employees, directors and non-employees is recognized based on the grant-date estimated fair values of the awards using the Black-Scholes option pricing model, or Black-Scholes. Stock-based compensation expense related to stock options and other stock based awards granted to employees and non-employees is recognized based on the grant-date fair value of the Company's common stock. The value is recognized as expense ratably over the requisite service period, which is generally the vesting term of the award. For stock options with performance-based vesting conditions, the Company records the expense for these awards based upon the fair value of the awards on the date of grant and the number of shares expected to vest based on the terms of the underlying award agreement and the requisite service periods. The Company adjusts the expense for actual forfeitures as they occur. Stock-based compensation expense is classified in the accompanying consolidated statements of operations based on the function to which the related services are provided.

### ***Income taxes***

The Company uses the liability method to account for income taxes. Under this method, deferred tax assets and liabilities are determined based on differences between the financial statement carrying amounts of existing assets and liabilities and their tax bases. Deferred tax assets and liabilities are measured using enacted tax rates applied to taxable income in the years in which those temporary differences are expected to be recovered or settled. A valuation allowance is established when necessary to reduce deferred tax assets to the amount expected to be realized.

The Company assesses the likelihood of deferred tax assets being realized. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized. In assessing the realizability of deferred tax assets, the Company considers whether it is more likely than not that some portion or all of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which the temporary differences representing net future deductible amounts become deductible.

The Company files U.S. federal and state income tax returns, as well as Swiss income tax returns. The Company's tax positions are subject to audit. Financial statement effects of uncertain tax positions are recognized when it is more likely than not, based on the technical merits of the position, that it will be sustained upon examination. The Company evaluates uncertain tax positions on a regular basis. The evaluations are based on a number of factors, including changes in facts and circumstances, changes in tax law, correspondence with tax authorities during the course of the audit, and effective settlement of audit issues. Interest and penalties related to unrecognized tax benefits are included within the provision for income tax. To date, the Company has not been subject to any interest and penalties.



### **Defined pension benefit obligation**

The Company maintains a mandatory pension for its employees in Switzerland through affiliation with the Swiss Life Collective BVG Foundation. All benefits in accordance with the regulations are reinsured in their entirety with Swiss Life Ltd within the framework of the corresponding contract. This plan is considered to be a defined benefit plan under GAAP.

The Company recognizes an asset for the plan's overfunded status or a liability for the plan's underfunded status in its consolidated balance sheets. Additionally, the Company measures the plan's assets and obligations that determine its funded status as of the end of the year and recognizes the change in the funded status within the consolidated statements of operations and comprehensive loss.

The Company uses an actuarial valuation to determine its pension benefit costs and credits. The amounts calculated depend on a variety of key assumptions, including discount rates and expected return on plan assets. Details of the assumptions used to determine the net funded status are described in Note 12. The Company's pension plan assets are assigned to their respective levels in the fair value hierarchy in accordance with the valuation principles described in the Fair Value of Financial Instruments section above.

### **Segments**

Operating segments are defined as components of an entity for which separate financial information is available and that is regularly reviewed by the chief operating decision maker, or CODM, in deciding how to allocate resources to an individual segment and in assessing performance. The Company's CODM is its chief executive officer. The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions.

### **Comprehensive income (loss)**

Comprehensive income (loss) is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. The Company's other comprehensive income (loss) includes adjustments to unrecognized pension benefit costs for Monte Rosa Therapeutics AG and changes in unrealized gains and losses from available-for-sale investments. The Company reported other comprehensive income of \$0.3 million and incurred other comprehensive loss of \$1.0 million, for the years ended December 31, 2022 and 2021, respectively.

### **Recently issued accounting pronouncements**

The Company has elected to use the extended transition period for complying with new or revised accounting standards as available under the Jumpstart Our Business Startups Act (JOBS Act).

In June 2016, the FASB issued Accounting Standards Update No. 2016-13, *Financial Instruments-Credit Losses: Measurement of Credit Losses on Financial Instruments*. ASU 2016-13 requires measurement and recognition of expected credit losses for financial assets. In April 2019, the FASB issued clarification to ASU 2016-13 within ASU 2019-04, *Codification Improvements to Topic 326, Financial Instruments-Credit Losses, Topic 815, Derivatives and Hedging, and Topic 825, Financial Instruments*, or ASU 2016-13. The guidance is effective for fiscal years beginning after December 15, 2022. The Company does not expect for ASU 2016-13 to have a material impact on its financial statements.

In August 2020, the FASB issued ASU No. 2020-06, *Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity*. ASU 2020-06 will simplify the accounting for convertible instruments by reducing the number of accounting models for convertible debt instruments and convertible preferred stock. Limiting the accounting models results in fewer embedded conversion features being separately recognized from the host contract as compared with current GAAP. Convertible instruments that continue to be subject to separation models are (i) those with embedded conversion features that are not clearly and closely related to the host contract, that meet the definition of a derivative, and that do not qualify for a scope exception from derivative accounting and (ii) convertible debt instruments issued with substantial premiums for which the premiums are recorded as paid-in capital. ASU 2020-06 also amends the guidance for the derivatives scope exception for contracts in an entity's own equity to reduce form-over-substance-based accounting conclusions. ASU 2020-06 will be effective for the Company beginning after December 15, 2023. Early adoption is permitted, but no earlier than fiscal years beginning after December 15, 2020, including interim periods within those fiscal years. The Company is currently assessing the impact adoption of ASU 2020-06 will have on the financial statements and disclosures.

