

Overview

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Founder and CEO

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Agenda

- The unmet need
- Technical solution: Drug-discovery platform AIDE³⁶⁰
 - Internal drug-discovery program – ARDS / vascular leak
 - AIDE³⁶⁰ partnerships
- Progress and traction
- Business model
- Current raise
- Team

Company Highlights

Company Overview

- Founded in 2020
- Experienced team with extensive biology, drug discovery, development, and commercialization expertise
- **Core expertise:** AI-assisted drug-discovery, pharmacology, and biology
- Internal therapeutic programs in endothelial vascular leak
- **National Science Foundation Award recipient December 2021**



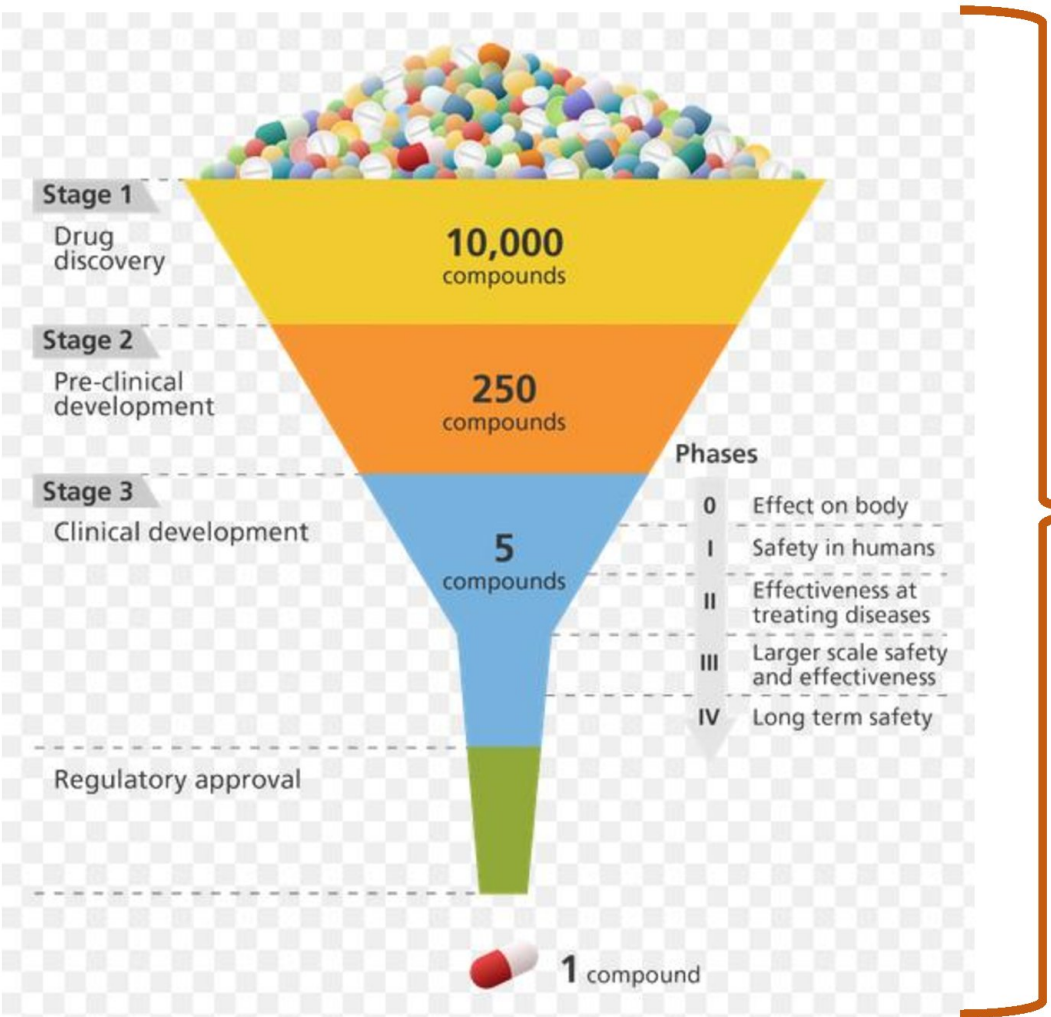
Pipeline

- Lead program: treatment for ARDS
- Other indications: diabetic macular edema, systemic capillary leak syndrome, chronic kidney disease, fibrosis

Intellectual Property and Financials

- Patent filed in 2020 / converted to PCT 2021 on methods of use, formulations and composition of matter
- Seeking \$2M Series A funding for operations, scale-up manufacturing, preclinical studies, and pre-IND FDA meeting

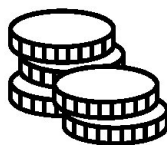
The problem: many drug candidates fail in the lab



Long: 12-15 years



Expensive: ~ \$3B



A key solution: perform most of the steps on the computer

Why?

