Next-Generation Precision Bi-Functional Antibody Drug Conjugates Corporate Presentation

February 2025

NASDAQ: AKTX akaritx.com

# AKARI THERAPEUTICS

## **Forward-Looking Statements**

This presentation includes expressed 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 Akari Therapeutics, Plc (the "Company") that involve risks and uncertainties relating to future events and the future performance of the Company. 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, post-closing operations and the outlook for the Company's business; the Company's targets, plans, objectives or goals for future operations, including those related to its product candidates; financial projections; future economic performance; and the assumptions underlying or relating to such statements. These statements are based on the Company'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: the risk that the Company may not realize the anticipated benefits of its merger with Peak Bio, Inc. (the "Merger") in the time frame expected, or at all; the ability to retain and hire key personnel; potential adverse reactions or changes to business relationships resulting from the Merger; 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; uncertainties as to the long-term value of the Company's American Depositary Shares ("ADSs") (and the ordinary shares represented thereby), including the dilution caused by the Company's issuance of additional ADSs (and the ordinary shares represented thereby) in connection with the Merger; 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 the Company's programs or product candidates; risks related to any loss of the Company's patents or other intellectual property rights; any interruptions of the supply chain for raw materials or manufacturing for the Company's product candidates, the nature, timing, cost and possible success and therapeutic applications of product candidates being developed by the Company and/or its collaborators or licensees; the extent to which the results from the research and development programs conducted by the Company, and/or its 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 the Company's product candidates; unexpected breaches or terminations with respect to the Company's material contracts or arrangements; risks related to competition for the Company's product candidates; the Company's ability to successfully develop or commercialize its product candidates; 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 the Company's product candidates; the Company's ability to maintain listing of its ADSs on the Nasdag Capital Market. 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. More detailed information about the Company and the risk factors that may affect the realization of forward-looking statements is set forth in the Company's filings with the SEC, copies of which may be obtained from the SEC's website at www.sec.gov. The Company assumes no, and hereby disclaims any, obligation to update the forward-looking statements contained in this press release.



# WE ARE AKARI THERAPEUTICS

Akari Therapeutics is an innovative targeted oncology company built on next-generation ADCs and a novel discovery engine



# Why Akari

#### Innovative Precision Antibody Drug Conjugates (ADCs) for the Treatment of Cancer

Discovery platform allows for generation of novel Bi-Functional ADC candidates with spliceosome inhibitor payload

Tunable Target, Linker and Payload

# A K A R I

#### Lead Candidate AKTX-101 (TROP2 PH1 ADC)

Significant advantages over current TROP2 ADCs observed in multiple preclinical models:

- Superior activity
- Prolonged survival
- Less resistance
- Better tolerability
- Prolonged survival in combination with checkpoint inhibitors (CPI)

#### Capital Efficient with Multiple Near-Term Milestones

- Lean team focused on Execution
- Opportunity for Non-Dilutive Capital Through Partnering of Legacy Pipeline
- BD Discussions ongoing with interested licensing/strategic partners

# ADCs Have Revolutionized Cancer Therapy, But Have Some Shortcomings

All Currently Approved ADCs Utilize One of Only Two Payload Toxin Classes, Which Are Known for Toxicity and Resistance Issues

Tubulin Inhibitors | DNA Damaging Agents

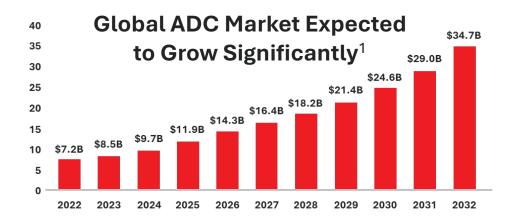
Limited Combination Ability with Other Key Therapies Like Anti-PD1/Anti-PDL1



Antibody drug conjugates market. Market.us. (2023, November 3).
 https://market.us/report/antibody-drug-conjugates-market/