### Recently adopted accounting pronouncements

On January 1, 2022, the Company adopted Accounting Standard Update or ASU No. 2016-02, *Leases (Topic 842)*, and its associated amendments using the modified retrospective transition approach by applying the new standard to all leases existing at the date of initial application and not restating comparative periods. There was no cumulative-effect adjustment recorded to retained earnings upon adoption. Under Topic 842, a lessee is required to recognize a lease liability and right-of-use (ROU) asset for all leases, unless the lease qualifies for the short-term lease exception. The new guidance also modified the classification criteria and requires additional disclosures to enable users of financial statements to understand the amount, timing, and uncertainty of cash flows arising from leases. Consistent with current guidance, a lessee's recognition, measurement, and presentation of expenses and cash flows arising from a lease continues to depend primarily on its classification. The Company elected the package of practical expedients permitted under the transition guidance, which allowed the Company to carryforward its historical lease classification, its assessment on whether a contract was or contains a lease, and its initial direct costs for any leases that existed prior to January 1, 2022. In addition, the Company elected the following transitional practical expedients: (1) the short-term lease exception and (2) to not separate its non-lease components for its real estate, vehicle and equipment leases. Upon the adoption of this standard, the Company recorded operating lease right-of-use assets of \$7.3 million and corresponding operating lease liabilities of \$7.4 million as of January 1, 2022. The difference between the value of the right-of-use assets and lease liabilities is due to the reclassification of existing deferred rent as of January 1, 2022.

In December 2019, the FASB issued ASU 2019-12, *Simplifying the Accounting for Income Taxes*, or ASU 2019-12. ASU 2019-12 eliminates certain exceptions related to the approach for intra-period tax allocation, the methodology for calculating income taxes in an interim period and the recognition of deferred tax liabilities for outside basis differences. It also clarifies and simplifies other aspects of the accounting for income taxes. This guidance is effective for fiscal years beginning after December 15, 2021, and interim periods within fiscal years beginning after December 15, 2022. The Company adopted ASU 2019-12 on January 1, 2022. The adoption of the standard was immaterial to the accompanying consolidated financial statements.

### 3. Fair value measurements

The following tables present information about the Company's financial assets and liabilities measured at fair value on a recurring basis and indicate the level of the fair value hierarchy utilized to determine such fair values (in thousands):

	As of December 31, 2022			
	Level 1	Level 2	Level 3	Total
<b>Current assets</b>				
Money market funds	\$ 50,633	\$ —	\$ —	\$ 50,633
Pension plan assets	—	5,320	—	5,320
Corporate debt securities	—	127,351	—	127,351
U.S. Treasury securities	—	80,563	—	80,563
Total assets measured at fair value	\$ 50,633	\$ 213,234	\$ —	\$ 263,867

	As of December 31, 2021			
	Level 1	Level 2	Level 3	Total
<b>Current assets</b>				
Money market funds	\$ 317,004	\$ —	\$ —	\$ 317,004
Pension plan assets	—	3,796	—	3,796
Total assets measured at fair value	\$ 317,004	\$ 3,796	\$ —	\$ 320,800

Money market funds are highly liquid investments and are actively traded. The pricing information on the Company's money market funds are based on quoted prices in active markets for identical securities. This approach results in the classification of these securities as Level 1 of the fair value hierarchy.

The fair value of pension plan assets has been determined as the surrender value of the portfolio of active insured members held within the Swiss Life Collective BVG Foundation collective investment fund and are classified within Level 2 of the fair value hierarchy.

Marketable securities consist of corporate debt securities and U.S. Treasury securities which are classified as available-for-sale pursuant to ASC 320, Investments—Debt and Equity Securities. Marketable securities are classified within Level 2 of the fair value hierarchy because pricing inputs are other than quoted prices in active

markets. The fair values of these investments are estimated by taking into consideration valuations obtained from third-party pricing services. The pricing services utilize industry standard valuation models, including both income- and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include reported trades of and broker/dealer quotes on the same or similar securities, issuer credit spreads, benchmark securities based on historical data and other observable inputs.

There were no transfers among Level 1, Level 2 or Level 3 categories in the years ended December 31, 2022 or 2021.

#### 4. Marketable securities

Marketable securities as of December 31, 2022, consisted of the following (in thousands):

Description	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Corporate debt securities	\$ 127,565	\$ 27	\$ (241)	\$ 127,351
U.S Treasury securities	80,798	2	(237)	80,563
Total	\$ 208,363	\$ 29	\$ (478)	\$ 207,914

As of December 31, 2022, the Company held 40 marketable securities, 31 of which were in an unrealized loss position. The aggregate fair value of securities in a loss position is \$164.9 million. There were no individual securities that were in a significant unrealized loss position as of December 31, 2022. The Company evaluates securities for other-than-temporary impairments based on quantitative and qualitative factors, and considers the decline in market value as of December 31, 2022, to be primarily attributable to the then current economic and market conditions. The Company neither intends to sell these investments nor concludes that it is more-likely-than-not that the Company will have to sell them before recovery of their carrying values. The Company also believes that it will be able to collect both principal and interest amounts due to it at maturity.