- In many diseases, proteins (also called targets) are not functioning properly. Binding of a drug to these targets can restore health and/or wellness.
- Most drug molecules bind to specific pockets or cavities at the surface of proteins.
- The number of small molecules that could bind to these pockets is almost infinite (cannot be investigated experimentally)
- Yet not all molecules can become a drug (e.g., toxicity...)
- With all the scientific data collected these last ~50 years, with novel algorithms and powerful computers, numerous steps can now be performed in silico, novel ideas can be generated and only the best hypotheses are tested experimentally using better assays. Designing drug candidate in silico is often referred to as computer-aided drug design or AI-assisted drug discovery

AI in Drug Discovery Cuts Timelines From 5+ Years to Months

Dr Nadia Tsao Jun 10, 2021

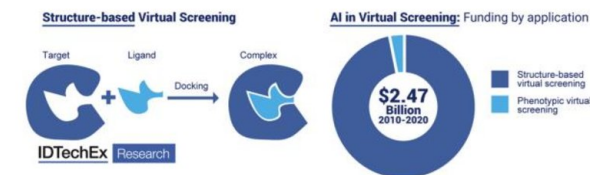


IDTechEx have recently published a new report, "[AI in Drug Discovery 2021: Players, Technologies, and Applications](#)", covering the use of artificial intelligence (AI), including machine learning (ML) and deep learning (DL), in the drug discovery process. The industry has received significant attention from investors and key players in the biopharma

industry during 2020, and 2021 continues to be a very exciting year for the industry.

The development of pharmaceutical drugs is a long and costly process. Companies in the pharmaceutical and biotechnology industries typically spend more than \$1 billion to bring a drug to market, in a process that often lasts 10 - 15 years. Moreover, the drug development process is very risky - up to 90% of drugs being developed do not reach commercialization. A technology that can contribute significantly to addressing any of these 3 pain points has the potential to quickly grow into a multibillion-dollar industry. AI has been successfully applied to speed up virtual screening, de novo drug discovery, and can be utilized to optimize compounds to have drug-like properties. Processes that typically take several years can be reduced to a matter of months.

**Structure-based
virtual screening is
the leading approach**



Structure-based virtual screening identifies molecules (ligands) that are predicted to bind to a biological structure (target). Structure-based virtual screening is the leading form of AI in drug discovery being funded today. Source: IDTechEx Research

Akttyva team's *in silico* tools and drug discovery expertise

- We have significant expertise in structure-based virtual screening with over 200 scientific publications in the field structural bioinformatics and chemoinformatics, computer methods often with applications to different therapeutic areas and protein targets

some of our studies on the cover page of scientific journals or books

- We use ~55 different computer methods and develop our own software packages
- We have 10 unique proprietary databases with millions of novel high quality compounds
- These tools evolve each month as we gain new knowledge



Akttiva AI-assisted Drug Discovery Engine

360° *in silico* / *experimental* analysis

Akttiva's AI-assisted Drug-discovery Engine
AIDE³⁶⁰

(2) AI-assisted virtual screening

Approved drugs



(3) ML with ADME and safety filters



(4) Disease models

In vitro human tissue 3D

In vivo model



Repurposed
Lead
(ARDS)

NCE Lead
(other indications)

(1) AI-assisted drug pocket discovery

NCEs



Model optimization

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Akttiva vascular leak drug candidate:

- Small molecule *in silico* drug repurposing: MK2 target



Drug Discovery Today

Available online 24 January 2022

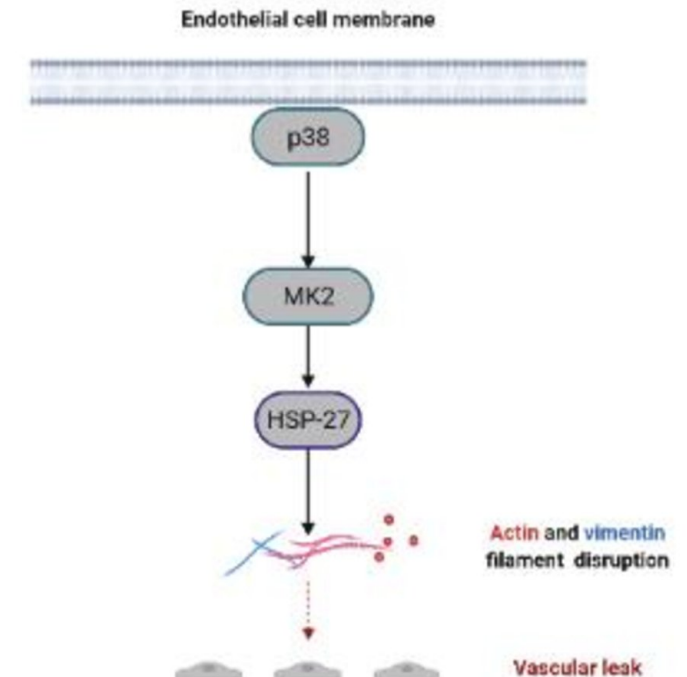
In Press, Corrected Proof



Post-screen (grey)

