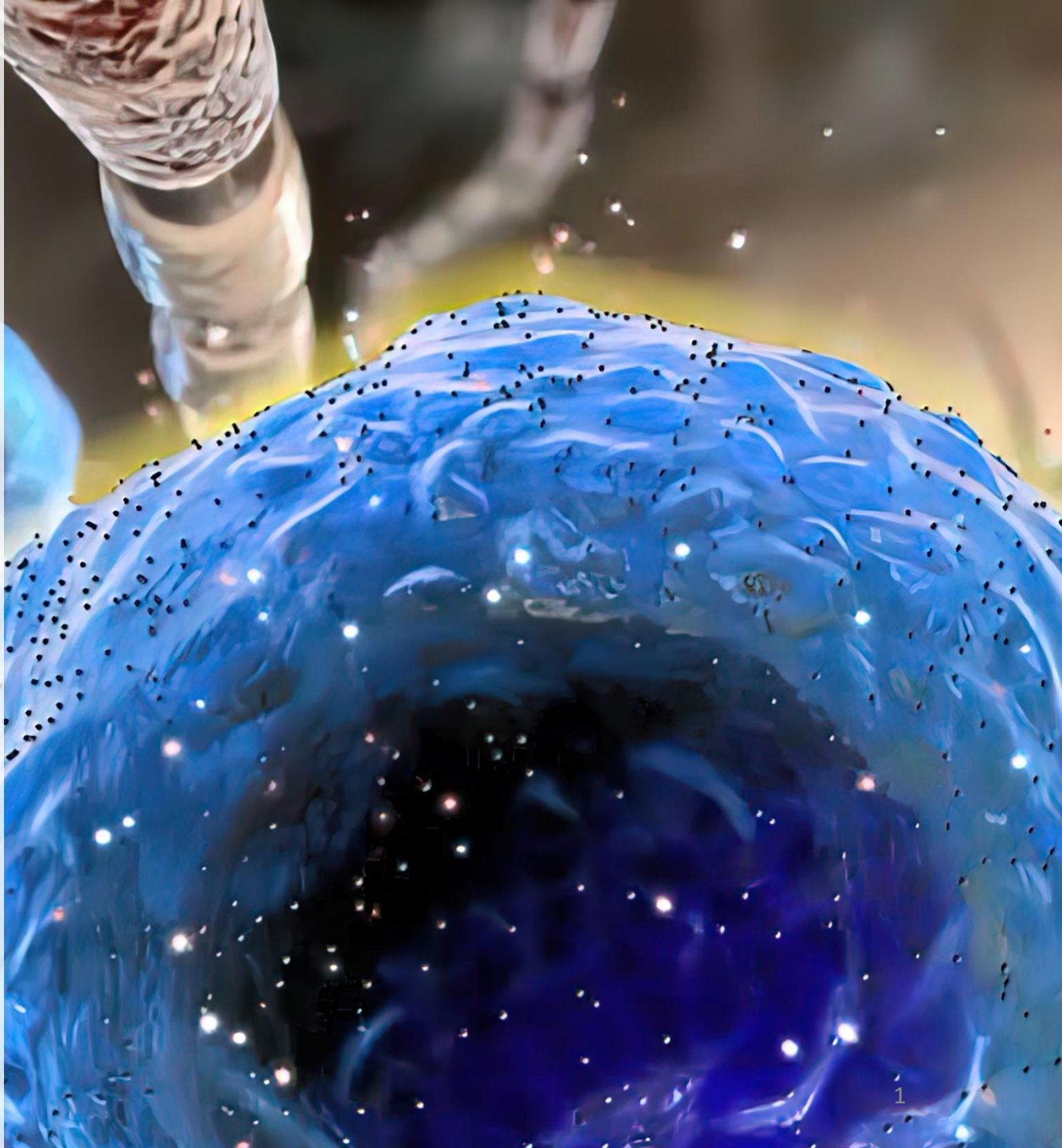
Akari Therapeutics

A Multi-Faceted Biotech Company

Q4-2024



Forward-Looking Statements

This communication relates to the proposed transaction pursuant to the terms of the Merger Agreement, by and among Akari, Pegasus Merger Sub, Inc., and Peak Bio. This communication includes express or implied forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), about the proposed transaction between Peak Bio and Akari and the operations of the combined company that involve risks and uncertainties relating to future events and the future performance of Akari and Peak Bio. Actual events or results may differ materially from these forward-looking statements. Words such as "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "future," "opportunity" "will likely result," "target," variations of such words, and similar expressions or negatives of these words are intended to identify such forward-looking statements, although not all forward-looking statements contain these identifying words. Examples of such forward-looking statements include, but are not limited to, express or implied statements regarding: the business combination and related matters, including, but not limited to, satisfaction of closing conditions to the proposed transaction, prospective performance and opportunities with respect to Akari or Peak Bio, post-closing operations and the outlook for the companies' businesses; Akari's, Peak Bio's or the combined company's targets, plans, objectives or goals for future operations, including those related to Akari's and Peak Bio's product candidates, research and development, product candidate introductions and product candidate approvals as well as cooperation in relation thereto; projections of or targets for revenues, costs, income (or loss), earnings per share, capital expenditures, dividends, capital structure, net financials and other financial measures; future economic performance, future actions and outcome of contingencies such as legal proceedings; and the assumptions underlying or relating to such statements. These statements are based on Akari's and Peak Bio's current plans, estimates and projections. By their very nature, forward-looking statements involve inherent risks and uncertainties, both general and specific. A number of important factors, including those described in this communication, could cause actual results to differ materially from those contemplated in any forward-looking statements. Factors that may affect future results and may cause these forward-looking statements to be inaccurate include, without limitation: uncertainties as to the timing for completion of the proposed transaction; uncertainties as to Peak Bio's and/or Akari's ability to obtain the approval of Akari's shareholders or Peak Bio's stockholders required to consummate the proposed transaction; the possibility that competing offers will be made by third parties; the occurrence of events that may give rise to a right of one or both of Akari and Peak Bio to terminate the merger agreement; the possibility that various closing conditions for the proposed transaction may not be satisfied or waived on a timely basis or at all, including the possibility that a governmental entity may prohibit, delay, or refuse to grant approval, if required, for the consummation of the proposed transaction (or only grant approval subject to adverse conditions or limitations); the difficulty of predicting the timing or outcome of consents or regulatory approvals or actions, if any; the possibility that the proposed transaction may not be completed in the time frame expected by Akari and Peak Bio, or at all; the risk that Akari and Peak Bio may not realize the anticipated benefits of the proposed transaction in the time frame expected, or at all; the effects of the proposed transaction on relationships with Akari's or Peak Bio's employees, business or collaboration partners or governmental entities; the ability to retain and hire key personnel; potential adverse reactions or changes to business relationships resulting from the announcement or completion of the proposed transaction; significant or unexpected costs, charges or expenses resulting from the proposed transaction; the potential impact of unforeseen liabilities, future capital expenditures, revenues, costs, expenses, earnings, synergies, economic performance, indebtedness, financial condition and losses on the future prospects, business and management strategies for the management, expansion and growth of the combined business after the consummation of the proposed transaction; potential negative effects related to this announcement or the consummation of the proposed transaction on the market price of Akari's American Depositary Shares or Peak Bio's common stock and/or Akari's or Peak Bio's operating or financial results; uncertainties as to the long-term value of Akari's American Depositary Shares (and the ordinary shares represented thereby), including the dilution caused by Akari's issuance of additional American Depositary Shares (and the ordinary shares represented thereby) in connection with the proposed transaction; unknown liabilities related to Akari or Peak Bio; the nature, cost and outcome of any litigation and other legal proceedings involving Akari, Peak Bio or their respective directors, including any legal proceedings related to the proposed transaction; risks related to global as well as local political and economic conditions, including interest rate and currency exchange rate fluctuations; potential delays or failures related to research and/or development of Akari's or Peak Bio's programs or product candidates; risks related to any loss of Akari's or Peak Bio's patents or other intellectual property rights; any interruptions of the supply chain for raw materials or manufacturing for Akari or Peak Bio's product candidates, the nature, timing, cost and possible success and therapeutic applications of product candidates being developed by Akari, Peak Bio and/or their respective collaborators or licensees; the extent to which the results from the research and development programs conducted by Akari, Peak Bio, and/or their respective collaborators or licensees may be replicated in other studies and/or lead to advancement of product candidates to clinical trials, therapeutic applications, or regulatory approval; uncertainty of the utilization, market acceptance, and commercial success of Akari's or Peak Bio's product candidates, and the impact of studies (whether conducted by Akari, Peak Bio or others and whether mandated or voluntary) on any of the foregoing; unexpected breaches or terminations with respect to Akari's or Peak Bio's material contracts or arrangements; risks related to competition for Akari's or Peak Bio's product candidates; Akari's or Peak Bio's ability to successfully develop or commercialize Akari's or Peak Bio's product candidates; Akari's, Peak Bio's, and their collaborators' abilities to continue to conduct current and future developmental, preclinical and clinical programs; potential exposure to legal proceedings and investigations; risks related to changes in governmental laws and related interpretation thereof, including on reimbursement, intellectual property protection and regulatory controls on testing, approval, manufacturing, development or commercialization of any of Akari's or Peak Bio's product candidates; unexpected increase in costs and expenses with respect to the potential transaction or Akari's or Peak Bio's business or operations; and risks and uncertainties related to epidemics, pandemics or other public health crises and their impact on Akari's and Peak Bio's respective businesses, operations, supply chain, patient enrollment and retention, preclinical and clinical trials, strategy, goals and anticipated milestones. While the foregoing list of factors presented here is considered representative, no list should be considered to be a complete statement of all potential risks and uncertainties. There can be no assurance that the proposed transaction or any other transaction described above will in fact be consummated in the manner described or at all. A more complete description of these and other material risks can be found in Akari's and Peak Bio's respective filings with the U.S. Securities and Exchange Commission (the "SEC"), including each of their Annual Reports on 10-K, for the year ended December 31, 2023 and 2022, respectively, subsequent periodic reports, and other documents that may be filed from time to time with the SEC. These risks, as well as other risks associated with the proposed transaction, are more fully discussed in the joint proxy statement/prospectus that are included in the registration statement on Form S-4 that was filed with the SEC on September 13, 2024 in connection with the proposed transaction. Such joint proxy statement/prospectus will be mailed or otherwise disseminated to Akari's shareholders and Peak Bio's stockholders when it becomes available. Any forward-looking statements speak only as of the date of this communication and are made based on the current beliefs and judgments of Akari's and Peak Bio's management, and the reader is cautioned not to rely on any forward-looking statements made by Akari or Peak Bio. Unless required by law, neither Akari nor Peak Bio is under no duty and undertakes no obligation to update or revise any forward-looking statement after the distribution of this document, including without limitation any financial projection or guidance, whether as a result of new information, future events or otherwise.

Additional Disclosures

Additional Information and Where to Find It

The Registration Statement on Form S-4 includes a prospectus of Akari and a joint proxy statement of Akari and Peak Bio. INVESTORS AND SECURITY HOLDERS ARE URGED TO READ CAREFULLY THE REGISTRATION STATEMENT ON FORM S-4, JOINT PROXY STATEMENT/PROSPECTUS AND OTHER RELEVANT DOCUMENTS FILED WITH THE SEC, AS WELL AS ANY AMENDMENTS OR SUPPLEMENTS THERETO AND ANY DOCUMENTS INCORPORATED BY REFERENCE THEREIN, IN THEIR ENTIRETY BECAUSE THEY CONTAIN IMPORTANT INFORMATION ABOUT THE PROPOSED TRANSACTION, RELATED MATTERS AND THE PARTIES TO THE PROPOSED TRANSACTION.

You may obtain a free copy of the Registration Statement on Form S-4, joint proxy statement/prospectus and other relevant documents that are on file with the SEC for free at the SEC's website at www.sec.gov. Copies of the documents filed with the SEC by Akari are available free of charge on Akari's website at http://investor.akaritx.com/ or by contacting Akari's Investor Relations Department at http://investor.akaritx.com/investor-resources/contact-us. Copies of the documents filed with the SEC by Peak Bio are available free of charge on Peak Bio's website at https://peak-bio.com/investors or by contacting Peak Bio's Investor Relations Department at https://peak-bio.com/contact.