#### 5. Property and equipment, net

Property and equipment, net, consist of the following (in thousands):

	December 31,	
	2022	2021
Laboratory equipment	\$ 17,766	\$ 12,315
Computer hardware and software	499	299
Furniture and fixtures	388	443
Leasehold improvements	2,660	1,119
Construction in process	12,013	852
Total property and equipment, at cost	\$ 33,326	\$ 15,028
Less: accumulated depreciation	(6,251)	(2,703)
Property and equipment, net	\$ 27,075	\$ 12,325

Depreciation expense for the years ended December 31, 2022, and 2021 was \$3.7 million and \$2.1 million, respectively.

#### 6. Accrued expenses and other current liabilities

Accrued expenses and other current liabilities consist of the following (in thousands):

	December 31,	
	2022	2021
Compensation and benefits	\$ 5,624	\$ 4,303
Accrued research and development	3,936	4,937
Other	5,020	840
Total other current liabilities	\$ 14,580	\$ 10,080

## 7. Leases

The Company determines if an arrangement is a lease at inception. Operating leases are included in operating lease right-of-use or ROU assets and operating lease liabilities in the consolidated balance sheets. The Company has no finance leases as of December 31, 2022.

ROU assets represent the right to use an underlying asset for the lease term and lease liabilities represent the obligation to make lease payments arising from the lease. Operating lease ROU assets and liabilities are recognized at commencement date based on the present value of lease payments over the lease term. As the Company's leases do not provide an implicit rate, management estimated the incremental borrowing rate based on the rate of interest the Company would have to pay to borrow a similar amount on a collateralized basis over a similar term. The Company uses its incremental borrowing rate based on the information available at commencement date in determining the present value of lease payments.

### *Summer Street Lease*

In September 2020, the Company entered into an operating lease agreement to lease 16,748 square feet of office and laboratory space at 645 Summer Street, Boston, Massachusetts or the Summer Street Lease with OPG MP Parcel Owner (DE) LLC or the Landlord. The original term of the Summer Street Lease expires in March 2026. On May 5, 2022, the Company entered into an Agreement for Termination of Lease with the Landlord which, subject to the Landlord executing a lease with a new tenant, provides the Company with the option to terminate the existing Summer Street Lease. On August 8, 2022, the termination condition was met. As a result, the operating lease ROU asset and operating lease liability were reduced by \$3.7 million to \$1.3 million and \$1.4 million, respectively, and the \$1.0 million security deposit associated with the lease was reclassified from long-term restricted cash to current restricted cash on the consolidated balance sheet. The Summer Street lease will terminate on June 1, 2023.

### *Klybeck Lease*

In March 2021, the Company entered into an operating lease agreement for office and lab space that occupies approximately 21,422 square feet located at Hochbergerstrasse 60C, 4057 Basel, Basel-City, Switzerland. The current term of the lease expires in March 2026.

### *Harrison Avenue Lease*

In December 2021, the Company entered into a non-cancelable lease agreement for 63,327 square feet of office and laboratory space to support its expanding operations or the Harrison Avenue Lease. The term of the lease commenced on April 1, 2022 and the Company's obligation to pay rent began on December 21, 2022. The initial term of the lease is 128 months following the commencement date at which point the Company has the option to extend the lease an additional 5 years. As of the lease commencement date, the Company has determined that it is not reasonably certain to exercise the option to extend the lease and has not included the extension period in the lease term. The annual base rent under the Harrison Avenue Lease is \$95.00 per square foot for the first year, which is subject to scheduled annual increases of 3%, plus certain costs, operating expenses and property management fees.

Pursuant to the terms of the Harrison Avenue Lease, the landlord will reimburse the Company for \$13 million of tenant improvements. The Company will reduce the ROU asset and record an asset for construction in progress as costs are incurred and reimbursed. These costs will be reclassified from construction in progress to leasehold improvements upon completion of the project. As of December 31, 2022, the Company had \$7.5 million receivable in reimbursable tenant improvements which is recorded as an other receivable on the consolidated balance sheet.

The components of lease expense for the year ended December 31, 2022, are as follows (in thousands):

	Year ended December 31, 2022
Operating lease expense	\$ 6,924
Variable lease expense	1,898
Total lease expense	\$ 8,822

The variable lease expenses generally include common area maintenance and property taxes. Of the total lease expense, \$7.8 million was recorded within research and development expenses and \$1.0 million was recorded

within general and administrative expenses in the consolidated statements of operations and comprehensive income (loss). There were no short-term lease costs in the year ended December 31, 2022.

The weighted average remaining lease term and discount rate related to the Company's leases are as follows:

	December 31, 2022
Weighted average remaining lease term (years)	9.7
Weighted average discount rate	9.9%

Supplemental cash flow information relating to the Company's leases for the year ended December 31, 2022 are as follows (in thousands):

	Year ended December 31, 2022
Right-of-use assets obtained in exchange for operating lease obligations	\$ 48,488
Cash paid for amounts included in the measurement of lease liabilities	\$ 1,654

The amortization of the ROU assets for the year ended December 31, 2022 was \$3.3 million.