Kinase signaling as a drug target modality for regulation of vascular hyperpermeability: A case for ARDS therapy development

Usamah S. Kayyali^a, Elizabeth Ghandakly^b, Natesh Singh^c, Bruno O. Villoutreix^{a,c}, Katya Tsaioun^{a,d}



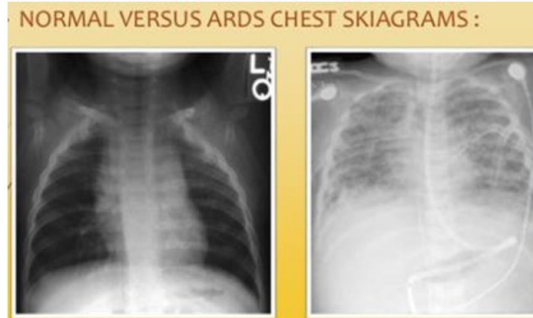
Problem: vascular leak underlying > 60 conditions

First indication: ARDS

Conditions associated with vascular leak

- **ARDS**
- Diabetic macular edema
- Acute kidney injury
- Chronic kidney disease
- Acute pancreatitis
- Fibrosis
- Ascites
- Systemic capillary leak syndrome
- Chemical, radiation and biothreats, brain injury
 - **BARDA priority**

Acute Respiratory Distress Syndrome (ARDS)



The reason for mortality in COVID-19 pandemic

Underlying cause:
Endothelial vascular leak

\$1.6B US market

> 400,000 cases
p.a.

14+ average days
in ICU

30-40% mortality
75,000
deaths/year

ARDS: a deadly condition with no treatment

Described as “wet lung” in 1914

Acute Respiratory Distress Syndrome (ARDS)

1 Required criteria (must meet all three)

- Timing within 1 week of clinical insult or new/worsening respiratory symptoms
- Chest XR shows bilateral opacities not fully explained by effusions, lobar/lung collapse, or nodules
- Respiratory failure not fully explained by cardiac failure/fluid overload

2 Risk factor

- Risk factor for ARDS present (e.g. pneumonia, trauma, sepsis, pancreatitis)
- Objective assessment (Echo) excludes hydrostatic edema if no risk factor present
- None of the above

3 Severity (Oxygenation)

- Mild: $\text{PaO}_2/\text{FiO}_2 >200$ to ≤ 300 mmHg with PEEP OR CPAP ≥ 5 cm H_2O
- Moderate: $\text{PaO}_2/\text{FiO}_2 >100$ to ≤ 200 mmHg with PEEP ≥ 5 cm H_2O
- Severe: $\text{PaO}_2/\text{FiO}_2 \leq 100$ mmHg with PEEP ≥ 5 cm H_2O
- None of the above

NORMAL VERSUS ARDS CHEST SKIAGRAMS :



The reason for mortality
in COVID-19 pandemic

Before COVID-19

> 400,000 cases
p.a.

14+ average days
in ICU

30-40% mortality
75,000
deaths/year

\$1.6B market

¹Uckun, F.M., Front.Pharmacol. 2020, 11:796 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7264370/#B8>

²2018 Data, <https://www.openaccessgovernment.org/acute-respiratory-distress-syndrome/43754/>

Standard of care vs. Akttyva's Solution

Current ARDS standard of care



News

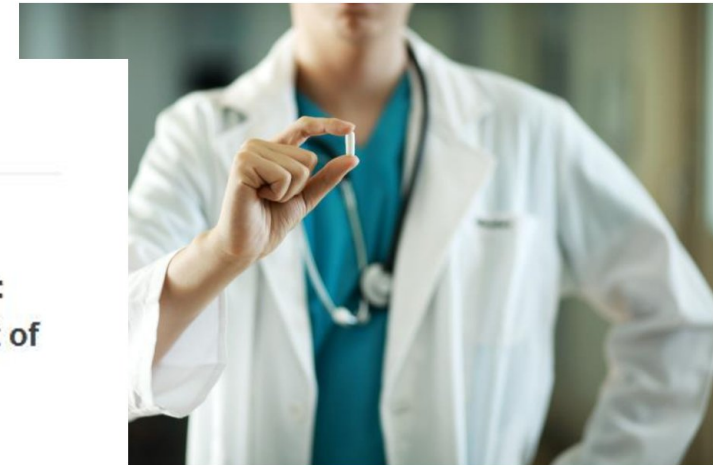


Classification of
Omicron (B.1.1.529):
SARS-CoV-2 Variant of
Concern

26 November 2021

- **Mechanical ventilation**
 - Goal: increase oxygenation
- **Problems:**
 - High delivery cost / ICU / skilled nursing
 - Mechanical damage to lung
 - Scarring / fibrosis
 - Palliative (30-40% mortality)