#### 2023 Sales from Approved ADCs

	Product	Toxin Class	2023 Sales
	Sacitzumab govitecan-hziy	DNA Damaging Agent	\$1.0B
lrs	ENHERTU <sup>®</sup> trastuzumab deruxtecan	DNA Damaging Agent	\$2.7B
Solid Tumors	tivdak tisotumab vedotin-1ftv tor njectum 40 mg	Microtubule Inhibitor	<\$100M
olid <sup>-</sup>	ado-trastuzumab emtansine ab wurdu. Waschick Fén intraxestikus vas	Microtubule Inhibitor	\$1.75B
S	PADCEV enfortumab vedotin- ejfv kycitos for VI kilozón 20 mg kils	Microtubule Inhibitor	\$1.3B
	Finland industry	Microtubule Inhibitor	\$150M
		Microtubule Inhibitor	\$750M
lors		Microtubule Inhibitor	\$1.5B
d Tun	Cynlonta. Incesturinab testinie-byl fer injection, fer internetion use · 16mg	DNA Damaging Agent	<\$100M
Liquid Tumors		DNA Damaging Agent	\$140M
		DNA Damaging Agent	<\$100M



5

# **Bi-Functional ADC Platform Targeting Cancer**

Highly Selective Cancer Cell Death Combined With Enhanced Immune System Engagement for Effective Tumor Eradication

Antibody Targeting Clinically Validated TROP2 Receptor on Tumor Cells

### Linker

Connects Anti-Tumor Payload to Targeting Antibody

 $\checkmark$ 

## Payload

Differentiated Novel PH1 Payload Disrupts Normal RNA Splicing, Leading to Cancer Cell Apoptosis

#### Potential to Overcome Shortcomings of Current ADCs

Low Off-Target
 Toxicity

Enhanced Activity as a Single Agent Potential to Overcome Tumor Resistance Mechanisms

Ability to Induce Epitope Spreading

 $\checkmark$ 



# **Next-Generation Precision ADC Pipeline**

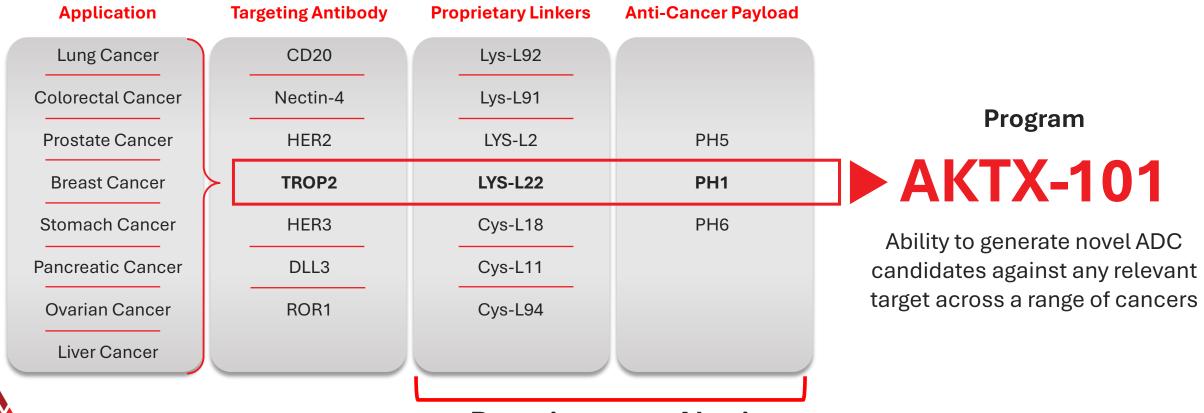
Program	Indication	Discovery	Preclinical	/ Clinical	Highlights
<b>AKTX-101</b> (TROP2 PH1 ADC) ADC with Novel Payload	Solid Tumors				<ul> <li>Novel Payload: PH1</li> <li>Advancing IND-enabling preclinical studies</li> <li>Pursue licensing / strategic partnership</li> </ul>
<b>AKTX-102</b> (Undisclosed Target) ADC with Novel Payload	Undisclosed				• Novel Payload: PH5 Payload targeting DNA Mismatch Repair (MMR) to generate neoepitopes
<b>AKTX-103</b> (Undisclosed Target) ADC with Novel Payload	Undisclosed				<ul> <li>Novel Payload: PH6         Payload targeting DNA             transcription in cancer cells and             co-opted immune cells         </li> </ul>