Participants in the Solicitation

Akari and Peak Bio and certain of their respective directors, executive officers, other members of management and employees, under SEC rules, may be deemed to be participants in the solicitation of proxies from the securityholders of Akari and Peak Bio in favor of the Business Combination. Securityholders of Akari and Peak Bio and other interested persons may obtain more information regarding the names and interests of Akari and Peak Bio directors and officers in the Business Combination in Akari and Peak Bio filings with the SEC, including in the definitive proxy statement/ prospectus, included in the Registration Statement. These documents can be obtained free of charge from the sources indicated above.

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Merger of Akari Therapeutics and Peak Bio Creates a Multi-Faceted Biotech Company

Diverse pipeline provides potential for multiple shots on goal

- *TROP2 PH1 ADC*: Antibody-drug conjugate (ADC) – pre-clinical program for solid tumors
- *PAS-nomacopan*: Geographic atrophy (GA) – pre-clinical program for ophthalmology
- *PHP 303 and nomacopan*: Multiple indications – phase 3-ready program offers near-term BD potential

Lead assets in areas of high unmet medical need provide multi-billion-dollar market opportunities in oncology and geographic atrophy

- Combines high unmet needs and large markets in oncology and ophthalmology
- Solid tumors represent ~90% of all tumors
- It is estimated that >1 million people in the USA have geographic atrophy

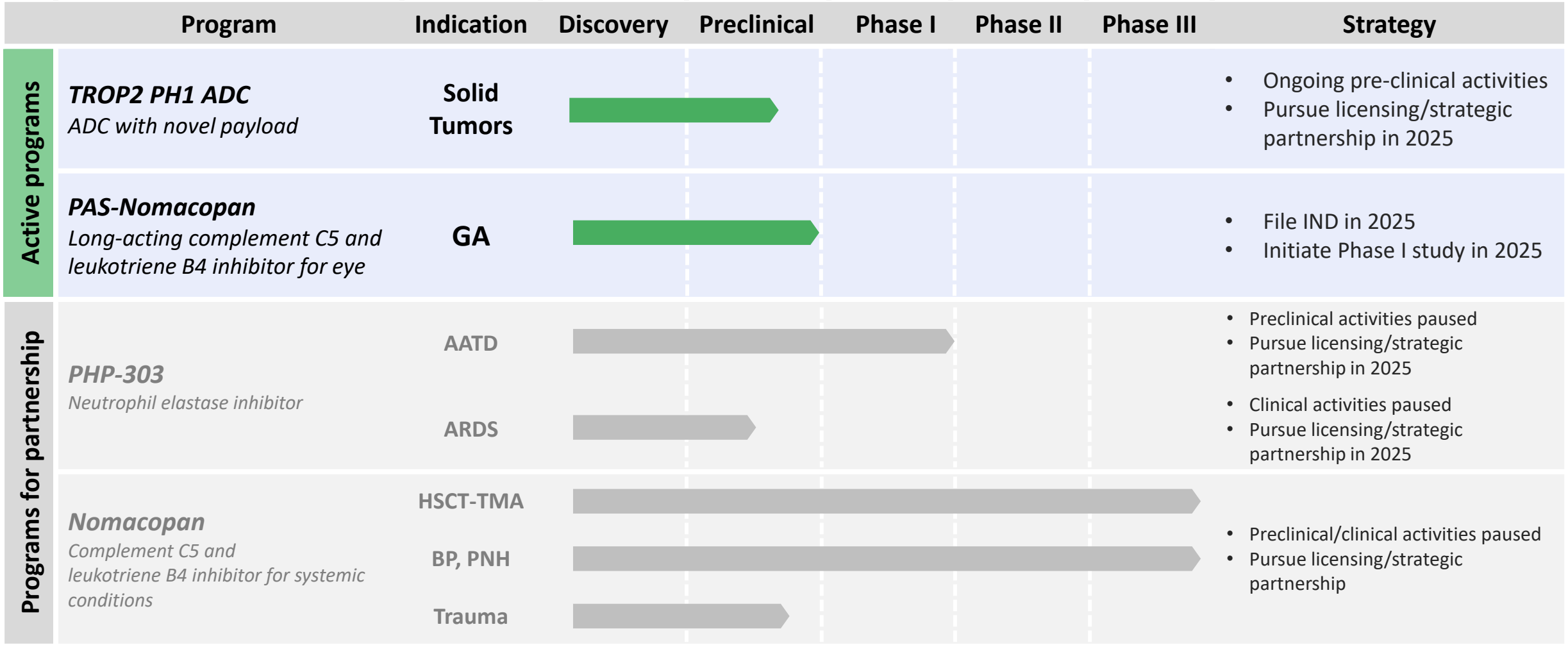
Lead programs leverage unique mechanisms of action backed by robust preclinical data sets that point to potential clinical benefit

- ADC franchise includes a wide array of cleavable and non-cleavable linkers as well as a payload that modulates the spliceosome
- PAS-nomacopan is a long-acting bispecific inhibitor of C5 and LBT4 in development for geographic atrophy
- Protected by broad intellectual property coverage

Merger brings end-to-end capabilities with a combined management team and board that brings proven track record of value creation in life sciences

- Merger results in significant operational efficiency for the company
- Funds to finance multiple value-creating near-term milestones

Prioritized Pipeline Focuses on Areas of High Unmet Medical Need



GA=Geographic atrophy. AATD= Alpha-1 anti-trypsin deficiency. ARDS= Acute respiratory distress syndrome. HSCT-TMA= Hematopoietic stem cell transplant-associated thrombotic microangiopathy. BP= Blood pressure. PNH= Paroxysmal nocturnal hemoglobinuria.

Led by a Management Team With Extensive Experience in Life Sciences

Samir Patel, M.D.
Interim President & CEO

Strategic leader with extensive operational, financial and commercial experience

dell children's medical center of central texas · CytoDyn · REZOLUTE · centocor · Johnson & Johnson · PranaBio INVESTMENTS

Wendy F. DiCicco
Interim CFO

Strategic financial leader with extensive background in life sciences

CENTINEL SPINE · FerGene · Imvax · EYEPOINT PHARMACEUTICALS · GLOBUS MEDICAL · quench · RENOVACOR

Miles Nunn
Chief Scientific Officer

Inventor of nomacopan and innovative scientist and discoverer

AKARI THERAPEUTICS · UK CEH · University of Oxford

Hoyoung Huh, M.D., Ph.D.
Chairman

Visionary investor/entrepreneur involved in start-up, management, and boards of numerous healthcare companies

4DMT · BiPar sciences · eidos · Facet Biotech · NEKTAR · PLIANT · REZOLUTE

Antibody Drug Conjugate (ADC)

- *Innovative platform*

Our ADCs Leverage Novel Linker Technology and Mechanism of Action

Traditional ADC Approach

Targeted killing of cancer cells by specific antibody coupled to a cytotoxic (payload)

- Over 70% of payloads in currently approved ADCs target tubulin or DNA*
- Industry standard payloads can have off-target effects and toxicities (e.g. ocular, hematologic, peripheral neuropathy) that may limit their use
- Majority of current payloads are substrates of drug efflux transporters called multi-drug resistance transporters permitting development of drug resistance in some cancer patients

**Topoisomerase and microtubule inhibitor payloads inhibit DNA replication and cancer cell division and* pyrrolobenzodiazepines (*PBD) payloads cross-link DNA*

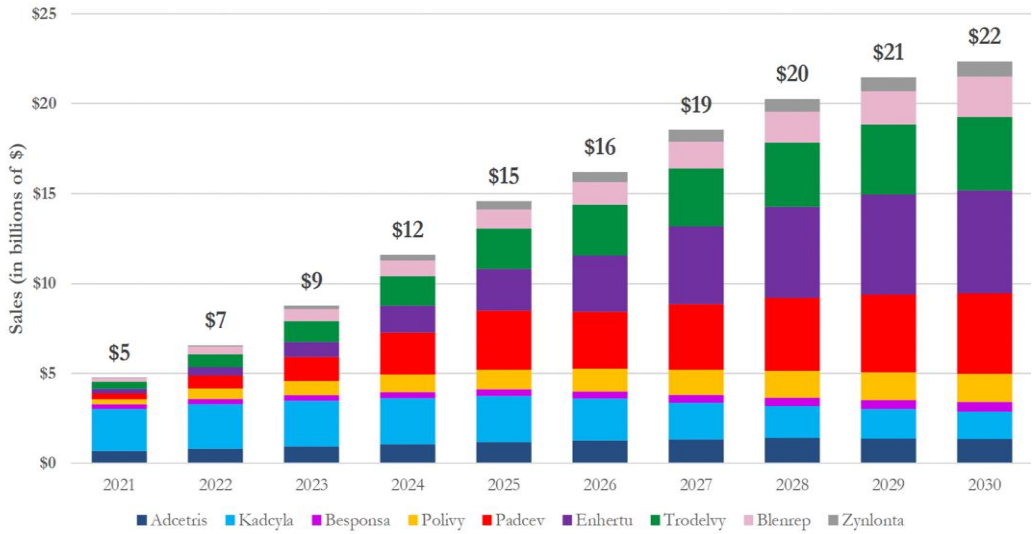
How is our ADC approach different?

Highly targeted killing of cancer cells and more potent engagement of immune system to kill cancer

- Differentiated **novel payloads** targeting proper **splicing of introns** (PH-1), **DNA mismatch repair** (PH-5) and **immune system mediated killing** of co-opted tumor cells/pro-tumor cells (PH-6)
- PH1 **enhances tumoricidal activity** beyond immediate cytotoxicity by **creating neoepitopes**, providing a 1-2 punch of initial cytotoxicity followed by prolonged immune-mediated cell death
- PH1 induced immune memory (B and T cells) can potentially re-engage when treated cancers recur countering resistance due to loss of target expression.
- PH1 has differentiated toxicity, relative to industry standard payloads
- PH1 (and potentially PH5 and PH6) payload is a poor substrate for MDR transporters that may decrease risk of patient developing drug resistance

ADC Market is Projected to Reach Over $22B by 2030

Approved Therapies Projected Revenue: $22B+ by 2030[1]



Note: Does not include Mylotarg or Lumoxiti as not broken out in consensus estimates; Padcev's ex-US portion/ Enhertu consensus estimates based off Astellas/ Daiichi's calendarization;
Note: Kadcyla/Polivy consensus in CHF, Blenrep in GBP; Padcev ex-US portion consensus portion in JPY; Converted to USD using 12/31/20 conversion rate

- ADC market projected to grow > 20% over the next few years
- Global Trop2 market expected to surpass $4 billion by 2026[1]
- Key Trop2 antibody market competitors include Daiichi Sankyo/AstraZeneca and Immunomedics/Gilead

*Strong Deal Flow Even for Pre-Clinical ADC Assets**

Partners	Asset	Target	Deal Type	Date	Phase	Deal Value
Multitude Therapeutics and Adcendo	ADCE-T02 ADC	Tissue Factor	Licensing	Aug-24	Pre-clinical	Upfront not revealed; Potentially >1b in milestones, Single-digit to low double-digit tiered royalties
Kelun-Biotech and Merck	SKB571	Undisclosed	Licensing	Aug-24	Pre-clinical	$35m upfront, $37.5m on option exercise, undisclosed sales milestones and tiered royalties
Aarvik Therapeutics and ArriVent BioPharma	Undisclosed ADC, novel platform	Unknown	Strategic Collaboration & Licensing	Aug-24	Pre-clinical	Upfront and opt-in undisclosed. Research funding, Option fees, and milestones ~$100m plus royalties
Biocytogen & Sotio and Ideaya Biosciences	Bispecific ADC	B7H3 x PTK7	Licensing	Jul-24	Pre-clinical	$6.5m Opt-in, $400m in milestones including $100m tied to development and regulatory events
Mabcare Therapeutics and DayOne	DAY301/ MTX-13	PTK-7	Licensing	Jun-24	Pre-clinical (IND enabled)	$55M upfront; Up to $1.2B exclusive commercial rights
Medilink and BioNtech	TMALIN ADC platform	Undisclosed	Licensing	May-24	Pre-clinical	$25M upfront; Up to $1.8B in milestones
Caris and Merck KGaA	Targets	Undisclosed	Licensing	Apr-24	Pre-clinical	Up to $1.4B in milestones
Sutro Biopharma and Ipsen	STRO-003	ROR1	Licensing	Apr-24	Pre-clinical	$90M upfront; Phase 1 by Ipsen $900M in milestones
AstraZeneca and LaNova	LM-305	GPRC5D	Licensing	May-23	Pre-clinical (IND approved)	$55M upfront; $545M milestones
BMS and Tubulis	Tubutecan payloads and p5 conjugation platform	Undisclosed	Collaboration	Apr-23	Pre-clinical	$22.75M upfront; $1B milestones
Merck and Kelun-Biotech	Undisclosed	Undisclosed	Licensing	Jul-22	Pre-clinical	$35M upfront; $901M milestones
ImmunoGen and Lilly	Camptothecins	Undisclosed	Licensing	Feb-22	Pre-clinical	$13M+$32.5M upfront; $1.7B milestones
Mersana and Janssen	Discovery of new ADCs	Up to 3 targets	Collaboration	Feb-22	Pre-clinical	$40M upfront; $1B milestones

* Does not reflect all preclinical ADC deals. Deals with undisclosed deal values left out. For e.g., Sony Corp. and Astellas (May-23), Ajinomoto and Exelixis (Jan-23), Sanofi and Seagen (Mar-22) etc.

