# Overview

March 1 2022

AKTTYVA THERAPEUTICS

Katya Tsaioun, Ph.D.
Founder and CEO
Katya@Akttyva.com
617-821-7095

# Agenda

- The unmet need
- Technical solution: Drug-discovery platform AIDE$^{360}$
  - Internal drug-discovery program – ARDS / vascular leak
  - AIDE$^{360}$ partnerships
- Progress and traction
- Business model
- Current raise
- Team

# Company Highlights

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## 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

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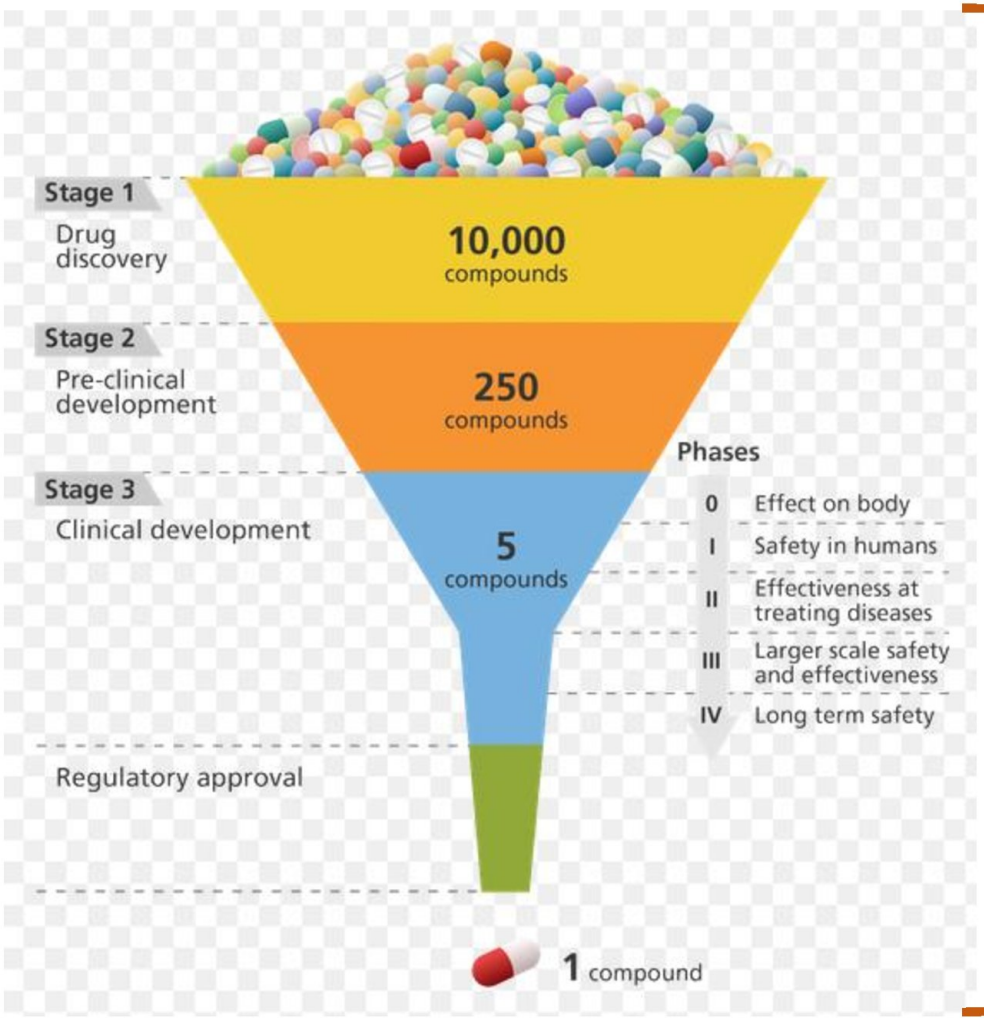


**Long: 12-15 years**

**Expensive: ~ $3B**

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

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**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 refer to as computer-aided drug design or AI-assisted drug discovery