Platform Technology to Fuel Pipeline with Ability to Generate Novel ADC Candidates Across a Range of Solid/Hematological Cancers

# Akari Platform Technology Can Fuel a Pipeline

Ability to Precisely Tune Assets for Purpose Allows for Multiple Program Development for Additional Licensing Partnerships



A KARI THERAPEUTICS

**Proprietary to Akari** 

## Novel PH1 Payload: Superior Activity With Potent Effect Across Various Tumors Types and Targets Using Platform Technology

In Vitro Studies Performed at Lower PH1 Drug Dose (Lower DAR)

Bladder Trop2<sup>Heterogenous</sup>

**Gastric Trop2**<sup>High</sup>

100 Trop2 PH1 (DAR4) Trodelvy (DAR8) (%) trop2 PH1 (%) trop2 PH1 (%) trodelvy (DAR8) (%) trop2 PH1 (%) trop2 PH1 (%) trodelvy (DAR8) (%) trop2 PH1 (%

Trop2

<sup>100</sup> → Trop2 PH1 (DAR4) <sup>80</sup> → Trodelvy (DAR8) → Isotype PH1

Cell Death (%)

60-

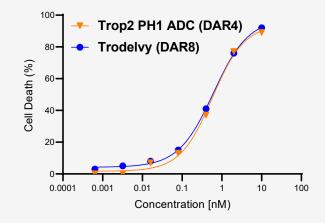
40-

20-

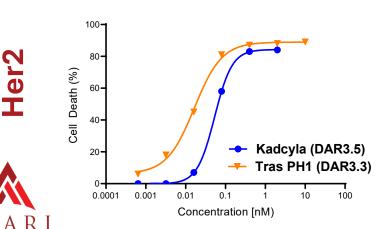
0.0001

0.001

#### Pancreatic Trop2<sup>High</sup>



Gastric Her2<sup>High</sup>



Breast Her2<sup>Low</sup>

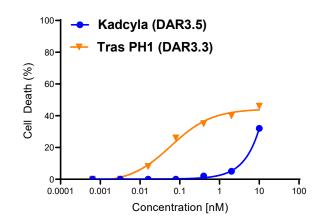
0.1

Concentration [nM]

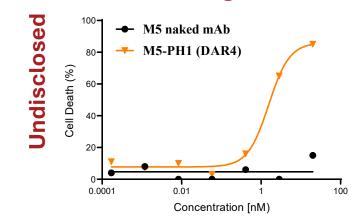
10

100

0.01



**NSCLC Target**<sup>Medium</sup>



These data are derived from comparative non-clinical studies and are not intended to serve as a basis for comparison with respect to Trodelvy's or any other clinical studies.

# **AKTX-101:** Novel Payload is a Spliceosome Inhibitor With Multiple Anti-Tumor Mechanisms

Novel Anti-Cancer Payload That Disrupts RNA Splicing Within Cancer Cells, Inducing Tumor-Specific Cell Death While Generating Immunostimulatory Effects and Minimizing Off-Target Toxicity

## Potential to Overcome Shortcomings of Current ADCs

#### Immunostimulatory Effects

Accumulation of mis-spliced proteins generates neoantigens that can be recognized by the immune system, potentially enhancing anti-tumor immunity

### **Reduced Off-Target Toxicity**

Proprietary linker and tumor selective antibodies that spare normal cells potentially reducing off-target toxicity