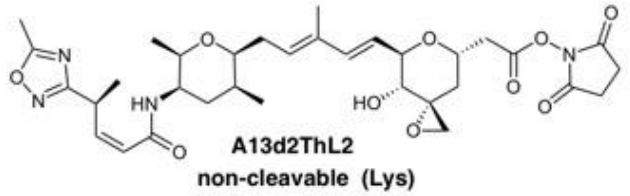
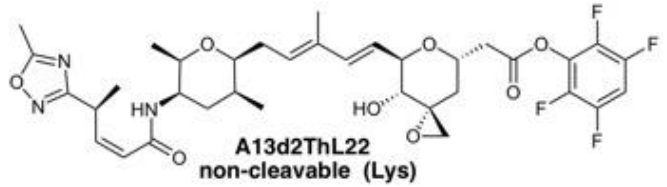
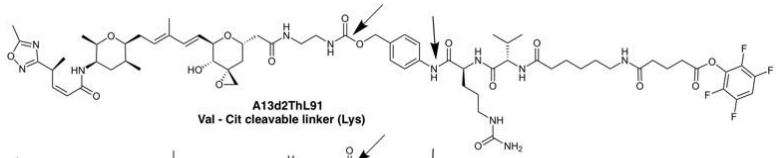
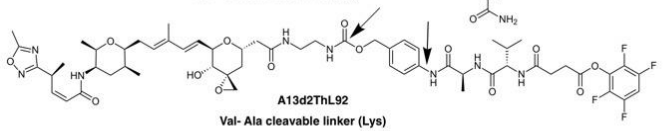
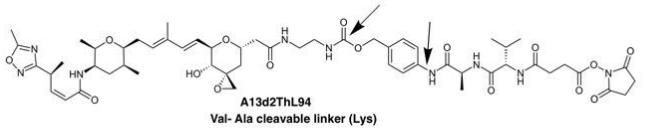
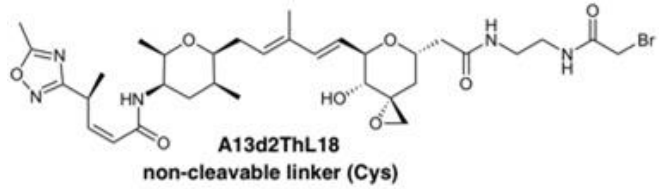
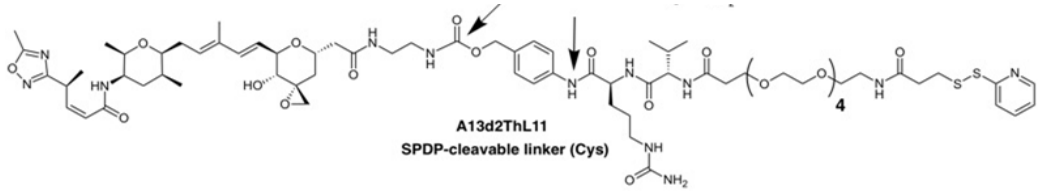
1. Evercore ISI Market Research Report: Health Care | Biotechnology / Drug Discovery, DEEP DIVE on ADCs - The Time Is Right, Now; June 2021
2. Global TROP2 Antibody Market & Clinical Trials Insight 2026; (Global TROP2 Antibody Market & Clinical Trials Report 2021-2026 - Ongoing Clinical Trials Assessment by Status, Phase & Region December 21, 2021 |Other Source(s): https://njbio.com/antibody-drug-conjugates/ and corporate websites (see deal table)

Novel Payload Platforms

- *Most advanced payload PH1 targets the spliceosome*
- *Linker toolkit for PH1 – leverages both cleavable and non-cleavable mechanisms*
- *Novel mechanisms of action*
  - *Generation of neoepitopes*
  - *Secondary immune mechanism of action*
  - *Selected for lack of binding to MDR transporters*

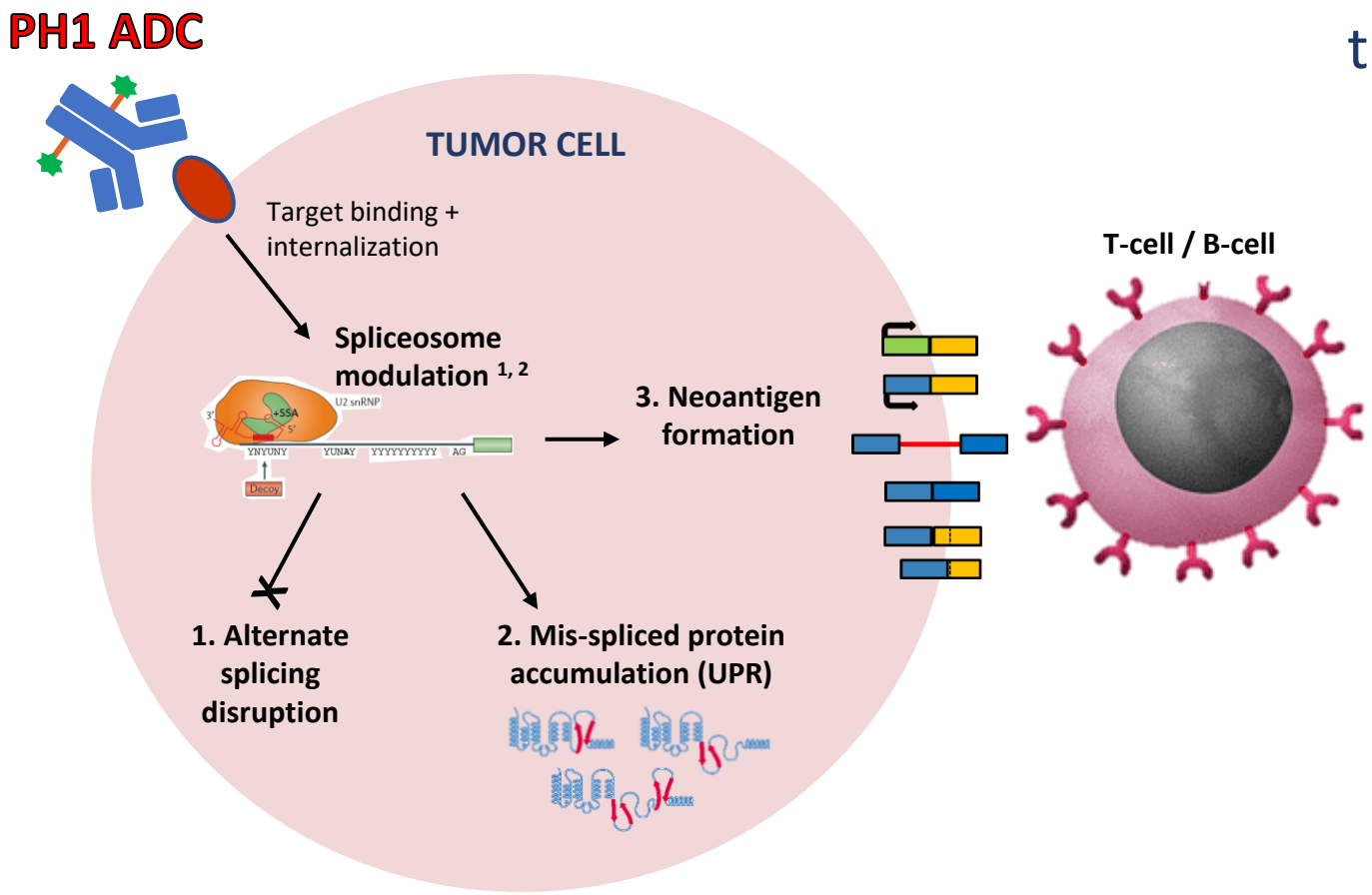
We Have Developed a Diverse Toxin Linker Toolkit for PH1 ADCs

Our Library Permits Selection of Optimal Linker for PH1 ADC Cytotoxic Potency*

Linkers	Non-Cleavable	Cleavable
Lys	L2  A13d2ThL2 non-cleavable (Lys) L22 (PH1)  A13d2ThL22 non-cleavable (Lys)	L91  A13d2ThL91 Val - Cit cleavable linker (Lys) L92  A13d2ThL92 Val- Ala cleavable linker (Lys) L94  A13d2ThL94 Val- Ala cleavable linker (Lys)
Cys	L18  A13d2ThL18 non-cleavable linker (Cys)	L11  A13d2ThL11 SPDP-cleavable linker (Cys)

*Tested *in vivo*.

PH1 Payload Is a Spliceosome Modulator With a Multi-Pronged Anti-Tumor Activity



By targeting normal splicing and tumor specific splicing of introns PH1:

1. **Disrupts tumor specific alternative splicing**, a fundamental process for tumor transformation and growth. Resulting mRNA decay deprives cancer cells of essential proteins.
2. **Causes accumulation of mis-spliced proteins** (majority of transcripts) inducing cell death by unfolded protein response (UPR) and endoplasmic reticulum stress.
3. **Generates neoantigens** (rare transcripts) that can stimulate the immune response.

1. Microbial and Natural Metabolites That Inhibit Splicing: A Powerful Alternative for Cancer Treatment Martínez-Montiel N et al (2016) http://dx.doi.org/10.1155/2016/3681094;
2. Altered RNA Processing in Cancer Pathogenesis and Therapy Obeng et al (2019) https://doi.org/10.1158/2159-8290.CD-19-0399

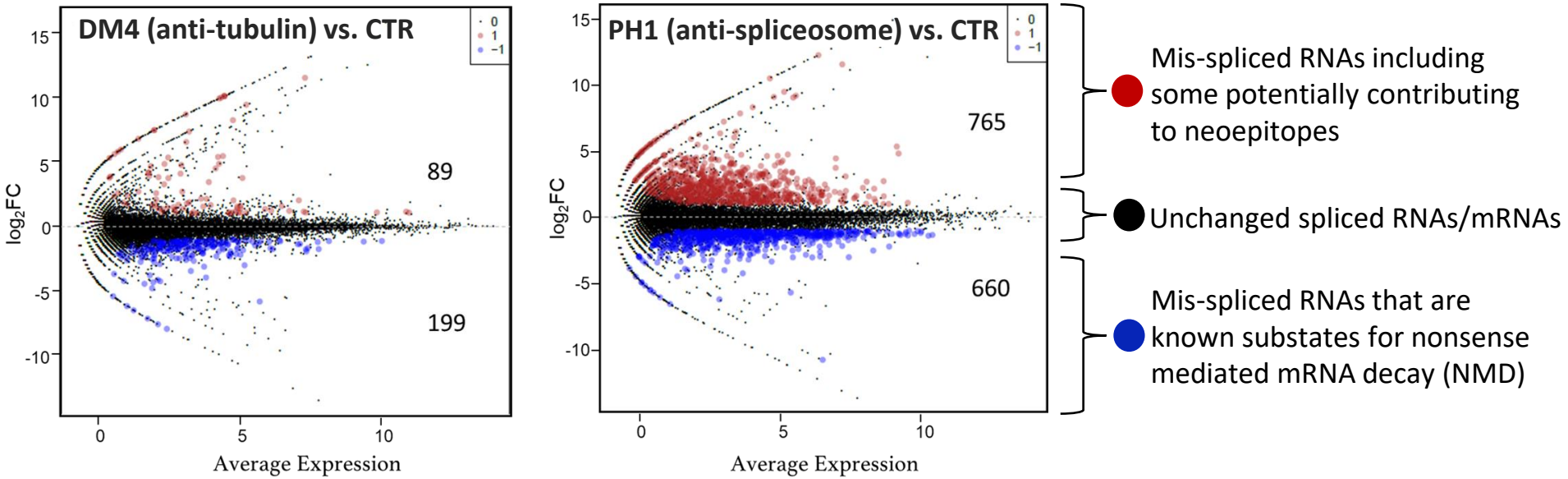
PH1 Greatly Elevates Abundance and Diversity of Mis-Spliced RNA