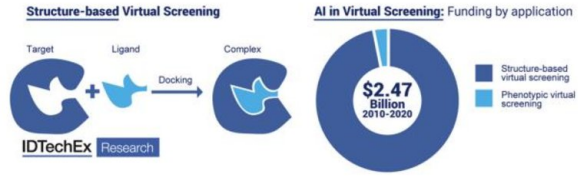
## AI in Drug Discovery Cuts Timelines From 5+ Years to Months

**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

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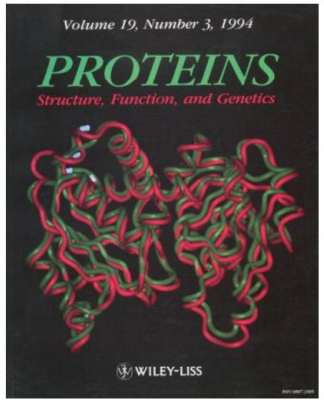
- **We have significant expertise in structure-based virtual screening with over 200 scientific publications in the field structural bioinformatics and chemoinformatics, computer methods often with applications to different therapeutic areas and protein targets**

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

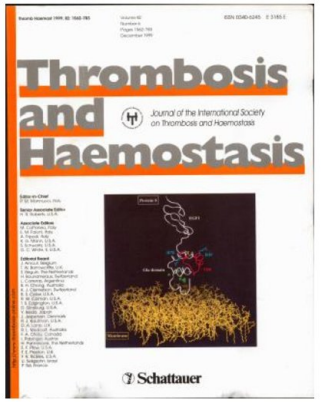
- **We use ~55 different computer methods and develop our own software packages**
- **We have 10 unique proprietary databases with millions of novel high quality compounds**
- **These tools evolve each month as we gain new knowledge**

1994



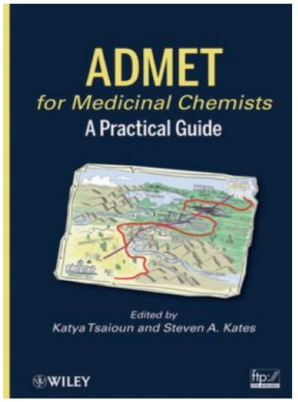

1997


1999

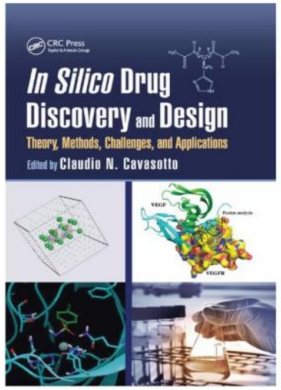



2001

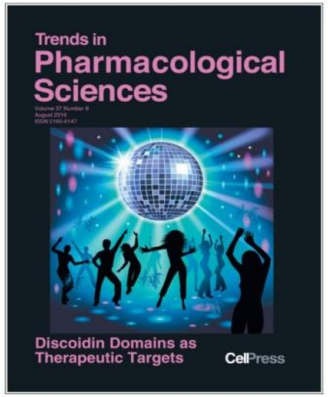

2010




2015




2016



# Akttyva AI-assisted Drug Discovery Engine

## 360° *in silico / experimental* analysis

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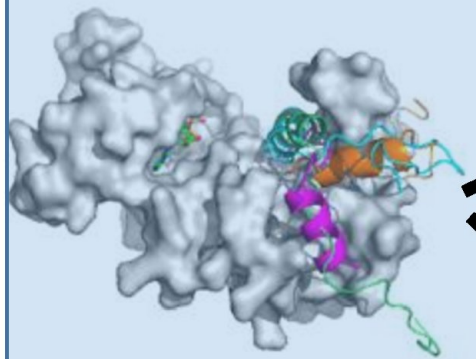
**Akttyva's AI-assisted Drug-discovery Engine**