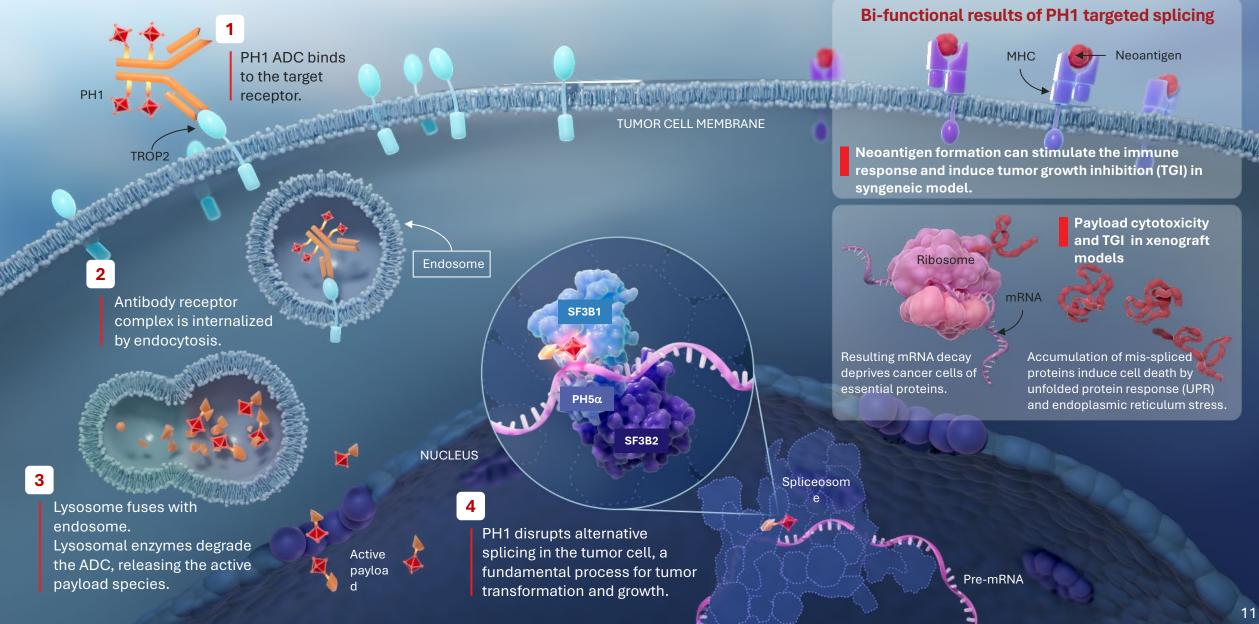
#### **Overcomes Resistance Mechanisms**

Appears to be a poor substrate for MDR transporters, which are often responsible for drug resistance in cancer therapy

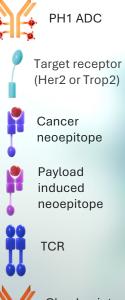
## Potential for Synergy With Immunotherapies

Immunomodulatory properties may synergize with checkpoint inhibitors and other immunotherapies

## **AKTX-101:** Direct Tumor Cell Cytotoxicity and Generation of Neoantigens Bi-Functional Payload Targeting the Spliceosome



## **AKTX-101:**



Checkpoint inhibitor

## Immune Response to Payload-Induced Neoantigens Extends Beyond ADC Target Receptor

T cell



Myeloid cells phagocytose and release granules

Myeloid cell

T cells recognize neoantigens and become primed for killing tumor cells

Synergy with checkpoint inhibitor therapies that further enhance immune response

Activation

B cells recognize neoantigens and become primed for killing tumor cells

B cell

Antibody response

#### MODERATELY IMMUNOGENIC CELL

#### TARGET<sup>LOW</sup> EXPRESSING CELLS

- Some cell death directly from lower payload concentrations
- Some payload-induced neoepitopes
- Immune cell mediated death

#### **HIGHLY IMMUNOGENIC CELL**

#### TARGET CEL

- Active payload kills majority of target cells
- Stimulates payload-induced necepitopes
   in survivors
- Resistant cells killed by immune response