Average (n=4 wells) expression of spliced RNA transcripts showing effect of DM4 and PH1 payloads compared to control

1 – 2 punch of PH1:

(1) Cytotoxicity by disrupting splicing

(2) Increased neoepitope formation



- Each dot represents a specific RNA derived by splicing
- PH1 treatment markedly increases both number and diversity of mis-spliced RNAs that may be eliminated by NMD (3x DM4) or contribute to neoepitopes (9x DM4)

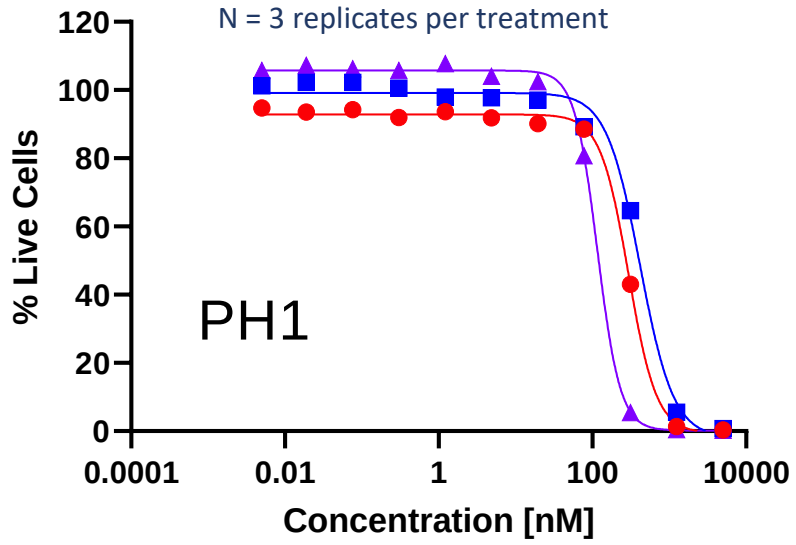
Source(s): Data on file, Internal Peak Bio Research Program reports

PH1 May Prevent Development of MDR-Mediated Resistance

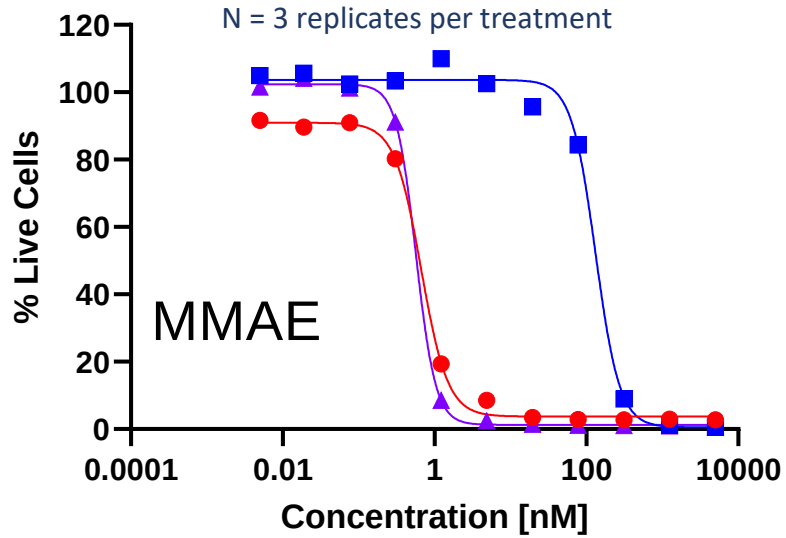
PH1 Is a Poor Substrate for MDR Transporters

Method:
Normal MES-SA cells & MES-SA cells selected for overexpression of MDR transporter 1/2 exposed *in vitro* to PH1 or anti-tubulin payload MMAE (monomethyl auristatin E), in presence or absence of MDR 1/2 inhibitor elacridar

- MES-SA uterine sarcoma cell line
- MES-SA cells expressing high levels of MDR transporter 1 and 2 which can pump toxins out of cells
- MES-SA cells with high MDR expression + MDR inhibitor elacridar



PH1 potency unaffected by overexpression of multidrug resistance (MDR) transporters



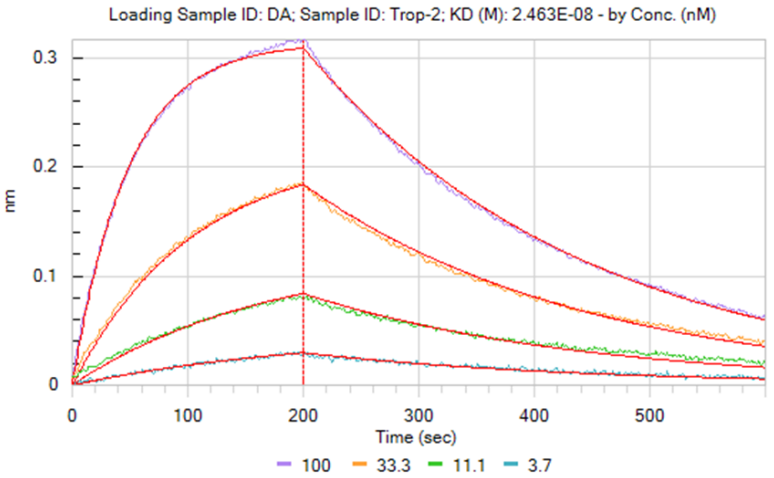
200X higher MMAE concentration required to kill cells overexpressing MDRs; inhibition of MDR 1/2 by elacridar restores MMAE potency

Trop2 PH1 ADC

- *Proprietary Trop2 mAb (M2.1)*
- *Optimization of payload linker*
- *Trophoblast cell surface antigen 2 (Trop2) PH1 ADC*
- *Low off-target activity*
- *Differentiated efficacy in xenograft model*
- *Potential increased efficacy as combination therapy*
- *Differentiated safety in NHP model*

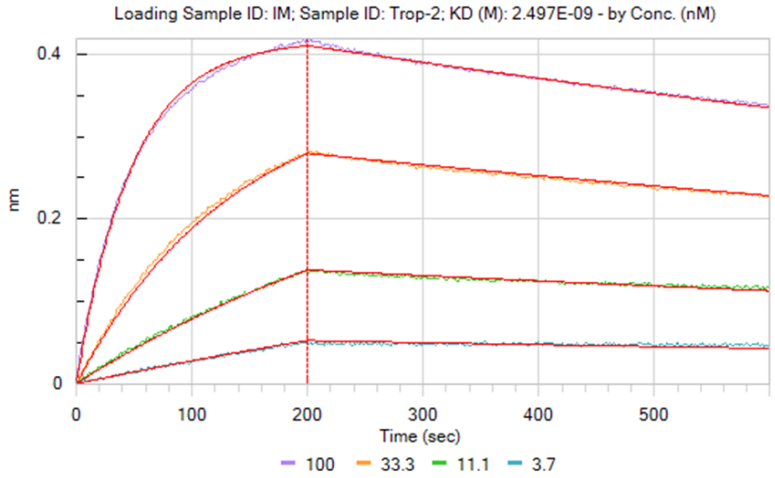
Our Trop2 mAb Demonstrates High Affinity for TROP2 Comparable to Trodelvy®

Daiichi mAb (Datopotamab DXd)



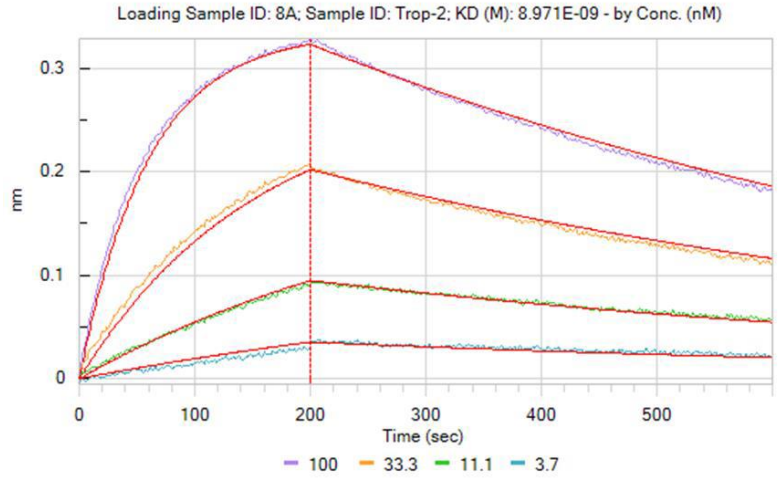
K_d: 24.6nM

Immunomedics mAb (Trodelvy®)



K_d: 2.50nM

PEAK Trop2 mAb (M2.1)



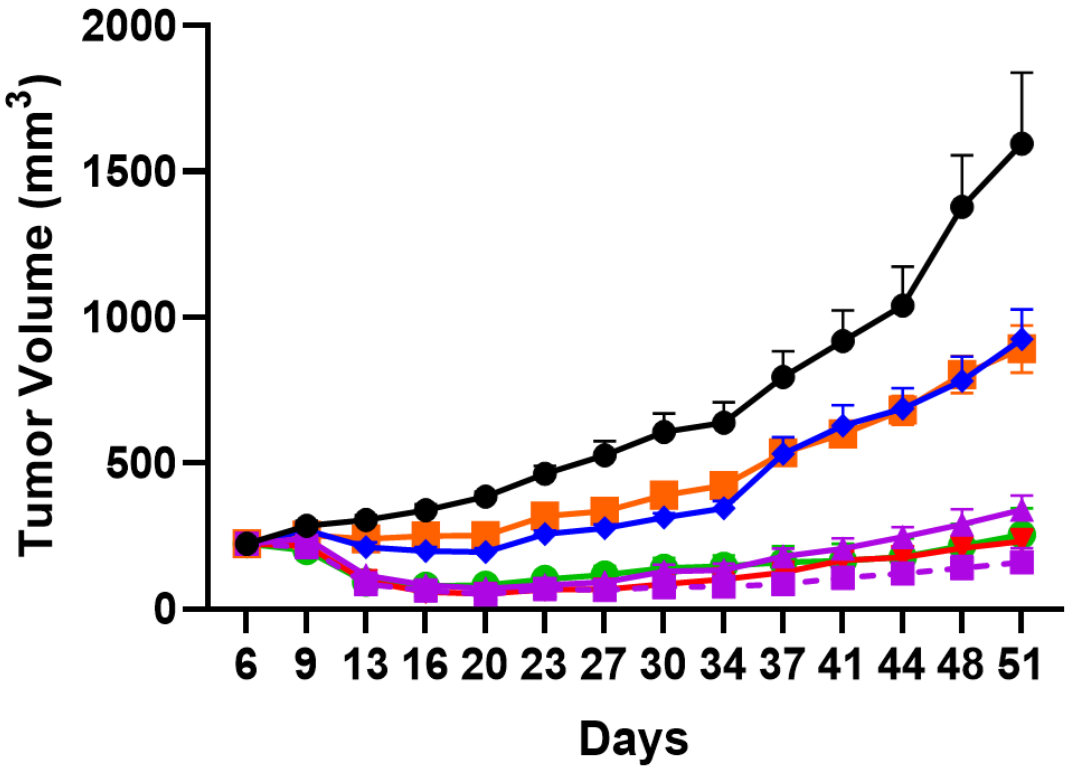
K_d: 8.97nM

- M2.1 variant has high binding affinity akin to that of Immunomedics mAb
- The Daiichi mAb (TINA) has a very distinct profile in comparison to the Immunomedics mAb (hRS7)

These data are derived from different non-clinical studies and clinical trials at different points in time, with differences in study/trial design and patient populations. As a result, comparisons cannot be made and no head-to-head non-clinical studies or clinical trials have been conducted.