Future undiscounted lease payments under non-cancelable leases as of December 31, 2022 for each of the years ending December 31 are as follows (in thousands):

Undiscounted lease payments	
2023	\$ 7,562
2024	6,982
2025	7,182
2026	7,053
2027	7,151
Thereafter	38,414
Total undiscounted lease payments	74,344
Less: Imputed interest	(27,343)
Total operating lease liability	\$ 47,001

Prior to January 1, 2022, the Company accounted for its leases in accordance with ASC Topic 840, *Leases*. As of December 31, 2021, the Company was committed under operating leases for its laboratory spaces and corporate offices. The future minimum lease payments under non-cancelable operating leases as of December 31, 2021 were as follows (in thousands):

2022	\$ 3,160
2023	8,353
2024	8,583
2025	8,820
2026	7,298
Thereafter	44,784
Total future minimum lease payments	\$ 80,998

## 8. Commitments and contingencies

### *License, collaboration and investment agreements*

In April 2018, the Company entered into license, collaboration and investment agreements with Cancer Research Technology Limited, or CRT, and The Institute of Cancer Research, or the ICR, for the purpose of development in the field of cereblon-mediated protein degradation, to support the Company's early product development activities as the Company built its internal capabilities (the "License and Collaboration"). Pursuant to the License and Collaboration, CRT and the ICR granted the Company exclusive and non-exclusive, worldwide, and sublicensable licenses under CRT's and the ICR's intellectual property rights in the field of cereblon mediated protein degradation to discover, research, develop, have developed, use, keep, make, have made, market, import, offer for sale, and sell products in the field of cereblon-mediated protein degradation.

In consideration for the rights granted under the License Agreement, the Company issued an aggregate of 1,132,984 common shares to CRT, the ICR and affiliated founding scientists pursuant to the Formation and Investment Agreement and paid CRT a technology access fee. The License Agreement will remain effective until terminated by written agreement between the Company, CRT and the ICR.



Upon execution of the License and Collaboration, the Company paid an immaterial access fee which was expensed to research and development in 2018. The research program conducted with the ICR with respect to cereblon-mediated protein degradation was completed as of December 31, 2020. However, the License and Collaboration Agreement continues until it is otherwise terminated under the terms and conditions stated within the agreement. There was no activity under this agreement for the year ended December 31, 2022.

Under the License and Collaboration, the Company may be obligated to make certain milestone payments for achieving specific clinical progression events for certain products, solely to the extent such products are subject to the License and Collaboration. If owed, such milestones would aggregate up to \$7 million for any covered first product candidate and \$3.5 million for any covered subsequent product candidate. In addition, the Company may be obligated to pay low single-digit royalties on net sales for any covered product successfully developed and commercialized in the field of cereblon-mediated protein degradation under the terms of the License and Collaboration on a country by country basis until the later of (i) the date when the manufacture, use, offer for sale, sale or importation of such product is no longer covered by a valid claim in the country of sale, use or manufacture; (ii) ten years from the first commercial sale of such product in the relevant country; and (iii) the expiry of any extended exclusivity period granted with respect to an orphan drug designation, pediatric designation or other exclusivity in the relevant country.

The License and Collaboration will remain effective until (i) the termination by either the Company or the ICR and CRT upon the bankruptcy or uncured breach of the other party, (ii) by the ICR and CRT if the Company should abandon all discovery, development and commercialization efforts for all products covered under the License and Collaboration; (iii) by the Company if it is determined the continued development of products covered under the License and Collaboration would be commercially unreasonable, scientifically unviable, illegal, unethical or impossible, with a 90-day notification period; or (iv) for any/no reason by written agreement of the Company and the ICR and CRT.

### ***Indemnification***

The Company, as permitted under Delaware law and in accordance with its certification of incorporation and bylaws and pursuant to indemnification agreements with certain of its officers and directors, indemnifies its officers and directors for certain events or occurrences, subject to certain limits, which the officer or director is or was serving at the Company's request in such capacity.

The Company enters into certain types of contracts that contingently require the Company to indemnify various parties against claims from third parties. These contracts primarily relate to (i) the Company's bylaws, under which the Company must indemnify directors and executive officers, and may indemnify other officers and employees, for liabilities arising out of their relationship, (ii) contracts under which the Company must indemnify directors and certain officers and consultants for liabilities arising out of their relationship, and (iii) procurement, service or license agreements under which the Company may be required to indemnify vendors, service providers or licensees for certain claims, including claims that may be brought against them arising from the Company's acts or omissions with respect to the Company's products, technology, intellectual property or services.

From time to time, the Company may receive indemnification claims under these contracts in the normal course of business. In the event that one or more of these matters were to result in a claim against the Company, an adverse outcome, including a judgment or settlement, may cause a material adverse effect on the Company's future business, operating results or financial condition. As of December 31, 2022 and 2021, the Company was not aware of any claims under indemnification arrangements and does not expect significant claims related to these indemnification obligations and, consequently, concluded that the fair value of these obligations is negligible. Therefore, no related reserves have been established.