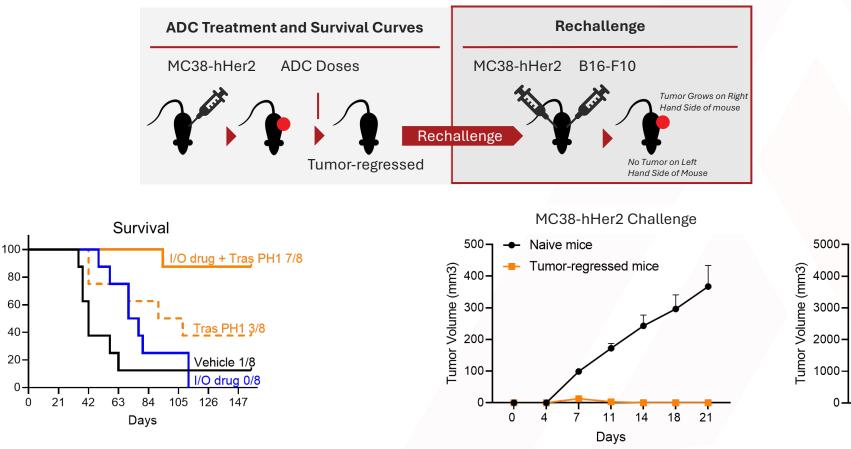
WEAKLY IMMUNOGENIC CELL

#### TARGET<sup>NONE</sup> EXPRESSING CELLS

Immune response targets surrounding cancer cells without a chemical bystander effect

## PH1 Payload Treated Mice Retained Immune Memory and Rejected Rechallenge with Tumor Cells

Potent Synergy With Checkpoint Inhibitor Has Potential to Cure Colorectal Tumors PH1 Induced Tumor-Specific Immune Memory





Tumor-regressed mice

11

Days

14

18

21

Naive mice

Percent survival

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## **AKTX-101:**

## Demonstrated Reduced Off-Target Toxicity in Preclinical Study

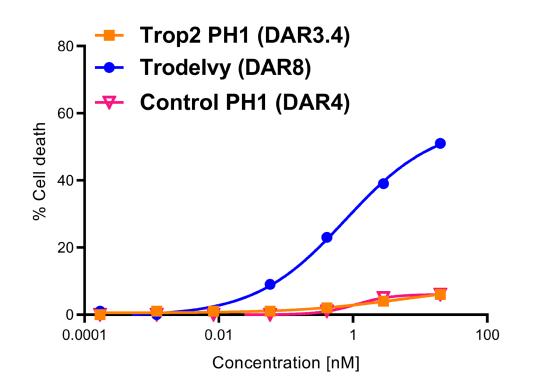
Limited effect on Normal Human Fibroblasts, an example of off-target toxicity of Trodelvy®

Proprietary Linker Only Releases PH1 Payload Upon Cell Internalization – No Leakage

Suggests Potential for Higher Therapeutic Index



#### Normal Human Fibroblasts TROP2<sup>none</sup>



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

These data are derived from comparative non-clinical studies and are not intended to serve as a basis for comparison with respect to Trodelvy's or any other clinical studies.

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# AKTX-101: Shown to Avoid Development of Resistance in Preclinical Study

PH1 Payload is Designed to Evade MDR Transporter Efflux Pumps and is unaffected by mutations in Tubulin or DNA Damage Pathways that confer resistance to microtubule and topoisomerase inhibitor payloads

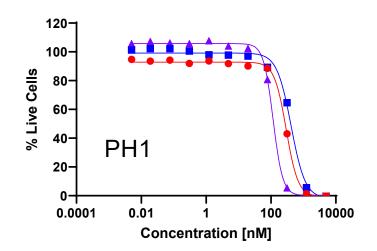
Patients who develop resistance to current TROP2 ADCs, may still be candidates for AKTX-101 due to differentiated PH1 payload mechanism