Akttyva Therapeutics



- **Small molecule**
 - Low cost, easy delivery
 - Multiple modes of administration
 - Address the root cause
 - Prevents ICU admission
 - Virus and mutations-agnostic

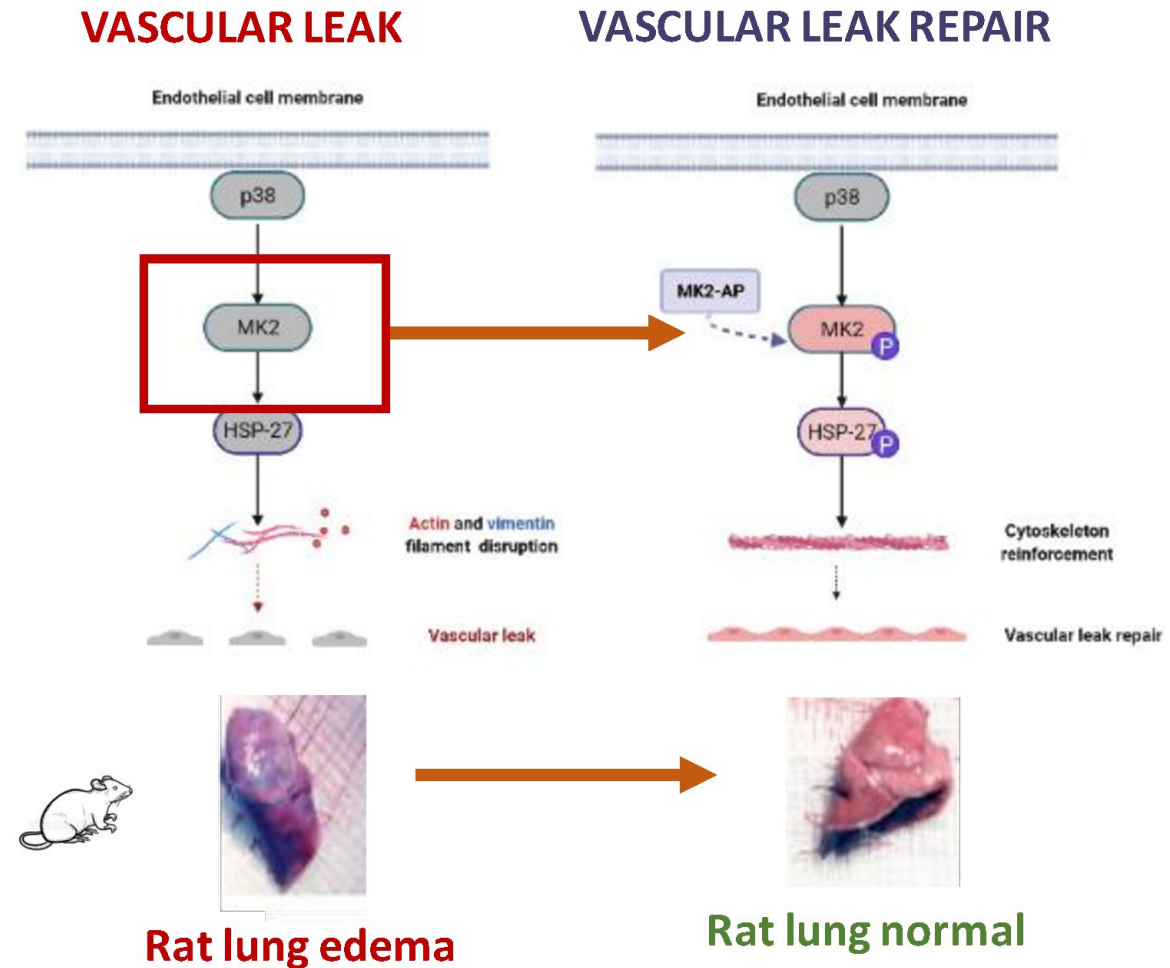
2015: Validated Approach to Stop ARDS

MK2 as the target:

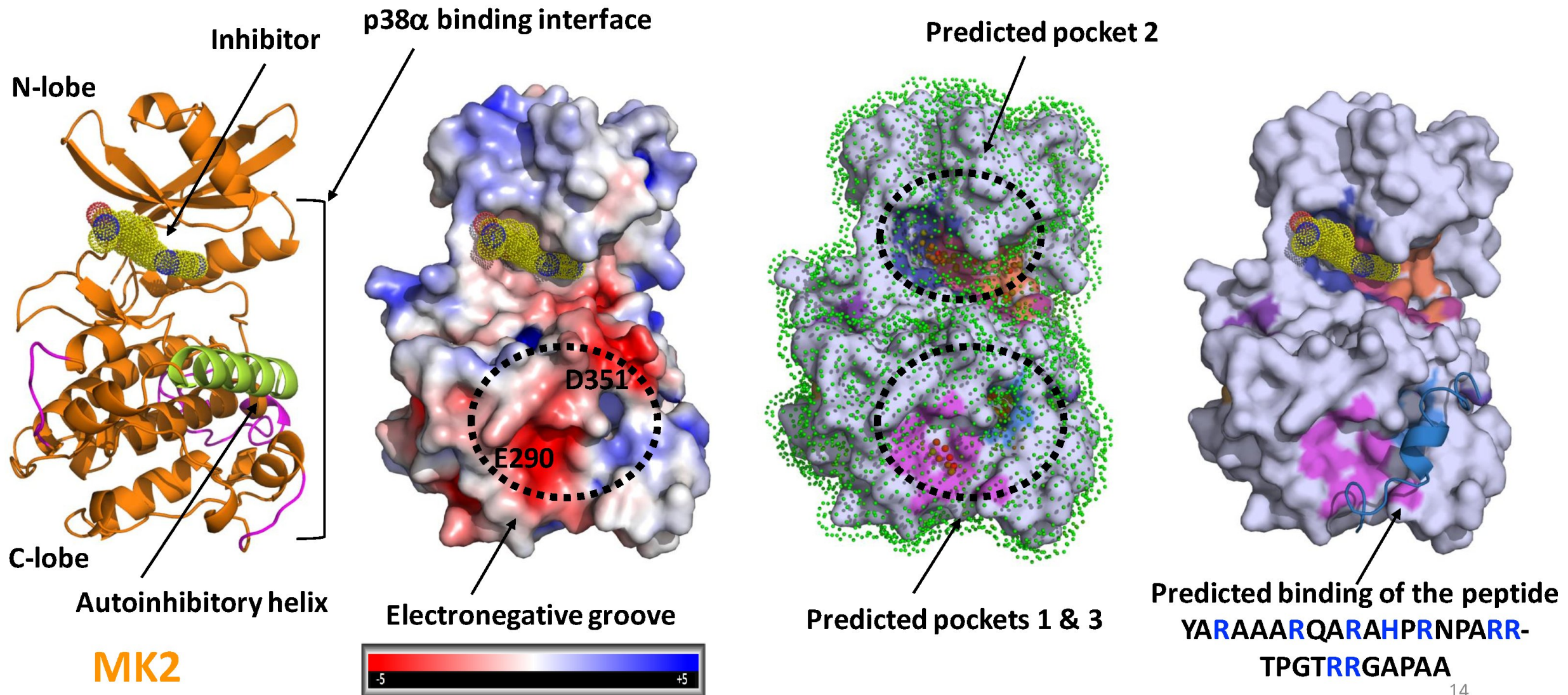
- **MK2** pathway involved in stress response when activated
- Pathway activation in endothelial cells stops vascular leak
- *In vivo* proof-of-concept established

The approach:

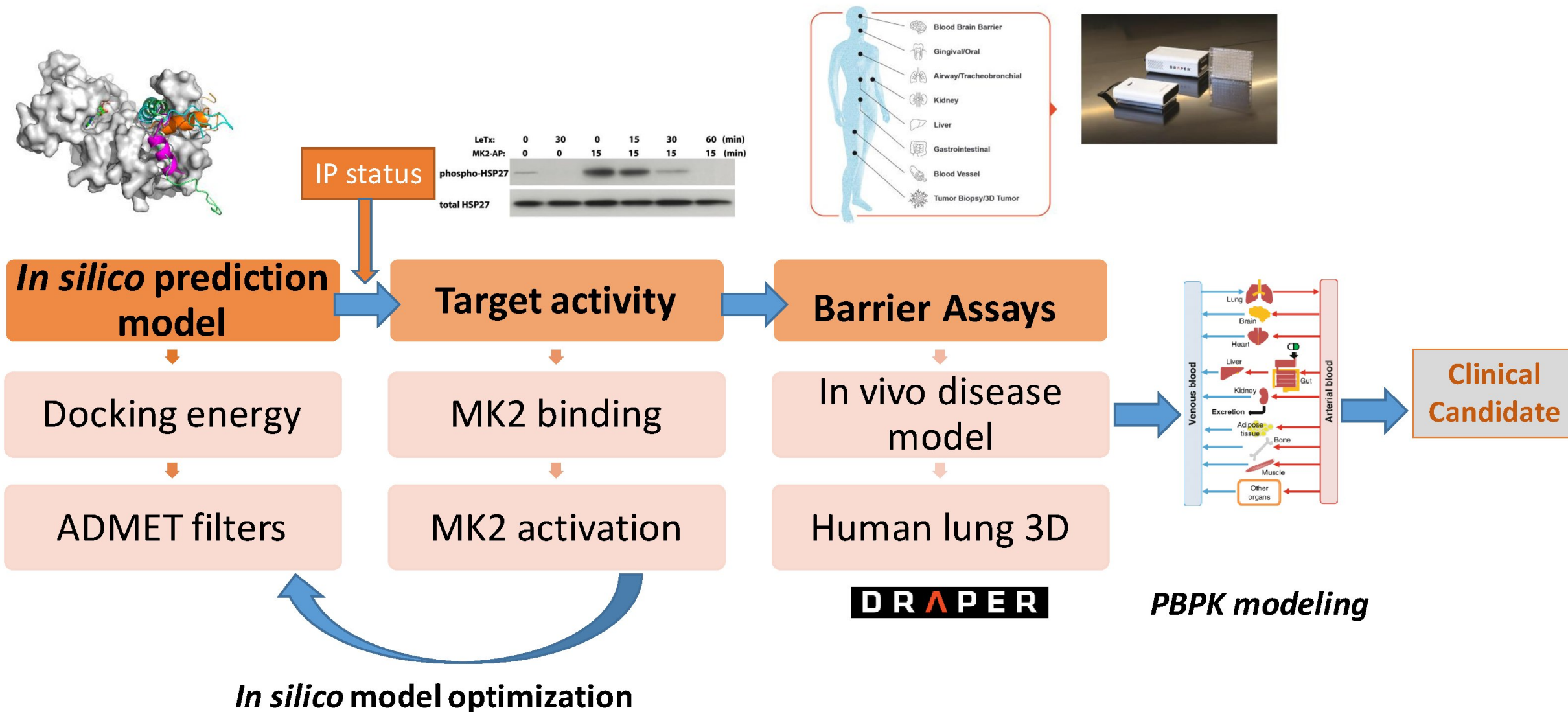
- Direct activation of **MK2 pathway** with small molecule to stop vascular leak
- **Agnostic to a specific virus, organ or toxic agent**



2021: AIDE³⁶⁰ identifies small molecule MK2 activators



Clinical candidate selection process



AIDE³⁶⁰: speed and precision

$$\text{HR} = \frac{\text{True active cmpds}}{\text{Selected hits assessed in vitro}} \times 100$$

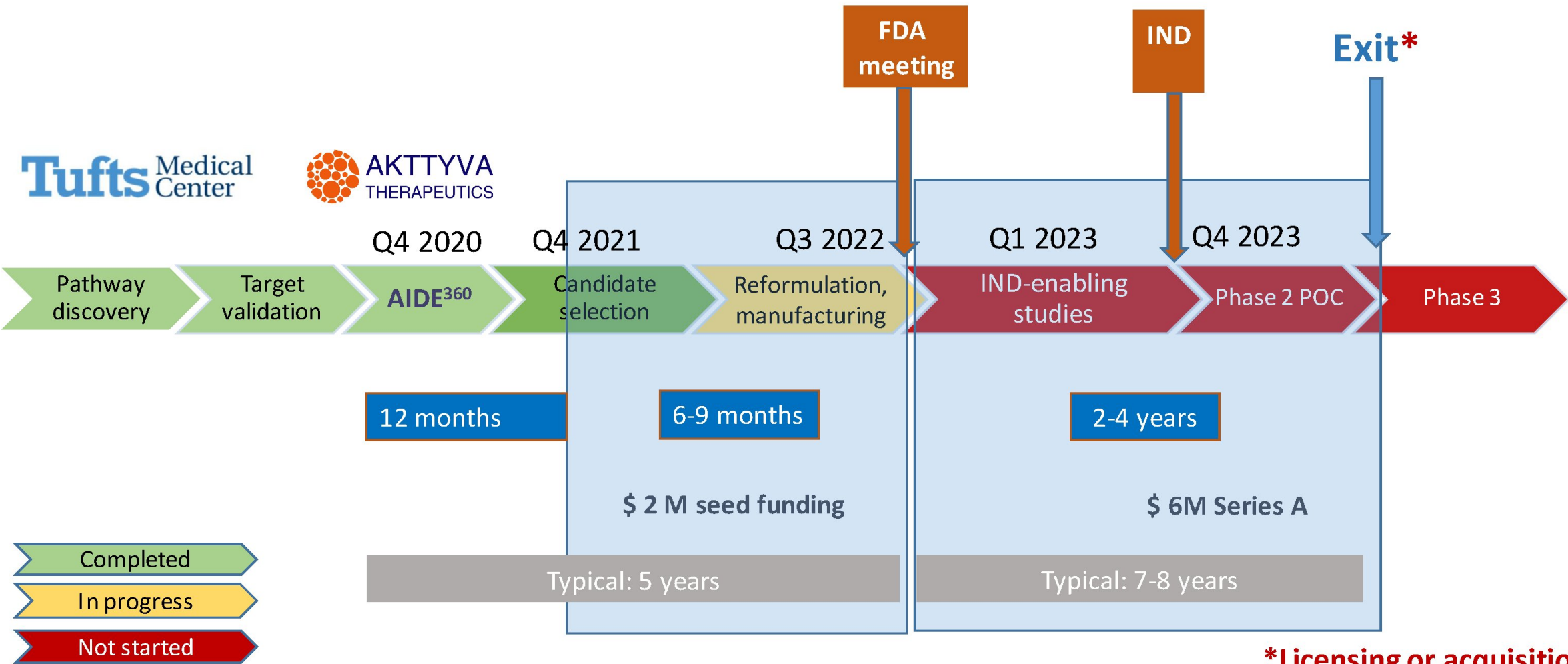
IC_{50} = [competitive inhibitor] producing a 50% inhibition]
(the smaller the better)