## **9. Equity**

### ***Undesignated Preferred Stock***

The Company had 10,000,000 shares authorized of undesignated preferred stock, par value of \$0.0001, of which no shares were issued and outstanding as of December 31, 2022.

### ***Common Stock***

The Company had 500,000,000 shares of common stock authorized, of which 49,445,802 shares were issued and 49,323,531 shares were outstanding at December 31, 2022.

The holders of common stock are entitled to dividends when and if declared by the board of directors, subject to the preferences applicable to outstanding shares of Convertible Preferred Stock. The board of directors has not declared any dividends and the Company has not paid any dividends.

The holders of common stock are entitled to one vote per share on all matters to be voted upon by the stockholders.

The Company has issued restricted stock to founders, employees and consultants, and expense for this restricted stock is recognized on a straight-line basis (see Note 10). The restricted stock generally vests monthly over 4 years.

### ***At-the-Market Offering***

In July 2022, the Company entered into a sales agreement, (the “Sales Agreement”), with Jefferies LLC, or Jefferies, pursuant to which the Company may offer and sell shares of its common stock having aggregate gross proceeds of up to \$100 million from time to time in “at-the-market” offerings through Jefferies, as the Company’s sales agent. The Company agreed to pay Jefferies a commission of up to 3.0% of the gross proceeds of any shares sold by Jefferies under the Sales Agreement. During the year ended December 31, 2022, the Company sold 2,482,008 shares of its common stock resulting in proceeds to the Company of \$19.7 million, net of offering costs of \$1.0 million.

## **10. Stock-based compensation**

### ***2020 Stock incentive plan***

The Company’s 2020 Stock Option and Grant Plan, or the 2020 Plan, provided for the Company to grant stock options, restricted stock, and other stock awards, to employees, non-employee directors, and consultants. Upon effectiveness of the 2021 Plan (as defined below), no further issuances will be made under the 2020 plan.

### ***2021 Stock incentive plan***

The Company’s 2021 Stock Option and Incentive Plan, or the 2021 Plan, was approved by the Company’s board of directors on May 28, 2021, and the Company’s stockholders on June 17, 2021, and became effective on the date immediately prior to the date on which the registration statement for the Company’s IPO was declared effective. The 2021 Plan provides for the grant of incentive stock options, non-qualified stock options, stock appreciation rights, restricted stock units, restricted stock awards, unrestricted stock awards, cash-based awards and dividend equivalent rights to the Company’s officers, employees, directors and consultants. The number of shares initially reserved for issuance under the 2021 Plan was 4,903,145, which will be automatically increased on each January 1st by 5% of the outstanding number of shares of the Company’s common stock on the immediately preceding December 31st or such lesser number of shares as determined by the Company’s compensation, nomination and corporate governance committee. As of December 31, 2022, 3,787,469 shares of common stock were available for issuance under 2021 Plan.

### ***2021 Employee stock purchase plan***

The Company’s 2021 Employee Stock Purchase Plan, or the 2021 ESPP, was approved by the Company’s board of directors on May 28, 2021, and the Company’s stockholders on June 17, 2021, and became effective on the date immediately prior to the date on which the registration statement for the Company’s IPO was declared effective. A total of 439,849 shares of the Company’s common stock were initially reserved for issuance under the 2021 ESPP which will be automatically increased on each January 1st through January 1, 2031, by the least of (i) 439,849 shares of the Company’s common stock, (ii) 1% of the outstanding number of shares of the Company’s common stock on the immediately preceding December 31 or (iii) such lesser number of shares of the Company’s common stock as determined by the plan administrator of the 2021 ESPP. As of December 31, 2022, 827,751 shares of common stock remained available for issuance under the 2021 ESPP.

## Stock option activity

The following summarizes stock option activity:

	Number of options	Weighted average exercise price	Weighted average remaining contractual term (years)	Aggregate intrinsic value (in thousands)
Outstanding—December 31, 2021	5,563,513	\$ 7.92	9.2	\$ 70,045
Granted	2,237,870	12.16		
Exercised	(117,552)	3.73		
Forfeited	(247,492)	11.70		
Outstanding—December 31, 2022	7,436,339	\$ 9.14	8.5	\$ 12,440
Vested or expected to vest—December 31, 2022	7,436,339	\$ 9.14	8.5	\$ 12,440
Options exercisable—December 31, 2022	2,376,226	\$ 7.32	8.2	\$ 6,208

The aggregate intrinsic value of options granted is calculated as the difference between the exercise price of the options and the estimated fair value of the Company's common stock. The weighted average grant date fair value of options granted in during the years ended December 31, 2022 and 2021 was \$8.44 and \$7.11 per share, respectively.

### Fair value of stock option awards

The Company estimates the fair value of stock option awards on the grant date using Black-Scholes. The fair value of options granted were estimated using the following weighted-average assumptions:

	Year ended December 31,	
	2022	2021
Expected term (years)	6.25	6.25
Expected volatility	78.82%	77.75%
Risk-free interest rate	2.02%	1.25%
Expected dividend yield	—%	—%

Black-Scholes requires the use of subjective assumptions which determine the fair value of stock-based awards. These assumptions include:

**Expected term:** The Company's expected term represents the period that options are expected to be outstanding and is determined using the simplified method. The Company does not have sufficient historical data to use any other method to estimate expected term.