**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

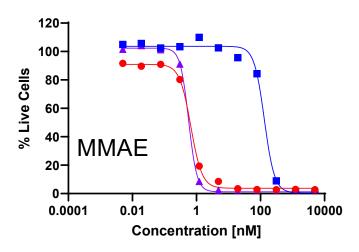
MES-SA uterine sarcoma cell line

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

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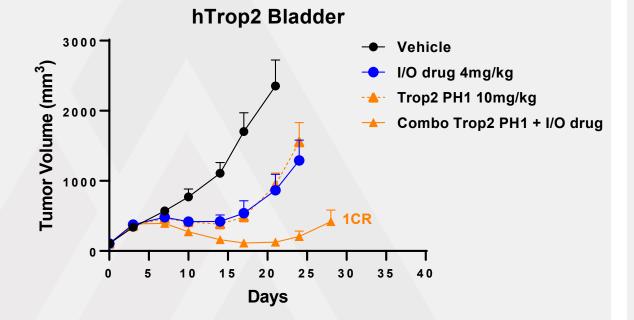
## **AKTX-101** Demonstrated Anti-Tumor Activity and Improved Overall Survival in Combination With Standard of Care I/O

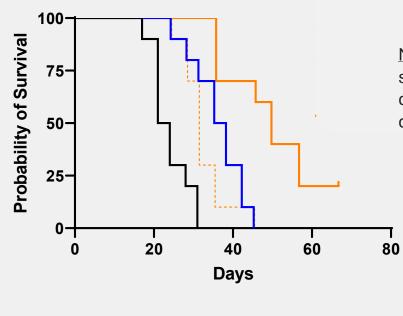
Mouse Bladder Syngeneic Cancer Tumor Model (Urothelial) Expressing Human TROP2 Protein

## Superior Anti-Tumor Efficacy In Combination With IO

Superior Overall Survival Combination With IO

**Kaplan Meier** 





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

Benefit in OS Compared to SOC and Superior in Combination With I/O



Comparable to SOC and Superior in Combination With I/O

## Significant Big Pharma Interest and Deal Flow in Early-Stage ADCs

Licensee	Licensor	Phase	Asset	Target	Date	Deal Type	Upfront Payment	Total Deal Highlights
<b>F</b> EPU BIOPHARMA	ARRIVENT	Preclinical	1 ADC	Undisclosed	1/2025	Licensing	\$47M	\$47M upfront + \$1.16B total milestones and royalties
biohaven <sup>®</sup>	Merus	Discovery	3 ADCs	Undisclosed	1/2025	Collaboration	Undisclosed	Research collaboration and license agreement to co-develop 3 ADCs
章联生物 MediLink Therapeutics		Preclinical	1 ADC	LRRC15	1/2025	Licensing	Undisclosed	Terms not disclosed
BIOCYTOGEN	Sotio MEMBER OF PPF GROUP	Preclinical	Multiple ADCs	Undisclosed	1/2025	Licensing	Undisclosed	Undisclosed upfront with up to \$325.5M in milestones and royalties on sales.
Synaffix	Mitsubishi Tanabe Pharma	Discovery	Undisclosed Research	Undisclosed	1/2025	Licensing	Undisclosed	Undisclosed upfront payment licensed.
Synaffix	Boehringer Ingelheim	Discovery	Undisclosed Research	Undisclosed	1/2025	Collaboration	Undisclosed	Undisclosed upfront with up to \$1.3B in milestones and royalty payments
<b>v</b> ararıs		Discovery	Undisclosed Research	Undisclosed	1/2025	Collaboration	Undisclosed	Undisclosed upfront with up to \$780M in milestones and royalty payments
Vela/igo	<b>AVENZO</b> THERAPEUTICS	Preclinical	VAC-103	EGFR x HER3	1/2025	Licensing	\$50M	\$50M upfront for rights outside of China, \$1.15B total dea potential + royalties.
DualǐtyBio 映圆生物	<b>AVENZO</b> THERAPEUTICS	Preclinical	AVZO-1418/DB-1418	EGFR/HER3	1/2025	Licensing	\$50M	\$50 million and will be eligible to receive up to approximately \$1.15 billion in development, regulatory an commercial milestone payments
Global Solution Provider	bioscience	Preclinical	3 ADCs	PTK7-ADC, MUC16-ADC, SEZ6-ADC	12/2024	Licensing	\$44M	\$44M upfront + \$265M in development and \$540M in commercial milestones, plus single-digit royalty (all 3 assets included)
Synaffix	ELEVATION	Preclinical	EO-1022	HER3	12/2024	Licensing	\$368M	\$368 million in upfront and clinical, regulatory, and commercial milestone payments, plus tiered royalties on net sales
Dual <sup>*</sup> tyBio <sup>映 圆 生 物</sup>	GSK	Preclinical	DB-1324	Undisclosed	12/2024	Licensing	\$30M	\$30M upfront, plus pre-option milestones and up to \$975 in milestones and tiered royalties on sales
TUBULIIS	GILEAD	Preclinical	Alco5 Tech	Undisclosed	12/2024	Licensing	\$20M	\$20M upfront, plus potential for \$30M option and up to \$415M in milestones and low double-digit royalties
<b>Vela⁄</b> igo	<b>AVENZO</b> THERAPEUTICS	Preclinical	VAC-103	Nectin4/ TROP2	11/2024	Option	\$50M	\$50 million and potential development, regulatory, and commercial milestone payments of up to approximately \$750 million in total, as well as tiered royalties on sales