**AIDE$^{360}$**

**(1) AI-assisted drug pocket discovery**



**(2) AI-assisted virtual screening**

***Approved drugs***

***NCEs***

**(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)

**Model optimization**

# Our Lead Program Discovered using AIDE$^{360}$

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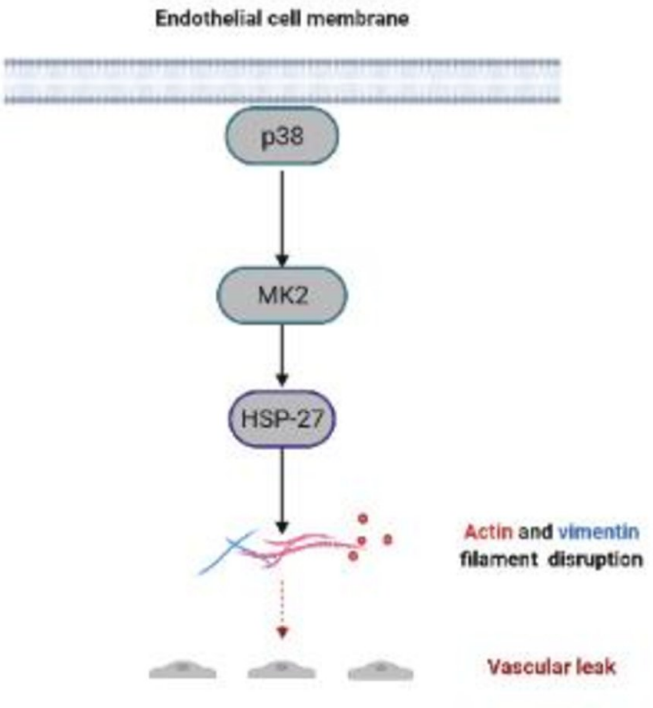
## Akttyva vascular leak drug candidate:

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




ELSEVIER

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

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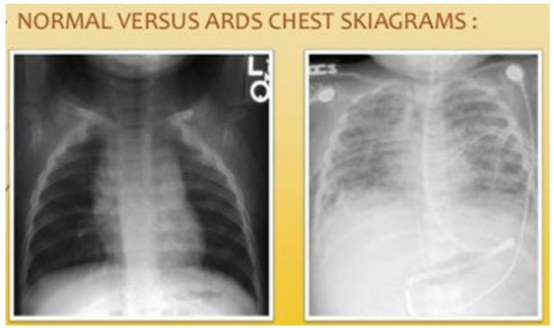
**Conditions associated with vascular leak**

- 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

**$1.6B US market**

> 400,000 cases p.a.

14+ average days in ICU

30-40% mortality 75,000 deaths/year

**Underlying cause:**

**Endothelial vascular leak**

# ARDS: a deadly condition with no treatment

## Described as “wet lung” in 1914

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### Acute Respiratory Distress Syndrome (ARDS)

**1 Required criteria (must meet all three)**

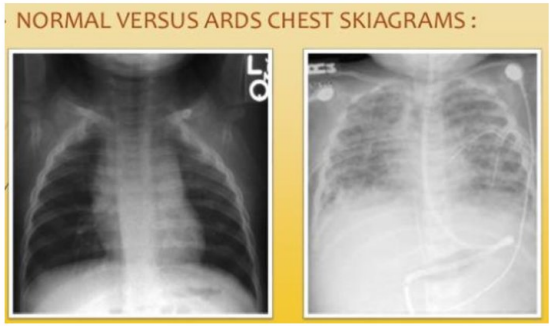
- Timing within 1 week of clinical insult or new/worsening respiratory symptoms
- Chest XR shows bilateral opacities not fully explained by effusions, lobar/lung collapse, or nodules
- Respiratory failure not fully explained by cardiac failure/fluid overload

**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: $PaO_2/FiO_2$ >200 to ≤300 mmHg with PEEP OR CPAP ≥5 cm $H_2O$
- Moderate: $PaO_2/FiO_2$ >100 to ≤200 mmHg with PEEP ≥5 cm $H_2O$
- Severe: $PaO_2/FiO_2$ ≤100 mmHg with PEEP ≥5 cm $H_2O$
- None of the above




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**

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

[2]2018 Data, https://www.openaccessgovernment.org/acute-respiratory-distress-syndrome/43754/

# Standard of care vs. Akttyva's Solution

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## *Current ARDS standard of care*