**Expected volatility:** The Company has limited information on the volatility of stock options as the shares were not actively traded on any public markets prior to June 24, 2021. The expected volatility was derived from historical stock volatilities of comparable peer public companies within its industry based on their similarities to the Company, including life cycle stage, therapeutic focus and size over a period equivalent to the expected term of the stock-based awards.

**Risk-free interest rate:** The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of the stock option grants.

**Expected dividend:** The Company has never paid dividends on its common stock and has no plans to pay dividends on its common stock. Therefore, the Company used an expected dividend yield of zero.

### **Restricted stock award activity**

Unvested restricted stock awards, or RSAs, as of December 31, 2022 and 2021, were granted to employees under the 2020 Plan. Restricted stock awards generally vest over a four year period provided the individual remains in continuous service of the Company.

The following summarizes restricted stock activity:

	Number of shares	Weighted average grant date fair value
Unvested restricted stock as of December 31, 2021	258,329	\$ 0.90
Vested	(136,058)	\$ 0.78
Unvested restricted stock as of December 31, 2022	122,271	\$ 1.04

The aggregate fair value of restricted stock that vested during the year ended December 31, 2022 and 2021 was \$1.5 million and \$5.2 million, respectively. The weighted average grant date fair value of restricted stock that vested during the year ended December 31, 2022 and 2021 was \$0.78 and \$1.13 per share, respectively.

### **Restricted stock unit activity**

Starting in 2022, the Company granted restricted stock units, or RSUs, to employees under the 2021 Plan. Each of the RSUs represents the right to receive one share of the Company's common stock upon vesting. The RSUs granted over two years provided the individual remains in continuous service of the Company. Accordingly, stock-based compensation expense for each RSU is recognized on a straight-line basis over the vesting term. The fair value of each RSU is based on the closing price of the Company's common stock on the date of grant.

The following summarizes restricted stock unit activity:

	Number of shares	Weighted average grant date fair value
Unvested restricted stock units as of December 31, 2021	—	
Granted	91,000	\$ 10.11
Unvested restricted stock units as of December 31, 2022	91,000	\$ 10.11

No RSUs vested during the year ended December 31, 2022.

### **Stock-based compensation expense**

Stock-based compensation expense is classified as follows (in thousands):

	Year ended December 31,	
	2022	2021
Research and development	\$ 5,582	\$ 2,606
General and administrative	6,082	2,594
Total stock-based compensation expense	\$ 11,664	\$ 5,200

As of December 31, 2022, total unrecognized stock-based compensation cost related to unvested stock options, restricted stock awards, and restricted stock units was \$31.1 million, \$0.1 million, and \$0.7 million, respectively. The Company expects to recognize this remaining cost over a weighted average period of 2.5 years, 1.0 years, and 1.5 years, respectively.

## **11. Income Taxes**

The Company has incurred net operating losses for all the periods presented. The Company has not reflected the benefit of any such net operating loss carryforwards in the accompanying consolidated financial statements. Domestic and foreign components of net loss are as follows (in thousands):

	Year ended December 31,	
	2022	2021
United States	\$ (17,232)	\$ (9,884)
Foreign	(91,269)	(64,074)
Net loss	\$ (108,501)	\$ (73,958)

The effective tax rate for the years ended December 31, 2022 and 2021 is different from the federal statutory rate primarily due to the valuation allowance against deferred tax assets as a result of insufficient sources of income. The reconciliation of the federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year ended December 31,	
	2022	2021
Income tax benefit at the federal statutory rate	21.0%	21.0%
State income taxes, net of federal benefit	6.2%	6.3%
Research and development tax credits	0.0%	1.2%
Foreign rate differential	(6.7)%	(6.9)%
Adjustment related to Preferred Stock Tranche Obligation	—	(0.3)%
Other	(0.7)%	(1.6)%
Change in valuation allowance	(19.8)%	(19.7)%
Total	0.0%	0.0%

Deferred income taxes reflect the net effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The principal components of the Company's deferred tax assets consisted of the following (in thousands):

	December 31,	
	2022	2021
Deferred tax assets		
Federal and state net operating loss carryforwards	\$ 26,136	\$ 14,529
Research and development tax credits	1,715	1,862
Capitalized research and development	1,151	—
Lease liability	13,173	—
Compensation related items	4,022	1,738
Other	149	58
Total deferred tax assets	\$ 46,346	\$ 18,187
Less: valuation allowance	(33,084)	(17,777)
Total net deferred tax assets	\$ 13,262	\$ 410
Deferred tax liabilities		
Right-of-use asset	(11,766)	—
Defined benefit plan adjustment	(375)	(125)
Prepaid insurance	(252)	—
Depreciation	(869)	(285)
Total deferred tax liabilities	(13,262)	(410)
Net deferred tax assets	\$ —	\$ —

The Company has incurred annual net operating losses in each year since inception. The Company has not reflected the benefit of any such net operating loss carryforwards in the financial statements. Due to the Company's history of losses, and lack of other positive evidence, the Company has determined that it is more likely than not that its net deferred tax assets will not be realized, and therefore, the net deferred tax assets are fully offset by a valuation allowance at December 31, 2022 and 2021. The Company increased its valuation allowance by \$15.3 million for the year ended December 31, 2022 in order to maintain a full valuation allowance against its deferred tax assets.