A K A R I

## **Proven Management Team**



Samir R. Patel, MD **Chief Executive Officer** 

Serial entrepreneur with more than 20 years of experience in life sciences with multiple successful exits





**Torsten Hombeck, PhD Chief Financial Officer** 

Seasoned executive with over 20 years of expertise in finance, capital markets and M&A





Miles Nunn, D. Phil **Chief Scientific Officer** 

Accomplished scientist and drug developer with over two decades of experience, including the discovery of nomacopan







Satyajit Mitra, PhD **Executive Director**, Head of Oncology

Scientist with 20 years in advancing novel oncology programs from early preclinical validation and lead selection through pipeline nomination



Research

## Highly Experienced, Involved, Knowledgeable Board to Help Steer Strategy and Execution



Hoyoung Huh, MD, PhD

Chairman Founder of Peak Bio Inc. and has held positions of Chief Executive Officer and Board Chairman since founding pH Pharma in 2015





#### Samir R. Patel, MD

Chief Executive Officer CEO since December of 2024, founder and principal of PranaBio Investments, has more than 20 years of experience in life sciences including co-founding Digital Therapeutics, LLC

Centocor Johnson Johnson



#### Ray Prudo, MD Director

Founder, Chairman, and CEO of Volution and its predecessor company, Varleigh Immuno Pharmaceuticals, and is currently a board member of several UK healthcare companies



#### James Neal, MS, MBA

Director More than 25 years' experience in forming and maximizing business and technology collaborations globally and in bringing novel products and technologies to market





#### Sandip I. Patel JD, BBA

Director

Involved in the formation, development, growth, and successful exits of several companies in the healthcare services and technology sector, insurance, and financial services





#### Robert Bazemore Director

Seasoned executive leader, board member and innovator with over 35 years experience in portfolio strategy, partnering, development and commercialization of novel therapeutics, predominantly in Oncology and Immunology

Johnson Johnson (Synageva) C centocor



#### Abizer Gaslightwala Director

25 years in the development and commercialization of novel medicines with extensive experience in Oncology; developed, launched, and driven growth of several oncology products and brands spanning cancers with a focus on targeted agents including HER2, VEGF, CD20, and EGFR

Johnson Johnson 🌓 Jazz Pharmaceuticals.