Hit rate = drug discovery success rate in finding bioactive molecules

Target A	Target A	Target MK2
High-throughput Screen (vitro - 2015)	Virtual Screen (silico + vitro 2016)	Virtual Screen (silico + vitro 2021)
10000 cmpds tested 10 hits 5 with $\text{IC}_{50} > 20 \text{ microM}$ 2 with IC_{50} between 10 and 20 microM 3 with $\text{IC}_{50} < 10 \text{ microM}$	500 cmpds tested 6 hits 2 with $\text{IC}_{50} < 20 \text{ microM}$ 4 with $\text{IC}_{50} < 10 \text{ microM}$	54 cmpds tested 5 hits 4 with EC_{50} between 15 and 20 microM 1 with $\text{IC}_{50} < 10 \text{ microM}$
Hit rate = 0.1	Hit rate = 1.2	Hit rate = 9.3
100-fold improvement over traditional drug-discovery		

Repurposed drug for ARDS treatment

Program designed for efficiency and speed to clinical PoC



*Licensing or acquisition

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Use of proceeds:

Internal programs:

ARDS:

- Disease model validation of lead candidate
- Clinical development plan
- Pre-IND meeting with FDA

Next Vascular leak indication:

- Use AIDE³⁶⁰ for NCE discovery for the next vascular leak indication

AIDE³⁶⁰ partnerships:

- Dedicated team to deliver virtual screening partnerships

Current funding:

- ✓ **\$259K** – National Science Foundation (NSF) award for AI platform advancement
- ✓ **\$200K closed**
- ✓ **Seed Raise: \$2 M**

Intellectual Property:

- Patent application: Compositions of matter, formulations and methods of use covering the small molecules filed in 2020, converted to PCT 11/12/21
- Additional filings planned on NCE modulators of MK2 and other members of the pathway (MK3, MK5)

Akttiva Business Model

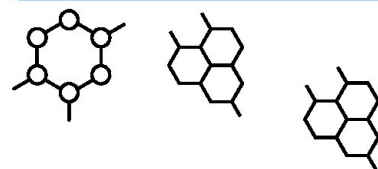
**Partnered
Programs**

Drug targets

**Internal
Programs**



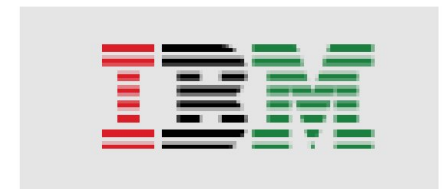
Leads



\$ -\$\$\$ Upfront
\$\$ Milestones
\$\$ Royalties

Progress and Traction

- ✓ AIDE³⁶⁰ platform in place:
 - ✓ Utilized for MK2 target:
 - ✓ More than 7,000 existing drugs have been docked to the MK2 pocket
 - ✓ >100 candidate drugs for repurposing identified
 - ✓ Activity assay established in the lab
 - ✓ 5 lead candidates identified based on experimental activity
- ✓ Lead candidate selected for clinical development in ARDS
- ✓ IBM partnership on AIDE³⁶⁰: free access to IBM cloud and business development
- ✓ Already in discussions with partner on co-development