- **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

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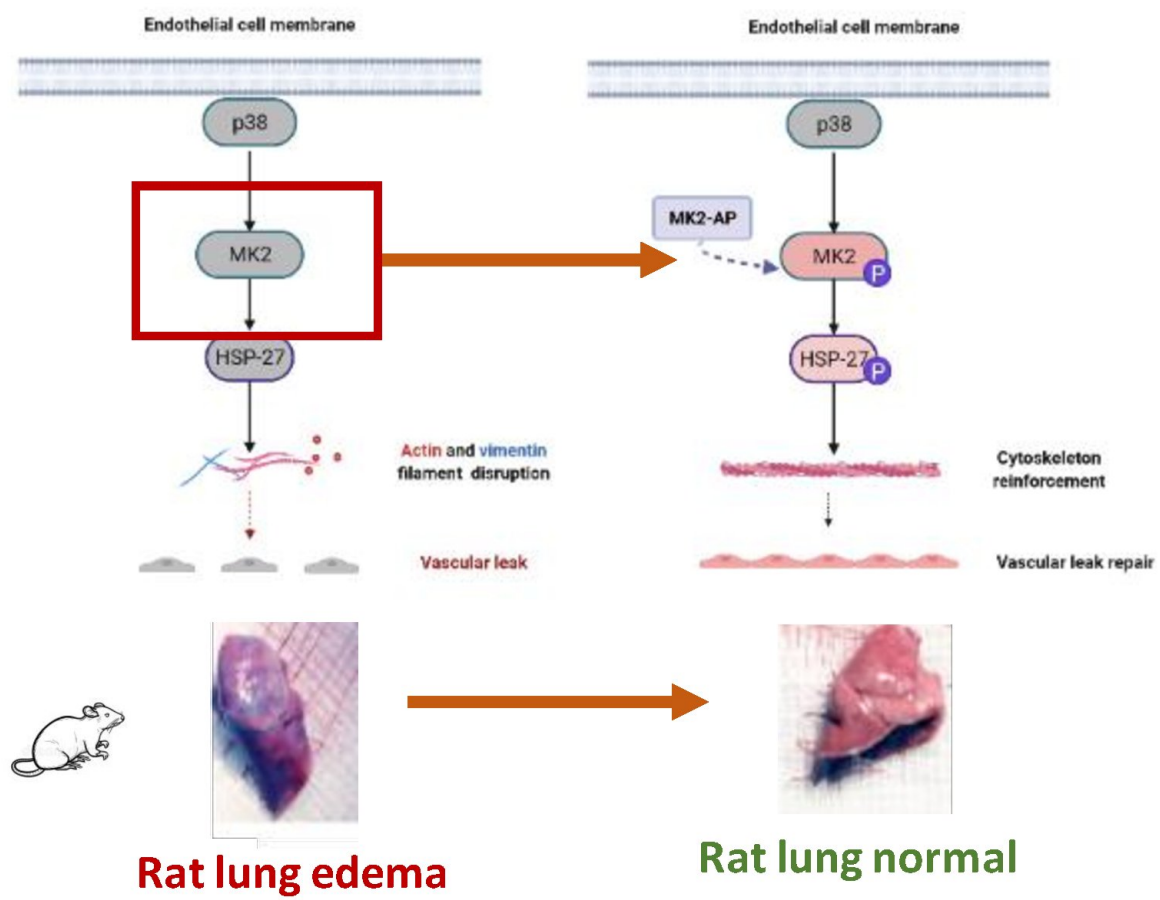
## MK2 as the target:

- **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




https://pubmed.ncbi.nlm.nih.gov/26066827/
Liu, Kayyali, J. Appl. Physiol, 2015

# 2021: AIDE$^{360}$ identifies small molecule MK2 activators

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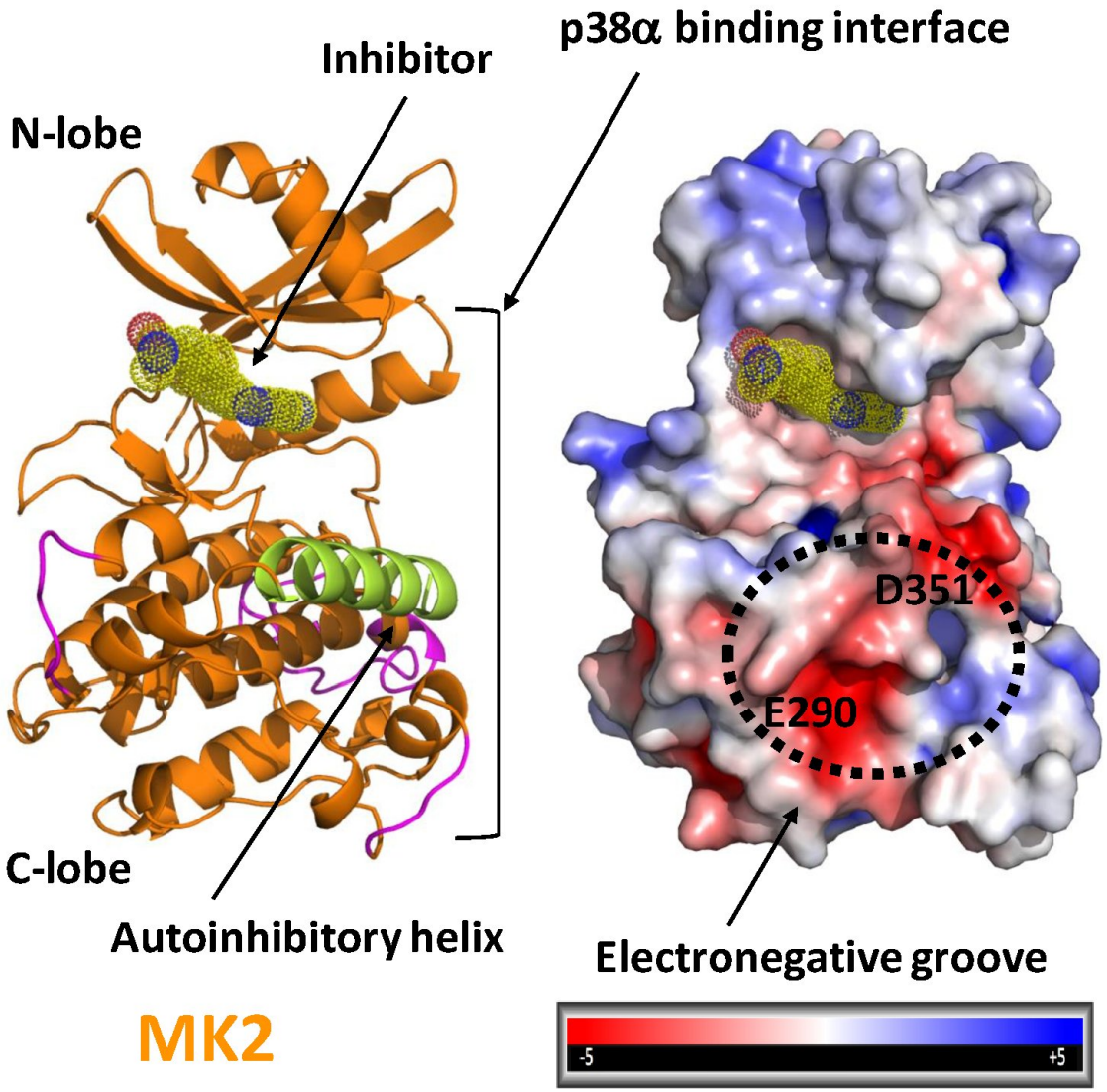