Trop2-PH1 ADC Linker Screen for Optimal Efficacy:
Lysine Conjugates With Non-Cleavable Linker Have the Highest Potency

hRS7 IgG1κ monoclonal antibody from Trodelvy® and was conjugated to PH-1 suite of linker toxins L2, L22 (PH1), L18 and L92 at the indicated drug antibody ratios (DAR)



Single dose of each drug at 3mg/kg
NCI-N87 gastric cancer model

		Experimental DAR
Vehicle		
L2 DAR8	Lys Non-cleavable linker	7.8
L2 DAR4	Lys Non-cleavable linker	3.7
L22	Lys Non-cleavable linker	4.5
L18	Cys non-cleavable linker	3.7
L92	Lys cleavable linker	4.5
Kadcyla	Anti-Her2 mAb-DM1, DAR	3.5

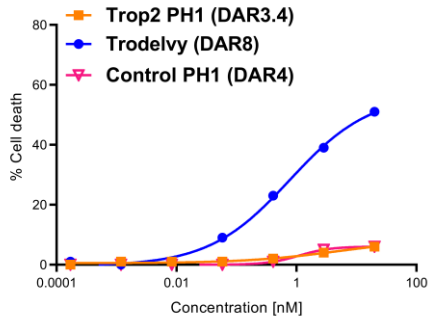
- Potency of Trop2 PH1 with lysine coupled non-cleavable linkers equivalent to Kadcyla in this model
- L2 DAR8 and L2 DAR4 equipotent
- Lysine coupled cleavable linker and cysteine coupled non-cleavable linker less potent

These data are derived from different non-clinical studies and clinical trials at different points in time, with differences in study/trial design and patient populations. As a result, comparisons cannot be made and no head-to-head non-clinical studies or clinical trials have been conducted.

Clinically Validated Trop2 Target as First Named PH1 Program

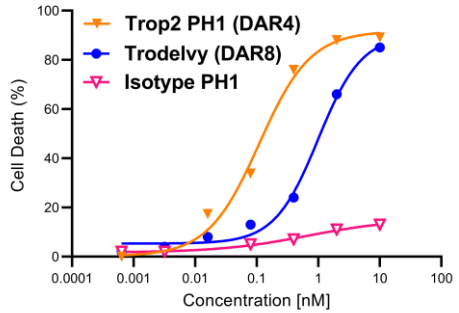
Trop2 PH1 ADC-potent *in-vitro* activity

Normal human fibroblasts



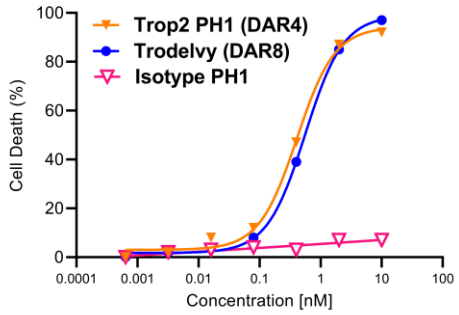
No cytotoxicity against normal human fibroblasts as observed in FIC (Attributed to superior linker stability)

NCI-N87 gastric Trop2^{high}



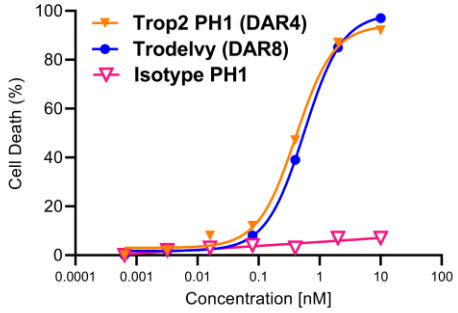
In gastric cancer, superior cytotoxicity at lower DAR than first-in-class (FIC) ADC therapy Trodelvy®

BxPC3 pancreatic Trop2^{high}



In pancreatic cancer cells, comparable cytotoxicity at lower DAR than FIC

RT112/84 bladder Trop2^{heterogenous}



In bladder cancer, comparable cytotoxicity at lower DAR than FIC

- Data (top R figure) shows superior specificity of Trop2 PH1 to cancer cells (possibly due to linker stability) compared to Trodelvy® which exhibits significant toxicity to normal fibroblasts (top L figure)
- Trop2 PH1 equal or more potent than Trodelvy® in NCI-N87 gastric cancer
- Trop2 PH1 equipotent compared to bystander-enabled Trodelvy® in Trop2high BxPC3 pancreatic cancer and in RT112/84 bladder cancer with heterogenous Trop2 expression (bottom R)
- Additional data on Trop2 PH1 killing of a wide range of tumor cell types *in vitro* in backup

SUPPORTS POTENTIAL UTILITY OF Trop2 PH1 ADC IN A WIDE RANGE OF SOLID TUMORS

These data are derived from different non-clinical studies and clinical trials at different points in time, with differences in study/trial design and patient populations. As a result, comparisons cannot be made and no head-to-head non-clinical studies or clinical trials have been conducted.

Payload Superiority of PH1 Over SN-38 on IMMU-132 Antibody Anti-Trop2-PH1 ADC-Induced Tumor Regression Is Dose Dependent

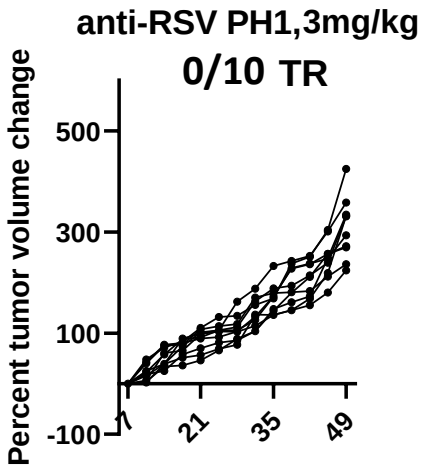
Method:

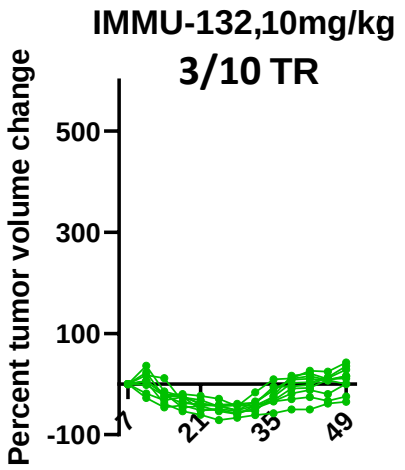
- Human NCI-N87 cell line used to model human gastric adenocarcinoma as subcutaneous xenografts in athymic BALB/c mice lacking an adaptive immune system
- In therapeutic mode, tumors allowed to grow, and mice randomized so average tumor size 200 mm^3 on Day 1
- Mice dosed on Days 1 and 8
- Tumor volumes measured throughout the study

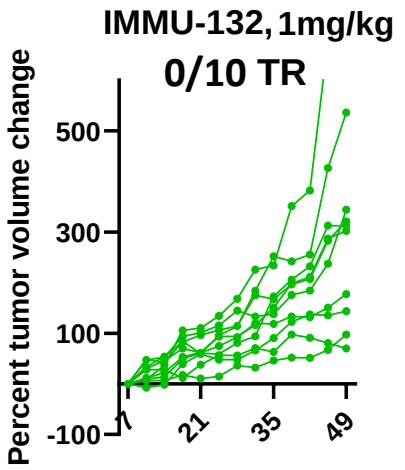
N = 10 tumors per arm

PH1 coupled to anti-Trop2 antibody exhibits significantly higher rate of tumor regression at a lower dose and DAR than SN38 coupled to anti-Trop2

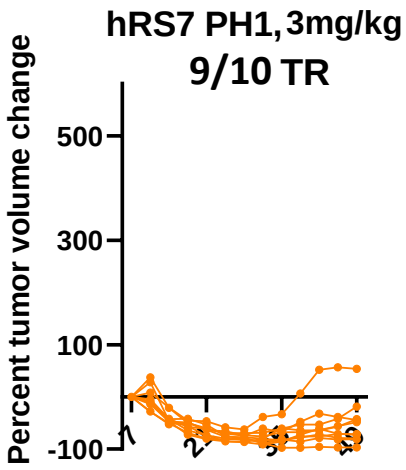
DAR8

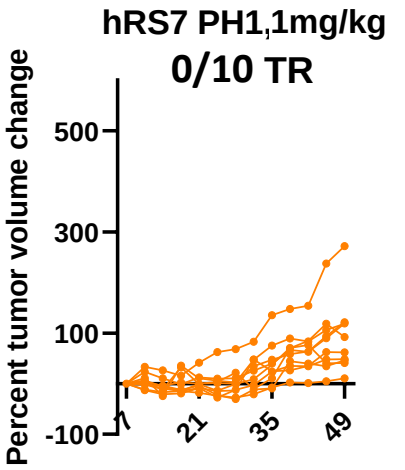






DAR4





ADCs used:

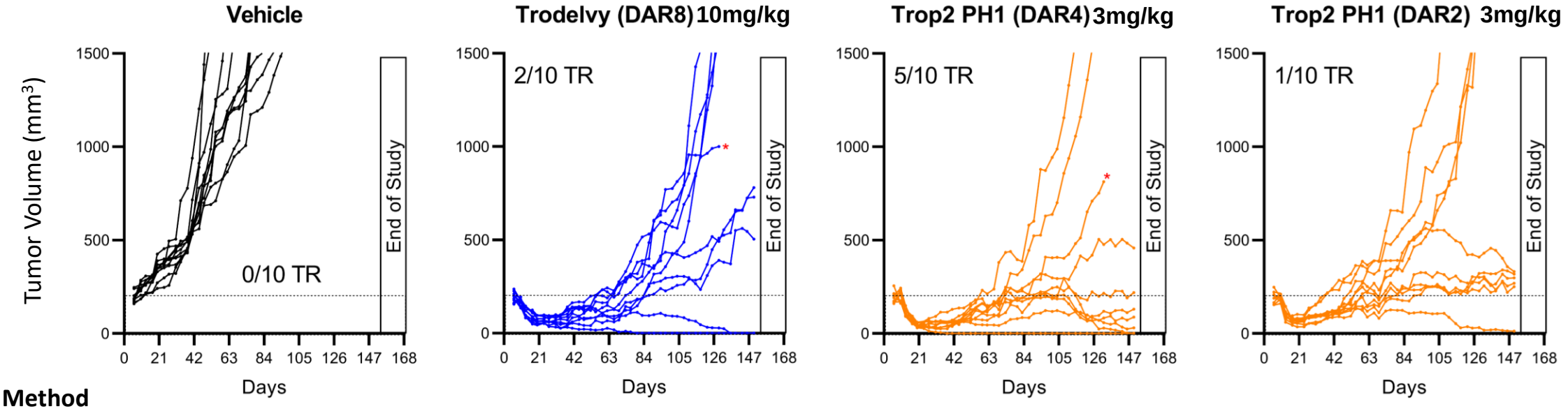
Anti-RSV PH1 = anti-respiratory syncytial virus isotype matched mAb conjugated to to PH1 NEGATIVE CONTROL ADC (no target on cell)

IMMU-132 = sacituzumab govitecan-hziy (Immunomedics) anti Trop 2 mAb hRS7 conjugated to SN-38 (an active metabolite of irinotecan), a topoisomerase I inhibitor. Derived in house, but expected similar to Trodelvy®
FIRST-IN-CLASS CONTROL

hRS7 PH1 = antitrophoblast cell-surface antigen 2 (Trop-2) monoclonal antibody conjugated to PH1

TR= Tumor regression. These data are derived from different non-clinical studies and clinical trials at different points in time, with differences in study/trial design and patient populations. As a result, comparisons cannot be made and no head-to-head non-clinical studies or clinical trials have been conducted.