As of December 31, 2022, the Company had federal net operating loss carryforwards, or NOLs, of \$3.9 million and federal tax credits of \$1.1 million available to offset tax liabilities. The Company's federal NOLs have an



indefinite life and federal tax credit carryforwards begin to expire in 2039. The Company also had gross foreign NOLs of \$191.1 million that begin to expire in 2026. The Company also had gross state NOLs of \$5.8 million and state tax credits of \$0.6 million which are available to offset state tax liabilities. The state NOLs begin to expire in 2039 and the state tax credit carryforwards begin to expire in 2035. Federal and state NOLs and tax credit carryforwards are also subject to annual limitations in the event that cumulative changes in the ownership interests of significant stockholders exceed 50% over a three-year period, as defined under Sections 382 and 383 of the Internal Revenue Code of 1986. The Company has not completed an analysis to determine if the NOLs and tax credits are limited due to a change in ownership. Should there be ownership changes that occurred, the Company's ability to utilize existing carryforwards could be substantially restricted.

The Tax Cuts and Jobs Act resulted in significant changes to the treatment of research and development, or R&D, expenditures under Section 174. For tax years beginning after December 31, 2021, taxpayers are required to capitalize and amortize all R&D expenditures that are paid or incurred in connection with their trade or business. Specifically, costs for US-based R&D activities must be amortized over five years and costs for foreign R&D activities must be amortized over 15 years – both using a midyear convention. During the year ended December 31, 2022, the Company capitalized \$4.0 million of R&D expenses.

The Company determines its uncertain tax positions based on whether and how much of a tax benefit taken by the Company in its tax filings is more likely than not to be sustained upon examination by the relevant income tax authorities.

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows (in thousands):

	Year ended December 31,	
	2022	2021
Unrecognized tax benefits, beginning of year	\$ —	\$ —
Additions for tax positions of prior years	2,235	—
Reductions for tax provisions of prior years	—	—
Unrecognized tax benefits, end of year	\$ 2,235	\$ —

The Company recognizes interest and penalties related to unrecognized tax benefits in U.S. Federal, state, and foreign income tax expense. For the year ended December 31, 2022, the unrecognized tax benefit generated was related to a reserve for the Federal and State Research and Development Credit of \$2.2 million. The Company had approximately \$2.2 million and \$0.0 of unrecognized tax benefit as of December 31, 2022, and 2021, respectively.

The Company files income tax returns in the U.S., Switzerland and Massachusetts. The Company is not currently under examination by any taxing authority for any open tax year. Due to net operating loss carryforwards, all years remain open for income tax examination. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service, or IRS, or state tax authorities to the extent utilized in a future period. No federal, foreign, or state tax audits are currently in process.

## 12. Employee retirement plans

### Defined benefit plan

The Company, in compliance with Swiss Law, is contracted with the Swiss Life Collective BVG Foundation for the provision of pension benefits. All benefits are reinsured in their entirety with Swiss Life Ltd within the framework of the contract.

The technical administration and management of the savings account are guaranteed by Swiss Life on behalf of the collective foundation. Insurance benefits due are paid directly to the entitled persons by Swiss Life in the name of and for the account of the collective foundation. The pension plan is financed by contributions of both employees and employer.

The contract between the Company and the collective foundation can be terminated by either side. In the event of a termination, the Company would have an obligation to find alternative pension arrangements for its employees. Because there is no guarantee that the employee pension arrangements would be continued under the same conditions, there is a risk, albeit remote, that a pension obligation may fall on the Company.

The pension assets are pooled for all affiliated companies; the investment of assets is done by the governing bodies of the collective foundation or by mandated parties. The risks of disability, death and longevity are reinsured in their entirety with Swiss Life Ltd.

The following table represents the changes in benefit obligations and plan assets and the net amount recognized on the consolidated balance sheets (in thousands):

	Year ended December 31,	
	2022	2021
<i>Change in benefit obligation:</i>		
Benefit obligation—beginning of period	\$ 5,975	\$ 2,284
Service cost employer	549	417
Contributions paid by employees	299	170
Interest cost	19	9
Contributions paid by plan participants	1,302	1,926
Benefits paid	(452)	(82)
Plan Amendment	(67)	(42)
Actuarial (gain) loss	(774)	1,293
Benefit obligation—end of period	\$ 6,851	\$ 5,975
<i>Change in plan assets:</i>		
Fair value of plan assets—beginning of period	\$ 3,799	\$ 1,217
Actual return on plan assets	(240)	226
Contributions paid by employer	610	340
Contributions paid by employees	299	175
Contributions paid by plan participants	1,302	1,926
Benefits paid	(452)	(85)
Fair value of plan assets—end of period	\$ 5,318	\$ 3,799
Defined benefit plan liability	\$ 1,533	\$ 2,176

The net pension costs was as follows (in thousands):

	Year ended December 31,	
	2022	2021
Service cost	\$ 549	\$ 417
Interest cost	19	9
Net pension cost	\$ 568	\$ 426