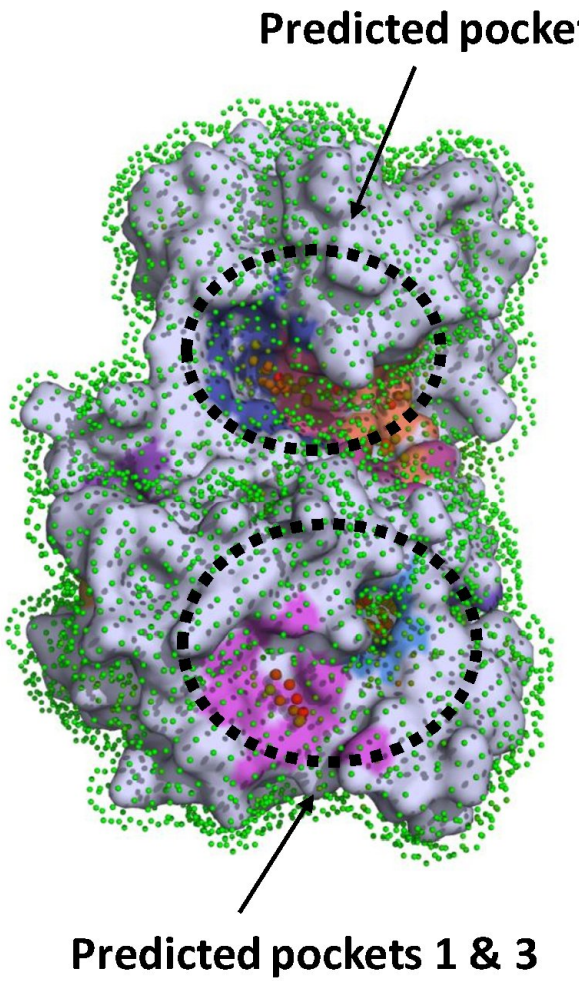


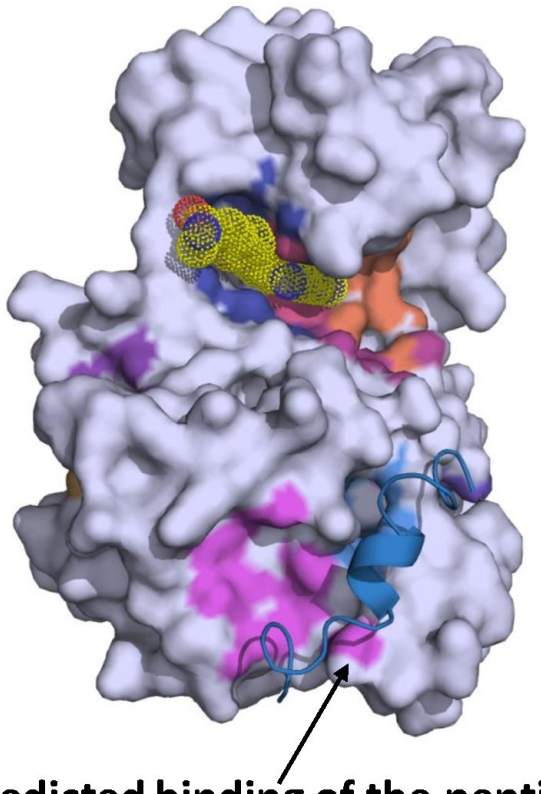

# Clinical candidate selection process

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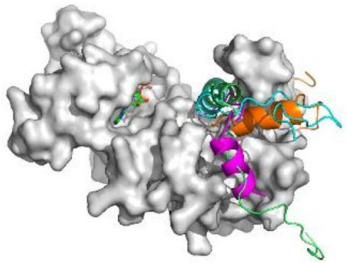
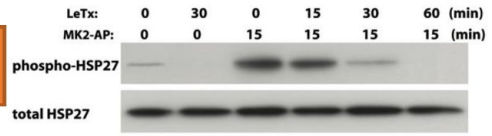
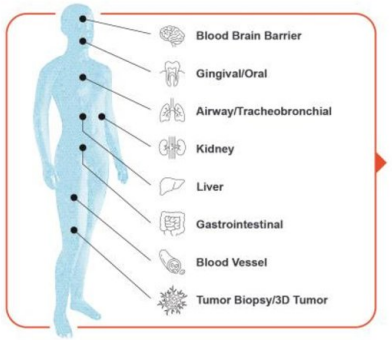