Trop2 PH1 ADC in Gastric Cancer Model:
Tumor Regression At Lower Drug-Antibody Ratio (DAR) and Lower Dose Than Trodelvy®



Method

- NCI-N87 cell xenograft model
- Mice dosed IV with ADC or vehicle on day 1 and day 8 post-randomization

At DAR4, TR in 50% of treated mice over a period of ~5 months

At DAR2, stable disease in 50% of treated mice over ~5 months

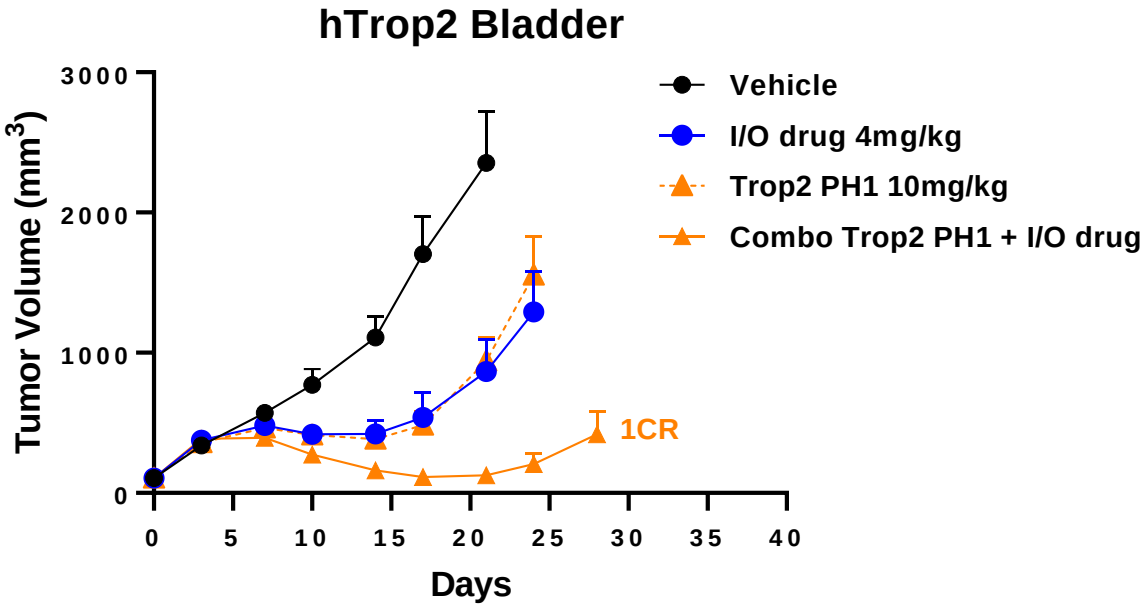
- Trop2-PH1 exhibits dose dependency and higher rate of tumor regression and long-term stabilization than Trodelvy® (Trop2-SN38 ADC)
- Prolonged duration of action of Trop2-PH1 likely due to induction of innate immune response

Group	TGI ± Std Err (day 20)	p Value vs Trop2 PH1 (DAR4) (day 20)	TGI ± Std Err (Day 41)	p Value vs Trop2 PH1 (DAR4) (day 41)
Trop2 PH1 (DAR 4)	**87.7 ± 1.0**		**90.3 ± 1.8**	
Trop2 PH1 (DAR 2)	**80.5 ± 1.8**	**0.00014**	**78.5 ± 3.2**	**0.0014**
Trodelvy (DAR 7.6)	**79.0 ± 2.1**	**0.000028**	**83.3 ± 2.4**	**0.035**

TR= Tumor regression. TGI=Tumor growth inhibition. These data are derived from different non-clinical studies and clinical trials at different points in time, with differences in study/trial design and patient populations. As a result, comparisons cannot be made and no head-to-head non-clinical studies or clinical trials have been conducted.

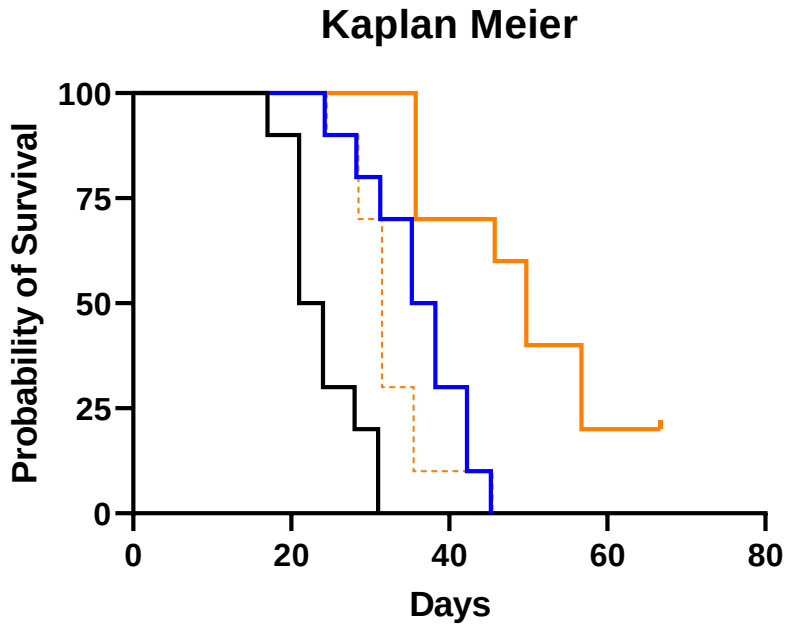
Trop2 PH1 ADC Combines With Standard-Of-Care Immunotherapy and Prolongs Overall Survival in Syngeneic Urothelial Cancer Model in Mice With Intact Immune System

Superior anti-tumor efficacy for Trop2 PH1 ADC plus SOC combination therapy



Trop2 PH1 ADC single agent efficacy is comparable to SOC

Improved OS for Trop2 PH1 ADC plus SOC combination therapy



Note: Patent pending so exact model, I/O drug and dosing not disclosed

Trop2 PH1 ADC single agent extends OS comparable to SOC

Efficacy against mouse bladder syngeneic cancer tumor model (urothelial) expressing human Trop2 protein

Trop2 PH1 ADC Safety By Intravenous Administration:
Proof-of-Concept Demonstrated Differentiated Safety Profile in NHP

- Doses examined 2mg/kg, 6mg/kg and 18mg/kg IV Q3W x 3 repeat doses at DAR2 and DAR4
  - 3 animals in each group, 2 sacrificed at end of dosing and 1 after further 3-week recovery period

- Maximum tolerated dose (MTD) 6 mg/kg caused mild-minimal or transient observations that reset to baseline within 2 weeks
  - Mild and reversible elevations in liver enzymes
  - Mild and reversible thrombocytopenia
  - Skin rash

- Differentiated safety profile from other competitor ADCs in clinic
  - No evidence of reported Trop2 related ADC toxicities such as neutropenia, peripheral neuropathy, stomatitis, or interstitial lung disease (ILD)
  - No nausea, vomiting or diarrhea at MTD

- Toxicity profile may allow combination with checkpoint inhibitors
  - No evidence of lung complications such as pneumonitis
  - No colitis or hypothyroidism

Summary of Trop2 PH1 ADC Characteristics

- **Nanomolar potency** against multiple types of solid tumors with potential **utility against wide range of cancers** either alone or in combination with I/O therapy
- **Superior specificity** to cancer cells (possibly due to linker stability) and unique **ability to generate neoepitopes**
- PH1 **payload efficacy is dose and DAR dependent** and appears to **induce innate and adaptive immunity** and anti-tumor immune memory evidenced by prolonged overall survival of mice after acute dosing
- **Promising safety in non-human primate** tox study with differentiated toxicity profile that may favor use with specific I/O therapies
- Trop2 mAb **ready for GMP manufacturing** development - lead selected, expressed and purified 30L scale and stability profile characterized

PASylated®-Nomacopan Geographic Atrophy (GA)

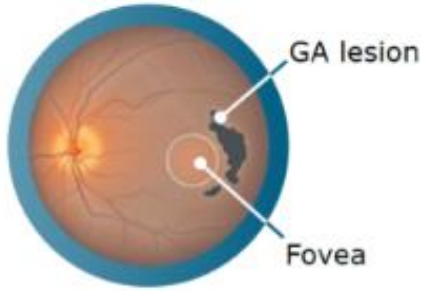
- *Bispecific inhibitor of C5 and LTB4*
- *Potential for 3 – 4 injections/year*
- *Potential for better safety than approved complement only drugs*

Nomacopan is the parent asset that was evaluated in two phase 3 clinical trials in hematopoietic stem cell transplant-related thrombotic microangiopathy (HSCT-TMA) and in paroxysmal nocturnal hemoglobinuria (PNH), while long-acting PASylated®-nomacopan is in the final stage of pre-clinical development as a potential treatment for geographic atrophy (GA)

Currently Approved Treatments in GA

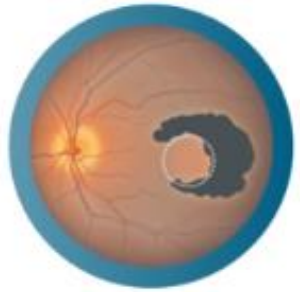
- GA is an advanced form of dry age-related macular degeneration (dAMD) with growth of atrophic lesions causing loss of photoreceptors and ultimately legal blindness in a median of *c.*6 years[1]
- Complement has an important role in driving the pathology[2] and lesion growth (see Figure on right) as demonstrated by the first recently approved (2023) treatments for GA which are both complement inhibitors:
  Izervay™/Astellas, anti-C5
  Syfovre™ /Apellis, anti-C3

Both approved drugs have been shown to decrease the growth rate of lesions



Non-central atrophy
Some loss of peripheral, low light vision

Growth of non-central atrophy
Loss of peripheral, low light vision



Starting to affect fovea
Loss of peripheral, low light vision; patches of lost central vision

Severe central atrophy
Loss of central vision leading to blindness

NOTE: Figure adapted from Fig 2 in reference 2 below

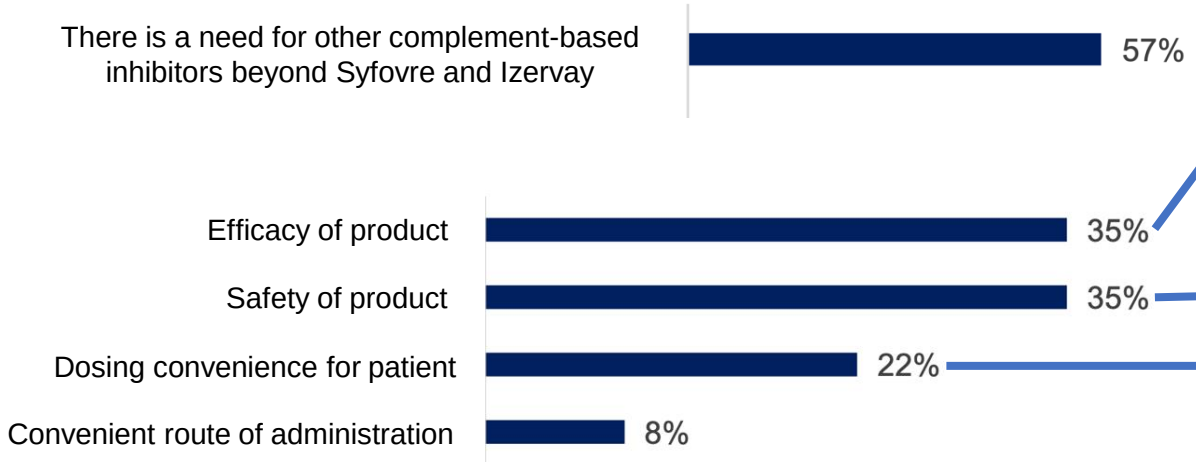
1. Linblad AS, Lloyd PC, et al. Change in area of geographic atrophy in the Age-Related Eye Disease Study: AREDS report number 26. Arch Opthalmol. 2009; 127: 1168-1174; 2. Boyer D, Schmidt-Erfurth U, et al. The pathophysiology of geographic atrophy secondary to age-related macular degeneration and the complement pathway as a therapeutic target. Retina 2017; 37: 819–835.