Team

Co-founded and led 16 companies
Brought 10 drugs to market
8 successful exits, 2 IPOs



**CEO,
Board Director**

Katya Tsaion, Ph.D. – 20+ years in biopharma; successful entrepreneur (founded Aprelica, an ADME-Tox CRO in 2006, successful exit to Evotec); expertise in mechanistic strategies of de-risking drug-discovery programs Executive Director of EBTC at Johns Hopkins Bloomberg School of Public Health

Serial entrepreneur,
De-risking drug candidates

Investor



Biology

Usamah S. Kayyali, Ph.D., MPH, DABT -Formerly, Associate Professor, Tufts Medical Center, discovered mechanisms of vascular permeability (\$2M NIH-funded research), demonstrated role of p38-MK2-HSP27 pathway in vascular permeability barrier regulation.

Pathway discovery and
validation



Head of Research



Mario DiPaola, Ph.D. – 25+ years in the pharma industry with roles in basic R&D, quality, CMC and regulatory functions in support of protein and small molecule development; regulatory filings (BLA/eCTD) for Alferon-N, Amevive, Sucraid, Authored/co-authored 60+ publications and co-inventor in 4 patents

Assay development,
biology

Investor



Chemistry

Bruno Villoutreix, Ph.D. - 25 years interface between molecular medicine / structural-bioinformatics / chemoinformatics, in silico drug design, ADME-Tox, small molecule PPI and protein-membrane modulators, Research Director at Inserm (French medical research Institute), Editor in Chief Frontiers in Drug Discovery

Biomolecular modeling



Board Director

Lana Gladstein, J.D. – Chief Legal Officer, Arranta Bio; previously EVP and General Counsel of Brammer Bio (bought by Thermo Fisher in 2019); formerly partner at Troutman Pepper and partner at Nutter, Boston, MA

Intellectual property



Board Director

Mark Tepper, Ph.D. Founder and C-level management for Corbus Pharmaceuticals (IPO 2014), Primatope Therapeutics (acquired), NKT Therapeutics, and RXi Pharma (IPO 2007). Previously held positions: CEO, Multiple Life Science startups, VP USA Research & Operations, EMD Serono; Bristol-Myers Squibb.



Corporate strategy



Advisors and mentors



Translational, M&A
expertise

Vanessa Carle, Ph.D.

Associate, **Pharma Ventures**

Expertise in drug discovery R&D, technology commercialization, translational drug-development projects and the start-up ecosystem, out-licensing partnerships. **Winner of MassChallenge Switzerland.**

PharmaVentures
— the deal experts —



Drug reimbursement
strategy

David Farber, J.D.

Partner, **King & Spaulding**, FDA &

Life Sciences Practice

Litigation, regulatory matters, and public policy, with a focus on healthcare, Medicare and Medicaid issues for pharmaceutical and medical device companies, hospitals and pharmacies. He is a recognized national expert on Medicare Secondary Payer issues.



Critical care physician

Prof. Hugh Montgomery, MB BS BSc FRCP MD FRGS FRI FFICM

Professor of Intensive Care
Medicine, University College
London

Conducted numerous clinical
trials in pulmonary indications
including ARDS indication



AI, ML Expert

Jonathan Dunne, Ph.D.

Principal Data Scientist at IBM. Jonathan has co-authored over 20 conference and Journal Papers in Cloud Outage Detection and Network QoS. He is also the holder of 250 software patents. His research interests include Service time Modelling and Queuing Theory. He also holds Level 3 - Distinguished Data Scientist certification from the Open Group. He is currently a member of the Association for Computing Machinery (ACM).



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Summary

- Akttyva is building a drug pipeline for indications with vascular leak pathology
- Akttyva is a leader in AI-enabled virtual screening
- The lead program (AKT-001) addresses indication #1 (ARDS)
- Within 12 months of \$2M investment Akttyva will:
 - Complete IND-enabling / bridging studies for AKT-001
 - Provide evidence of binding to target by structural biology studies
 - Obtain a list of NCE hits for the indication #2 identified
 - Set up HTS experimental binding and functional assays cascade
- Aiming to raise >\$10M in Series A round beginning of 2023. Milestones:
 - AKT-001 in phase 2a in ARDS patients
 - NCE lead and a backup for indication #2 are in advanced preclinical development

Who we are



Inventors of proprietary virtual screening platform AIDE³⁶⁰

Internal drug pipeline: vascular leak in > 60 indications

Advanced therapeutic program ready for IND-enabling studies

Experienced management team

Substantially de-risked by NSF, partnerships, angel funding

Contact:

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Thank you!