IP status




***In silico* prediction model**

Docking energy

ADMET filters

**Target activity**

MK2 binding

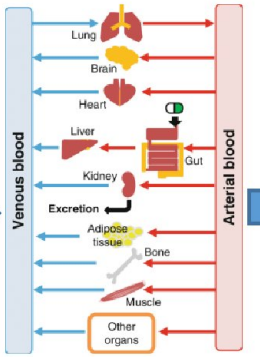
MK2 activation

**Barrier Assays**

In vivo disease model

Human lung 3D

DRAPER




***PBPK modeling***

**Clinical Candidate**

***In silico* model optimization**

# AIDE$^{360}$: speed and precision

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

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

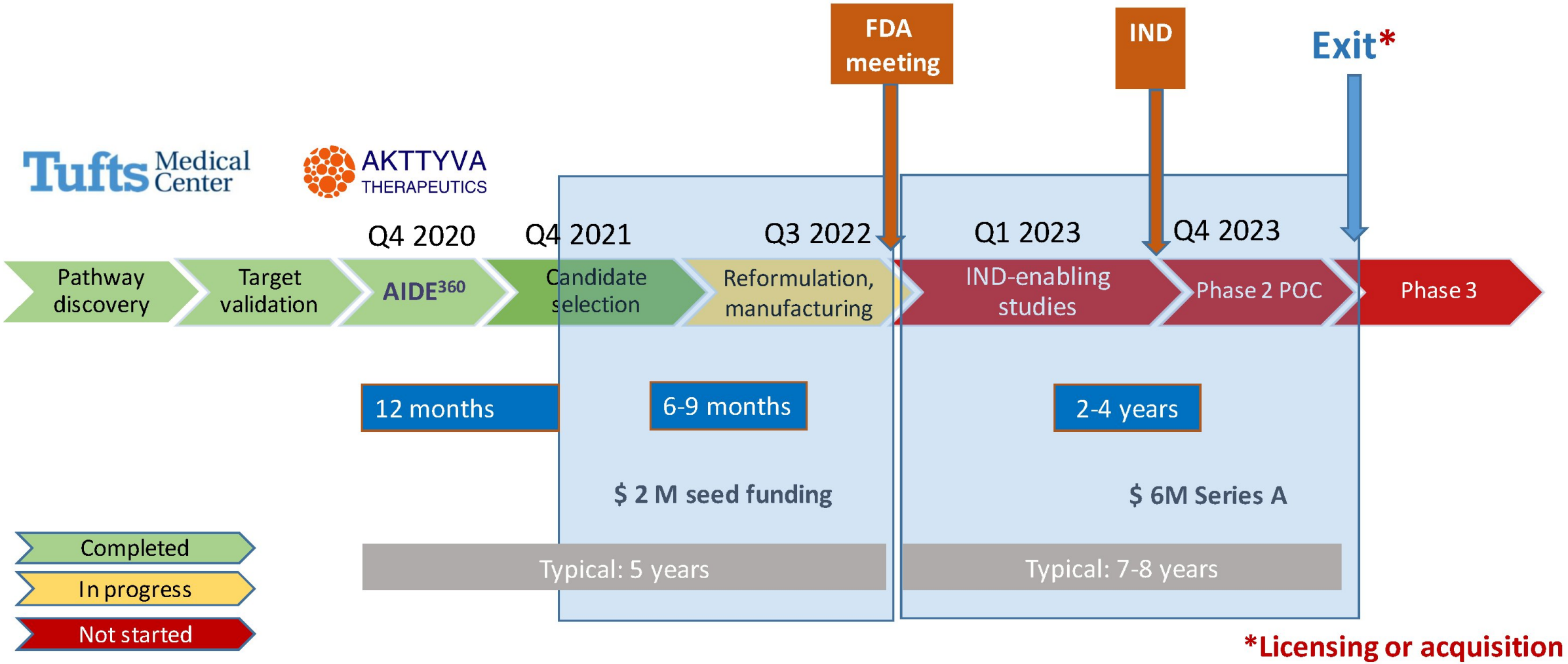
**Hit rate = drug discovery success rate in finding bioactive molecules**

| Target A | Target A | Target MK2 |
|---|---|---|
| **High-throughput Screen (vitro - 2015)** | **Virtual Screen (silico + vitro 2016)** | **Virtual Screen (silico + vitro 2021)** |
| **10000 cmpds tested**<br>**10 hits**<br>5 with $IC_{50}$ > 20 microM<br>2 with $IC_{50}$ between 10 and 20 microM<br>3 with $IC_{50}$ < 10 microM | **500 cmpds tested**<br>**6 hits**<br>2 with $IC_{50}$ < 20 microM<br>4 with $IC_{50}$ < 10 microM | **54 cmpds tested**<br>**5 hits**<br>4 with $EC_{50}$ between 15 and 20 microM<br>1 with $IC_{50}$ < 10 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