PAS-Nomacopan Is Designed to Address Unmet Needs in GA Identified by Retinal Specialists

MIZUHO Mizuho Securities USA LLC

U.S. Equity Research **November 1, 2023**

Results from Proprietary Survey of Retinal Specialists



NOTE: ≤ 3% of retinal specialists highlighted: Dosing convenience for physician; Physician practice economics; price/reimbursement; and compliance

PAS-nomacopan's target product profile

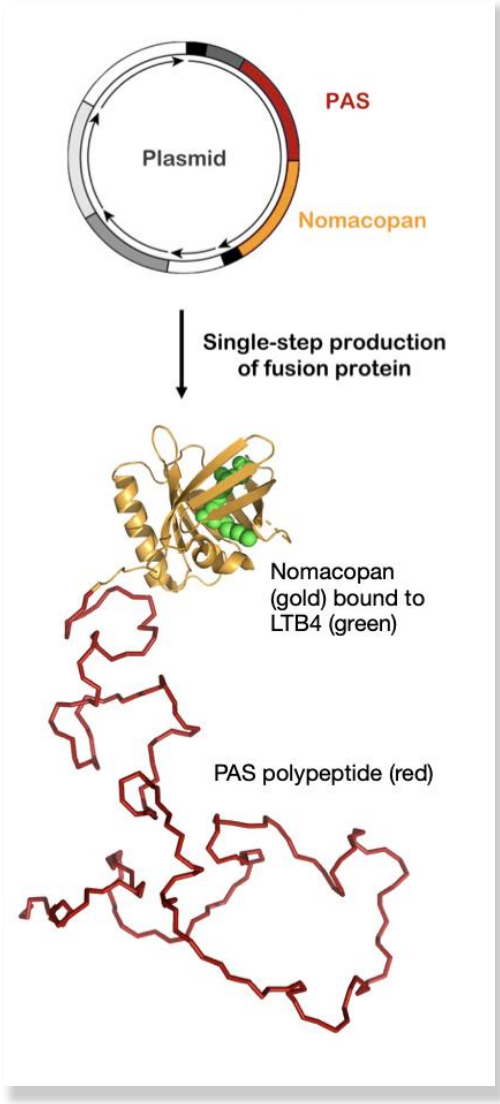
Inhibition of two proinflammatory pathways in eye has potential to improve efficacy over complement only inhibitors

LTB4 inhibition can prevent VEGF-A overexpression[1,2], which may drive new onset CNV caused[3,4] by the approved drugs

PASylation® technology enables potential for only 3 to 4 intravitreal (IVT) injections each year vs 6 – 12 for approved therapies[5,6]

1. Sasaki F, Sonoda K-H, et al. Leukotriene B4 promotes neovascularisation and macrophage recruitment in murine wet-type AMD models. *JCI Insight* 2018; 2. Eskandarpour M, Nunn MA, et al. Review – Immune-mediated retinal vasculitis in posterior uveitis and experimental models: the leukotriene (LT)B4-VEGF axis. *Cells* 2021;. **3.** Liao DS, Grossi FV, et al. Complement C3 inhibitor pegcetacoplan for geographic atrophy secondary to age-related macular degeneration - a randomized phase 2 trial. *Opthalmol.* 2019. **4.** Jaffe GJ, Westby K, et al. C5 inhibitor avacincaptad peg for geographic atrophy due to age-related macular degeneration - a randomized pivotal phase 2/3 trial. *Ophthalmol.* 2021; **5.** HIGHLIGHTS OF PRESCRIBING INFORMATION. IZERVAY™ (avacincaptad pegol intravitreal solution); **6.** HIGHLIGHTS OF PRESCRIBING INFORMATION. SYFOVRE™ (pegcetacoplan injection), for intravitreal use. These data are derived from different non-clinical studies and clinical trials at different points in time, with differences in study/trial design and patient populations. As a result, comparisons cannot be made and no head-to-head non-clinical studies or clinical trials have been conducted.

What is PASylated®(PAS)-Nomacopan?



PAS-nomacopan is a long-acting bispecific inhibitor of complement C5 and leukotriene B4 (LTB4) derived from nomacopan by fusion of a 600 amino acid proline-alanine-serine (PAS) repeat

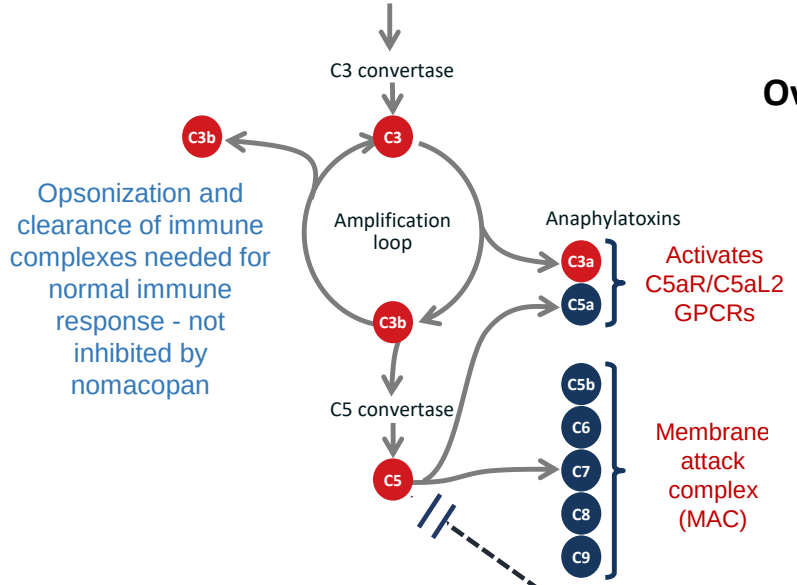
- PASylation[1] is a biological alternative to expensive chemical addition of synthetic polymers such as polyethylene glycol (PEG). Like PEG, PAS greatly increases the hydrodynamic radius of proteins.
- PAS-nomacopan has a hydrodynamic radius of 9.3nm and nomacopan 2.5nm.[2] Hydrodynamic radius is normally strongly associated with residency time in the eye.[3]
- PAS-nomacopan has full biochemical activity versus C5 (K_D 25pM)[4] and LTB4 (K_D 255pM)[2] with potency equivalent to nomacopan.
- PAS-nomacopan is expressed in a proprietary strain of bacteria and needs no post purification chemical coupling as it is manufactured with PAS fused in frame to the N-terminal of nomacopan (see figure).

1. Gebauer M, Skerra A. Prospects of PASylation® for the design of protein and peptide therapeutics with extended half-life and enhanced action. Bioorg Med Chem. 2018; 26: 2882-2887; 2. Akari data on file; 3. Crowell SR, Wang K, et al. Influence of charge, hydrophobicity, and size on vitreous pharmacokinetics of large molecules. Transl Vis Sci Technol. 2019; 8 :1; 4. Kuhn N, Schmidt CQ, et al. PASylated covers a C5-specific complement inhibitor with extended pharmacokinetics, shows enhanced anti-haemolytic activity in vitro. Bioconjugate Chem. 2016; 27: 2359-2371.

PAS-Nomacopan Inhibits Two Pathways That Can Cause Damaging Inflammation, While Preserving Beneficial Immune Functions

Complement (C5) inhibition

Complement system activated by IgG, foreign carbohydrate, damage associated molecular patterns (DAMPs), and cell surfaces not recognized as 'self'



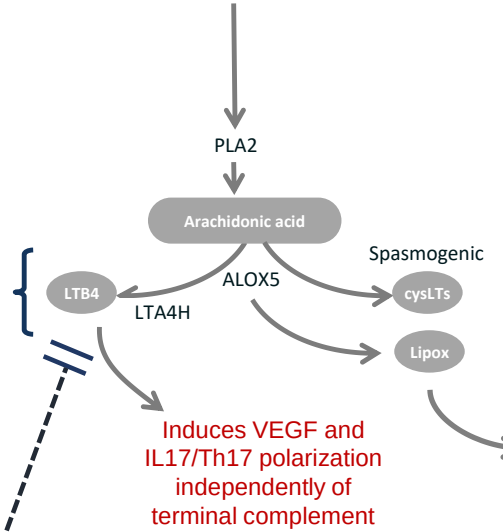
Opsonization and clearance of immune complexes needed for normal immune response - not inhibited by nomacopan

Activates C5aR/C5aL2 GPCRs

Membrane attack complex (MAC)

Leukotriene (LTB4) inhibition

Eicosanoid system activated by Fc receptor engagement, cytokines, and terminal complement products



Activates BLT1/BLT2 GPCRs

Induces VEGF and IL17/Th17 polarization independently of terminal complement

Anti-inflammatory lipoxins - not inhibited by nomacopan

Overlapping proinflammatory effects caused by complement & LTB4

- Granulocyte activation
- Phagocyte activation
- Induction of cytokines
- Induction of chemokines
- Procoagulant effects
- Cell lysis / Activation
- Modulation B and T cells

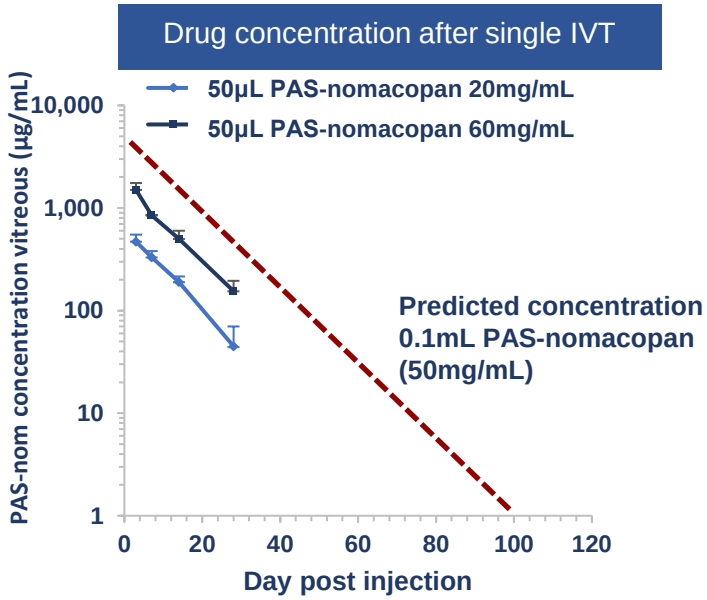
By inhibiting C5 activation, prevents formation of the MAC and C5a which signals through 2 cell surface GPCRs

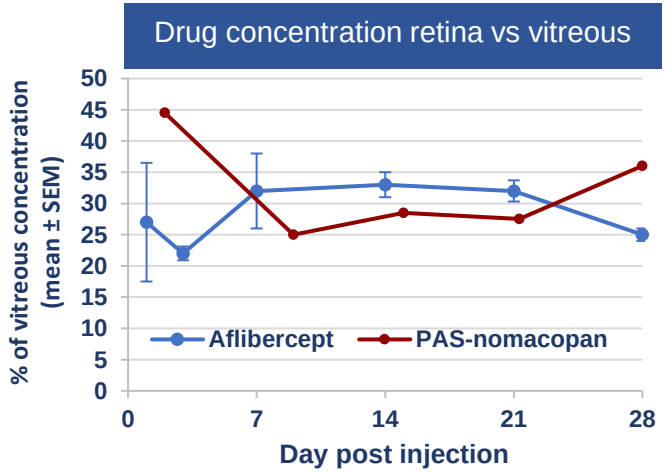
PAS-nomacopan

By sequestering LTB4, prevents interaction of the proinflammatory eicosanoid with its 2 cell surface GPCRs

Both complement and leukotriene pathways are active within the eye

Development of Long-Acting PAS-Nomacopan: Current Data and Potential Final IND-Enabling Steps





- **Data from non-clinical studies supports potential dose interval of 3 months or longer:**
  - Half-life rabbit vitreous 7.4 – 8.4 days with good bioavailability in other eye tissues (retina and RPE/choroid). Positive relationship between dose (1 mg or 3 mg/eye) and drug concentration in vitreous was observed (see Figures L).
  - Drug tolerated in rabbit non-GLP studies with some evidence of immune response akin to other biological drugs (such as anti-VEGFs) injected to eye.
- **GMP drug substance (DS) manufacturing needed for phase 1 study completed**
  - Full-scale (1500L) batch of GMP DS manufactured with good yield and analytical methods and specifications suitable to support intravitreous administration.
- **Pre-IND meeting completed – providing clarity on path to IND**
- **Completing drug product (DP) manufacture and toxicology studies to potentially enable IND clearance in 2025**

Source: PAS-nomacopan data generated from internal studies. These data are derived from different non-clinical studies and clinical trials at different points in time, with differences in study/trial design and patient populations. As a result, comparisons cannot be made and no head-to-head non-clinical studies or clinical trials have been conducted.