🔁 Pfizer



## **Upcoming Expected Value Driving Milestones**

## Building a Next-Generation Precision Bi-Functional ADC Platform

## Ongoing and Near-Term

- Present anticipated PH1 Payload Preclinical Data at Scientific Conference
- Complete additional IND-enabling preclinical studies for AKTX-101
- Generate additional validating data on novel payloads to support pipeline
- Round out Executive Team with critical hires
- Seeking licensing/strategic partner for AKTX-101 (TROP2 PH1 ADC)

## Legacy Pipeline Assets

## Ongoing

BD Efforts To Secure Development Partners And Provide Non-Dilutive Capital



# **Assets Beyond ADC Platform**

Opportunity for Non-Dilutive Capital Through Ongoing BD Activities to Secure Development Partner for Inactive Programs

Program	Indication	Discovery / Preclinical / Phase 1 / Phase 2 / Phase 3 /	Global Market Opportunity
<b>PAS-Nomacopan</b> Long-Acting Complement C5 & Leukotriene B4 Inhibitor for Eye	Geographic Atrophy		<b>\$23</b> Billion <sup>1</sup>
PHP-303	Alpha-1 Antitrypsin Deficiency		<b>\$1.4</b> Billion <sup>2</sup>
Neutrophil Elastase Inhibitor	Acute Respiratory Distress Syndrome		\$3.4 Billion <sup>3</sup>
<b>Nomacopan</b> Complement C5 & Leukotriene B4 Inhibitor for Systemic	Bullous Pemphigoid; Paroxysmal Nocturnal Hemoglobinuria		>\$5 Billion <sup>4</sup>
Conditions	Trauma		<b>\$15</b> Billion⁵



- 1. Geographic atrophy (GA) market size, Share report, 2024-2032. Geographic Atrophy (GA) Market Size, Share Report, 2024-2032. (n.d.). https://www.snsinsider.com/reports/geographic-atrophy-ga-market-2480
- 2. Alpha-1 antitrypsin deficiency market size & forecast 2034. Size & Forecast 2034. (n.d.). https://www.imarcgroup.com/alpha-1-antitrypsin-deficiency-market
- 3. Global acute respiratory distress syndrome (ARDS) treatment market size: Mordor Intelligence. Mordor Intelligence Market Research Company. (n.d.). https://www.mordorintelligence.com/industry-reports/acute-respiratory-distress-syndrome-treatment-market
- 4. Paroxysmal nocturnal hemoglobinuria treatment market 2030. Paroxysmal Nocturnal Hemoglobinuria Treatment Market 2030. (n.d.). https://www.grandviewresearch.com/industry-analysis/paroxysmal-nocturnal-hemoglobinuria-pnh-market
- 5. Trauma Care Centers Market Size & Share Report, 2022-2030. (n.d.). https://www.grandviewresearch.com/industry-analysis/trauma-care-centers-market

# Why Now

Next-Generation Precision Antibody Drug Conjugates (ADC) Candidates for the Treatment of Cancer

## **Innovative Bi-Functional ADC**

#### **Platform Technology**

Customizable Targets by Tumor, Novel Payloads, Unique Linkers to Generate a Pipeline of Superior ADCs for Out-Licensing Opportunities

## AKTX-101 (TROP2 PH1 ADC)

Next-Generation Precision Bi-Functional ADC With Novel Spliceosome Inhibiting Payload Designed to Overcome Limitations of Current ADCs

## Significant Deal-Flow for Early-Stage ADC

Continued Recent Momentum of ADC Deals Underscores Big Pharma Growing Interest and Engagement for Potential Deal



Capital Efficient Strategy Focused on Execution Ongoing Robust BD Effort to Secure Licensing/Strategic Partner for AKTX-101 and Potential for Upside From Licensing of Non-Core Assets

Next-Generation Precision Bi-Functional Antibody Drug Conjugates **Investor Relations** 

JTC Team aktx@jtcir.com (908) 824-0775

# AKARI THERAPEUTICS