# Funding needs and IP

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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 AIDE$^{360}$ for NCE discovery for the next vascular leak indication

AIDE$^{360}$ 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)

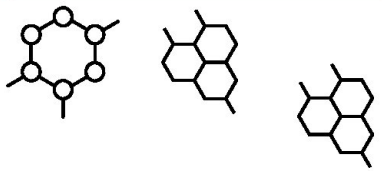
# Akttyva Business Model

**Partnered Programs**

Drug targets


**Internal Programs**

Leads



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

# Progress and Traction

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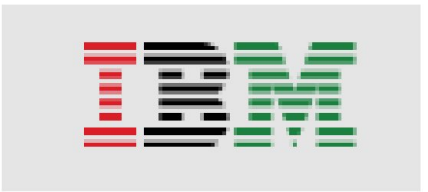
- ✓ AIDE$^{360}$ platform in place:
  - ✓ Utilized for MK2 target:
    - ✓ More than 7,000 existing drugs have been docked to the MK2 pocket
    - ✓ >100 candidate drugs for repurposing identified
    - ✓ Activity assay established in the lab
    - ✓ 5 lead candidates identified based on experimental activity
- ✓ Lead candidate selected for clinical development in ARDS
- ✓ **IBM partnership on AIDE$^{360}$: 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

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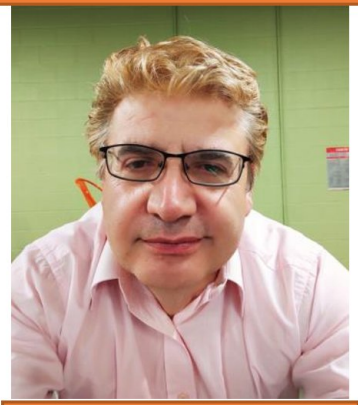
Serial entrepreneur, De-risking drug candidates

## CEO, Board Director

**Katya Tsaioun, Ph.D.** – 20+ years in biopharma; successful entrepreneur (founded Apredica, 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

Investor

cyprotex the ADME Tox specialists



Assay development, biology

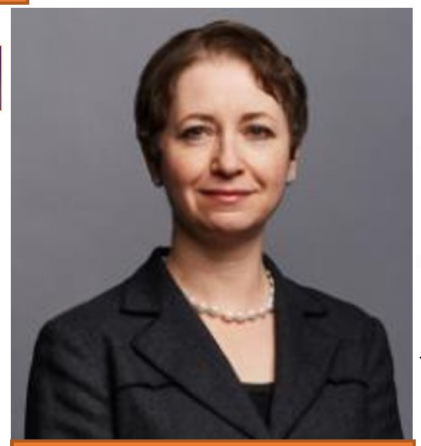
## Head of Research

Biogen

**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

Investor

charles river



Intellectual property

## 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

ARRANTABIO

ThermoFisher SCIENTIFIC

brammer bio

Pathway discovery and validation

## 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.

Tufts Medical Center

Biomolecular modeling

## 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

Inserm La science pour la santé From science to health

Corporate strategy

RXi

CORBUS PHARMACEUTICALS

## 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.





Bristol-Myers Squibb

# Advisors and mentors

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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

BRIGHAM HEALTH
BWH BRIGHAM AND WOMEN'S HOSPITAL

IBM

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).

# Summary

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- 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

AKTTYVA THERAPEUTICS

Inventors of proprietary virtual screening platform AIDE$^{360}$

**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:

Katya Tsaioun

Katya@akttyva.com

617-821-7095

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Thank you!