IVT Injected Drugs for Treatment of GA Are Potential Blockbusters

5 million people worldwide have GA

>1 million people in the U.S. are living with GA[1-3]

The GA treatment market is expected to have CAGR of 7%+ and may exceed $36 billion USD by 2032

Apellis

IVERIC BIO
An Astellas Company

Market cap $3.3 billion
as of Oct 10, 2024

Astellas acquisition for $5.9 billion
as of Jul 11, 2023

Value creation

- GA is a blockbuster market with significant unmet needs that PAS-nomacopan may address
- PAS-nomacopan GA program value and likelihood of partnering may increase significantly if IND clearance is received in 2025 and if subsequent clinical studies can be successfully completed

1. CDC https://www.cdc.gov/vision-health-data/prevalence-estimates/amd-prevalence.html
2. AMDF Geographic Atrophy | American Macular Degeneration Foundation. https://www.macular.org/about-macular-degeneration/geographic-atrophy
3. Bakri et. al. 2023 Geographic atrophy: Mechanism of disease, pathophysiology, and role of the complement system – PMC. https://pmc.ncbi.nlm.nih.gov/articles/PMC10408405/

Nomacopan

- *Phase 3-ready*
- *Efficacy and safety validated in PNH*

PHP-303

- *5th generation inhibitor selective for bioactive form of neutrophil elastase*
- *In phase 1 multiple ascending study, 5-40 mg 1x daily PHP-303 regimen achieved >90% neutrophil elastase inhibition with largely grade 1 AEs*

Available for licensing/strategic partnership

Nomacopan and PHP-303 Are Phase 2 and 3-Ready Clinical Assets Available for Licensing and Strategic Partnership

Summary of nomacopan opportunity

- Phase 3-ready
- Recombinant compact globular (16.7kDa) protein
- Administered by subcutaneous injection for systemic indications
- Robust manufacturing process in bacteria at 1500L scale
- Clinical data (phase 1, 2 and 3) from 76 patients and healthy volunteers shows drug well tolerated
- Cumulative total human exposure 35 years
- Clinical efficacy demonstrated in **paroxysmal nocturnal hemoglobinuria (PNH)** and supported in **bullous pemphigoid (BP)**

Summary of PHP-303 opportunity

- Phase 2-ready program
- 5th generation small molecule inhibitor of neutrophil elastase (NE)
- Administered oral once daily tablet
- Robust manufacturing process developed by Bayer
- Clinical phase 1 data from 60 healthy volunteers shows drug well tolerated and exhibits highly effective dose dependent inhibition of NE
- Phase 2 EU CTAs and protocols approved for PHP-303 trial in **Alpha-1 antitrypsin disease (AATD)** of the lung

Value creation

- Clinical programs with significant commercial potential offers near-term BD potential

1. Jore MM, Johnson S, Sheppard D, et al. Structural basis for therapeutic inhibition of complement C5. Nat Struct Mol Biol. 2016;23:378-386; 2. Roversi P, Ryffel B, Togbe D, et al. Bifunctional lipocalin ameliorates murine immune complex-induced acute lung injury. J Biol Chem. 2013;288:18789. murine immune complex-induced acute lung injury. J Biol Chem. 2013;288(26):18789-18802.

Akari Therapeutics Is a Multi-Faceted Biotech Company

Diverse pipeline provides potential for multiple shots on goal

Lead assets in areas of high unmet medical need provide multi-billion-dollar market opportunities in oncology and geographic atrophy

Lead programs leverage unique mechanisms of action backed by robust preclinical data sets that point to potential clinical benefit

Merger brings end-to-end capabilities with a combined management team and board that brings proven track record of value creation in life sciences

Supplementary Slides

Nomacopan

- *Phase 3-ready*
- *Efficacy and safety validated in PNH*

PHP-303

- *5th generation inhibitor selective for bioactive form of neutrophil elastase*
- *In phase 1 multiple ascending study, 5-40 mg 1x daily PHP-303 regimen achieved >90% neutrophil elastase inhibition with largely grade 1 AEs*

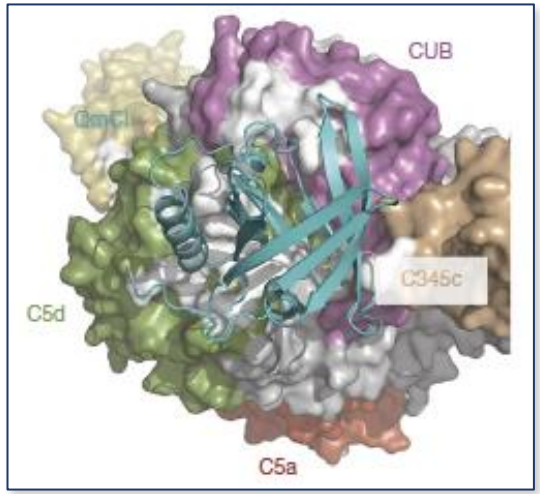
Available for licensing/strategic partnership

Nomacopan Is a Novel Bispecific Recombinant Protein

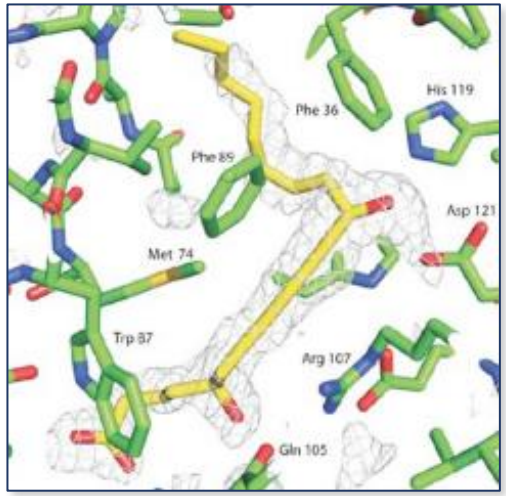
Summary of nomacopan's properties

- Phase 3-ready
- Recombinant compact globular (16.7kDa) protein
- Administered by subcutaneous injection for systemic indications
- Robust manufacturing process in bacteria at 1500L scale
- Clinical data (phase 1, 2 and 3) from 76 patients and healthy volunteers shows drug well-tolerated
- Cumulative total human exposure 35 years
- Clinical efficacy demonstrated in **paroxysmal nocturnal hemoglobinuria (PNH)** and supported in **bullous pemphigoid (BP)**

Detailed understanding of C5 and LTB4 binding that is relevant to both nomacopan and PAS-nomacopan



High resolution structure of nomacopan (blue) bound to human **complement C5**[1]



High resolution structure of nomacopan capture of **LTB4** (yellow)[2]

1. Jore MM, Johnson S, Sheppard D, et al. Structural basis for therapeutic inhibition of complement C5. Nat Struct Mol Biol. 2016;23:378-386; 2. Roversi P, Ryffel B, Togbe D, et al. Bifunctional lipocalin ameliorates murine immune complex-induced acute lung injury. J Biol Chem. 2013;288:18789. murine immune complex-induced acute lung injury. J Biol Chem. 2013;288(26):18789-18802.

Potential Paths Forward for Monetization of Nomacopan Asset

Partner or license nomacopan for:

A) An acute treatment indication such as trauma or traumatic brain injury using current formulation

B) Indication such as PNH for ROW (*i.e.* ex US/EU/Japan) using current formulation

- Leverage existing PNH data e.g. by reinitiating AK580 phase 3 trial and long-term safety trial AK581
- Price annual cost per patient highly competitively to encourage widest possible use
- Design trials to show that LTB4 inhibition has benefit in PNH in addition to C5 inhibition e.g. downregulates prothrombotic biomarkers
- Post approval for complement treatment naïve patients test if risk of thrombotic event lower on nomacopan than on complement only inhibitors

C) Develop slow-release formulation for clinical testing in either any disease currently treated with complement C5 inhibitors (lower risk approach) OR other chronic indications mediated by complement and/or LTB4

- List of diseases currently treated by inhibition of C5 activation includes PNH, myasthenia gravis (MG), atypical hemolytic uremic syndrome (aHUS) and neuromyelitis optica (NMO)
- Ensure highly competitive pricing/low annual cost per patient to encourage widest possible use
- Design trials to show that LTB4 inhibition has benefit in addition to C5 inhibition

PHP-303

- *5th generation inhibitor selective for bioactive form of neutrophil elastase*
- *In Ph1 multiple ascending study, 5-40 mg 1x daily PHP-303 regimen achieved >90% neutrophil elastase inhibition with largely grade 1 AEs*

Available for licensing/strategic partnership

PHP-303 Is a Potentially Best-in-Class Neutrophil Elastase Inhibitor (NEI) for Treatment of Alpha-1 Antitrypsin Deficiency (AATD)

Next Generation NEI

- PHP-303 is a small molecule, **oral QD**, reversible and highly selective NEI potentially addressing shortfalls of previous therapies
- PHP-303 can be an ideal solution for disease conditions where NE imbalance is an important contributor to disease

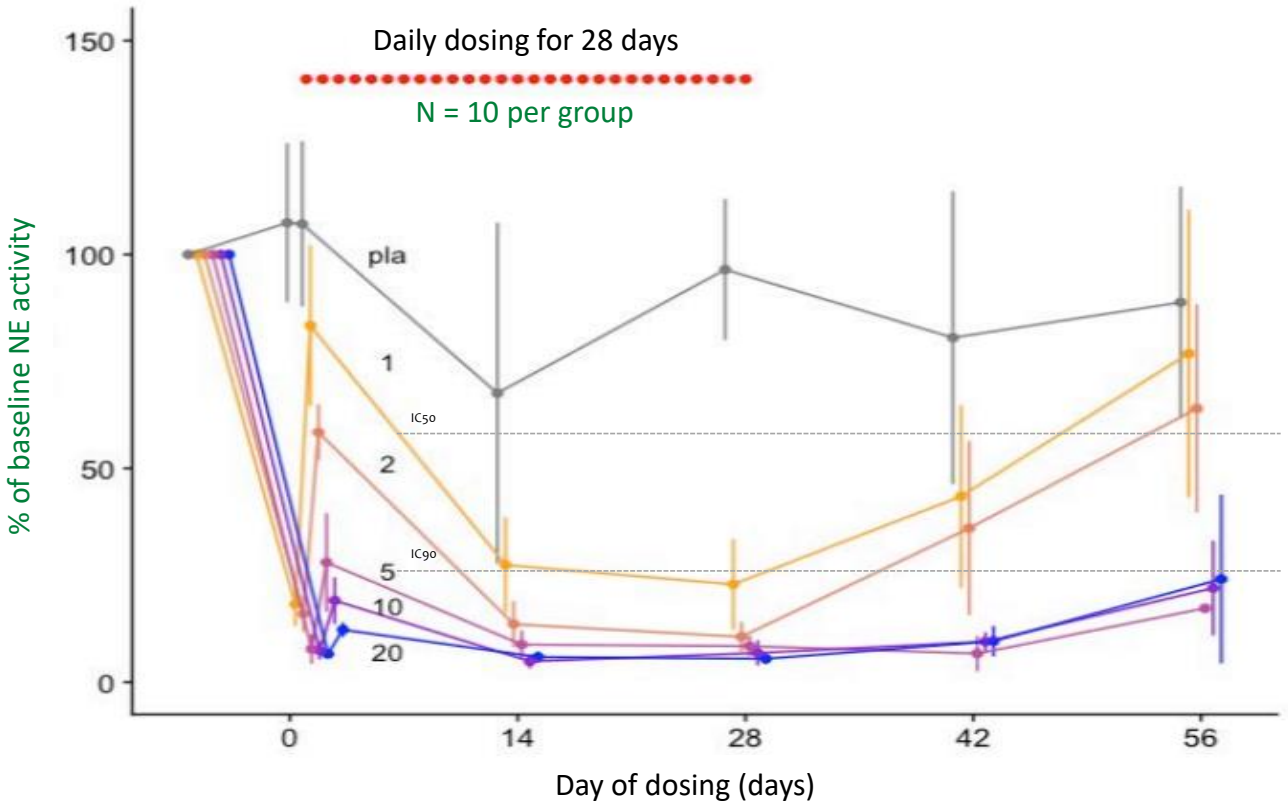
PHP-303 Addresses the Unmet Medical Need in AATD

- Demonstrated dose-dependent NE Inhibition with largely grade 1 AEs in phase 1 clinical trials
- NE likely important determinant in AATD progression (chronic inflammatory imbalance); PHP-303 inhibits bioactive form of the enzyme
- Orphan disease status likely in US and EU
- Untapped potential with large delayed and/or misdiagnosed population
- Cost-effective alternative to current treatments

Value creation

- Phase 2-ready program and asset with significant commercial potential offers near-term BD potential

Dose-Dependent Inhibition of NE Activity by PHP-303 in Phase 1 Multiple Ascending Dose Study



An opportunity to develop a phase 1 derisked asset in an area of unmet medical need

- Sustained, dose-dependent suppression NE activity
- ~90% inhibition of NE activity by doses >5mg QD
- PHP-303 well-tolerated with largely grade 1 toxicities
- Phase 2 EU CTAs and protocols approved for PHP-303
- FDA has accepted Aα-Val 360 and isodesmosine/ desmosine as surrogate biomarkers for lung damage for alvelestat (competitor NEI) program
- Orphan disease potential for additional period of exclusivity
- Supported by grant from Alpha-1 project advocacy group