The provision for pension benefit obligation recognized in other comprehensive loss was as follows (in thousands):

	Year ended December 31,	
	2022	2021
Actuarial gain (loss) arising from experience adjustments	\$ 774	\$ (1,293)
Defined benefit cost for the year recognized in other comprehensive loss	\$ 774	\$ (1,293)

The assumptions used to measure the projected benefit obligation and net pension costs were as follows:

	Year ended December 31,	
	2022	2021
Inflation rate	1.25%	0.50%
Discount rate	2.30%	0.35%
Interest rate on savings accounts	1.00%	0.45%
Expected rate of return on assets	2.30%	0.45%
Salary increase	1.25%	1.00%
Social Security increase	1.25%	0.50%
Pension increase	0.00%	0.00%
Retirement age	100% Male 65 Female 64	100% Male 65 Female 64
Mortality and disability rates	BVG 2020 Table	BVG 2020 Table

Estimated benefit payments, which reflect future expected service, are expected to be paid as follows (in thousands):

	December 31,
2023	\$ 660
2024	\$ 693
2025	\$ 717
2026	\$ 735
2027	\$ 753
2028-2032	\$ 4,239

### Defined contribution plan

In February 2021, the Company adopted a defined contribution plan intended to qualify under Section 401(k) of the Internal Revenue Code covering all eligible U.S. based employees of the Company. All employees are eligible to become participants of the plan immediately upon hire. Each active employee may elect, voluntarily, to contribute a percentage of their compensation to the plan each year, subject to certain limitations. The Company reserves the right, but is not obligated, to make additional contributions to this plan. The Company makes safe-harbor match contributions of 100% of the first 4% of each participant's eligible compensation. The Company recorded \$0.5 million and \$0.3 million matching 401(k) contribution related expense during the years ended December 31, 2022 and 2021, respectively.

## 13. Net loss per common share

Basic and diluted net loss per share attributable to common stockholders is calculated as follows (in thousands except share and per share amounts):

	Year ended December 31,	
	2022	2021
Net loss	\$ (108,501)	\$ (73,958)
Net loss per share attributable to common stockholders—basic and diluted	\$ (2.30)	\$ (2.96)
Weighted-average number of common shares used in computing net loss per share—basic and diluted	47,227,370	25,000,124

The following outstanding potentially dilutive securities have been excluded from the calculation of diluted net loss per common share, as their effect is anti-dilutive:

	December 31,	
	2022	2021
Stock options to purchase common stock	7,436,339	5,563,513
Restricted stock awards	122,271	258,329
Restricted stock units	91,000	—

## **14. Related parties**

The Company paid \$0.4 million in contract research and development expenses to Tempus Labs, Inc. for the years ended December 31, 2022, and 2021. A member of the Company's Board of Directors served as an officer of Tempus Labs, Inc. until May 2022. Tempus Labs, Inc. is no longer a related party as of December 31, 2022.

## **15. Subsequent events**

On March 10, 2023, Silicon Valley Bank (SVB) was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation as receiver. At the time of the closure, the Company had cash totaling about 2% of our total cash, cash equivalents, and marketable securities held in operating accounts and money market accounts at SVB. The Company received full access to this cash on March 13, 2023.

## **BOARD OF DIRECTORS**

**Markus Warmuth, M.D.**  
President, Chief Executive Officer  
and Director

**Alexander Mayweg**  
Managing Director at Versant  
Venture Management, LLC.  
President of Ridgeline Discovery

**Ali Behbahani**  
General Partner on the healthcare  
team of New Enterprise Associates,  
Inc.

**Kimberly L. Blackwell**  
Chief Executive Officer of Zentalis  
Pharmaceuticals, Inc.

**Andrew Schiff**  
Managing Partner of Aisling Capital

**Chandra P. Leo**  
Investment Advisor on the private  
equity team at HBM Partners AG

**Christine Siu**  
Chief Operating Officer in Residence  
of BridgeBio Pharma Inc.

**Jan Skvarka, Ph.D, MBA**  
Executive Chairman of GentiBio, Inc.  
and DEM BioPharma, Inc.

## **EXECUTIVE OFFICERS**

**Markus Warmuth, M.D.**  
President, Chief Executive Officer  
and Director

**Ajim Tamboli, CFA.**  
Chief Financial Officer

**Owen B. Wallace, Ph.D.**  
Chief Scientific Officer

**Filip Janku, M.D., Ph.D.**  
Chief Medical Officer

**Jullian G. Jones, Ph.D.**  
Chief Business Officer

**Philip Nickson, Ph.D.**  
General Counsel

**Sharon Townson, Ph.D.**  
Chief Technology Officer

**John Castle, Ph.D.**  
Chief Data Scientist

## **CORPORATE HEADQUARTERS**

645 Summer Street, Suite 102  
Boston, MA 02210

## **INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

Deloitte & Touche, LLP  
200 Berkeley St 10th floor, Boston,  
MA 02116

## **TRANSFER AGENT**

Computershare Trust Company, N.A.  
150 Royall Street , Canton, MA,  
02021

## **INVESTOR RELATIONS**

[ir@monterosatx.com](mailto:ir@monterosatx.com)