

An abstract graphic of flowing, overlapping ribbons in shades of purple, blue, and orange, creating a sense of movement and depth, serves as a background for the slide.

# Driving innovative therapeutics across the finish line

**Corporate Presentation**

APRIL 5, 2024

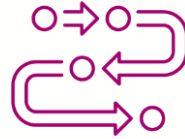
# Forward-Looking Statements

*This presentation contains “forward-looking statements.” These statements include words like “may,” “expects,” “believes,” “plans,” “scheduled,” and “intends,” and describe opinions about future events. These include statements regarding management's expectations, beliefs and intentions regarding, among other things, the GENESIS trial, the plans and objectives of management for future operations, regulatory filings submitted to the FDA, commercial potential of motixafortide, including generic entrants, and our financial condition and results of operations. These forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause the actual results, performance or achievements of BioLineRx to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. Factors that could cause BioLineRx's actual results to differ materially from those expressed or implied in such forward-looking statements include, but are not limited to: the initiation, timing, progress and results of BioLineRx's preclinical studies, clinical trials, and other therapeutic candidate development efforts; BioLineRx's ability to advance its therapeutic candidates into clinical trials or to successfully complete its preclinical studies or clinical trials; BioLineRx's receipt of regulatory approvals for its therapeutic candidates, and the timing of other regulatory filings and approvals and the potential need for post-approval studies; the clinical development, commercialization and market acceptance of BioLineRx's therapeutic candidates; BioLineRx's ability to obtain access to relevant markets for its approved products, as well as its ability to obtain viable pricing and reimbursement of those products; BioLineRx's ability to establish and maintain corporate collaborations; BioLineRx's ability to integrate new therapeutic candidates and new personnel; the interpretation of the properties and characteristics of BioLineRx's therapeutic candidates and of the results obtained with its therapeutic candidates in preclinical studies or clinical trials; the implementation of BioLineRx's business model and strategic plans for its business, approved products and therapeutic candidates; the scope of protection BioLineRx is able to establish and maintain for intellectual property rights covering its approved products and therapeutic candidates and its ability to operate its business without infringing the intellectual property rights of others; estimates of BioLineRx's expenses, future revenues, capital requirements and its needs for and ability to access sufficient additional financing; risks related to changes in healthcare laws, rules and regulations in the United States or elsewhere; competitive companies, technologies and BioLineRx's industry; statements as to the impact of the political and security situation in Israel on BioLineRx's business; and the impact of the COVID-19 pandemic and the Russian invasion of Ukraine, which may exacerbate the magnitude of the factors discussed above. These and other factors are more fully discussed in the "Risk Factors" section of BioLineRx's most recent annual report on Form 20-F filed with the Securities and Exchange Commission on March 26, 2024. In addition, any forward-looking statements represent BioLineRx's views only as of the date of this presentation and should not be relied upon as representing its views as of any subsequent date. BioLineRx does not assume any obligation to update any forward-looking statements unless required by law.*

# Fully integrated, commercial stage biopharmaceutical company



We aim to develop and commercialize **best-in-class therapeutics** for patients



Our expert team combines many decades of **end-to-end expertise** in drug development and commercialization



Our presence **in leading biotechnology hubs** provides tremendous opportunity for strategic partnerships, talent, and operations

We pursue ***life-changing therapies*** in oncology and rare diseases

# Drug development powered by experts, fueled by passion

Team of **seasoned specialists** comprising every expertise needed to successfully bring a drug from bench to market, including CMC, nonclinical and clinical development, business, finance and commercialization



**Philip Serlin, CPA, MBA**  
CHIEF EXECUTIVE OFFICER



**Mali Zeevi, CPA**  
CHIEF FINANCIAL OFFICER



**Ella Sorani, PhD**  
CHIEF DEVELOPMENT OFFICER



**Tsipi Keren-Lehrer, BSC, LLB**  
HEAD OF BUSINESS DEVELOPMENT  
AND STRATEGIC ADVISOR



**Holly May, MBA**  
PRESIDENT, BIOLINERX USA

# Value Creation Through Program Execution



## **Sustainable Growth via Commercialization of Best-in-Class Stem Cell Mobilization Agent**

- US FDA approval (Fall 2023) of APHEXDA® (motixafortide) for mobilization of hematopoietic stem cells for autologous transplantation in patients with multiple myeloma
- Commercialization in Asia with partner Gloria Biosciences. Targeting other territories
- Label expansion development program underway through Phase 1 study of stem cell mobilization for gene therapies in patients with sickle cell disease (initial data Q4 2024)\*

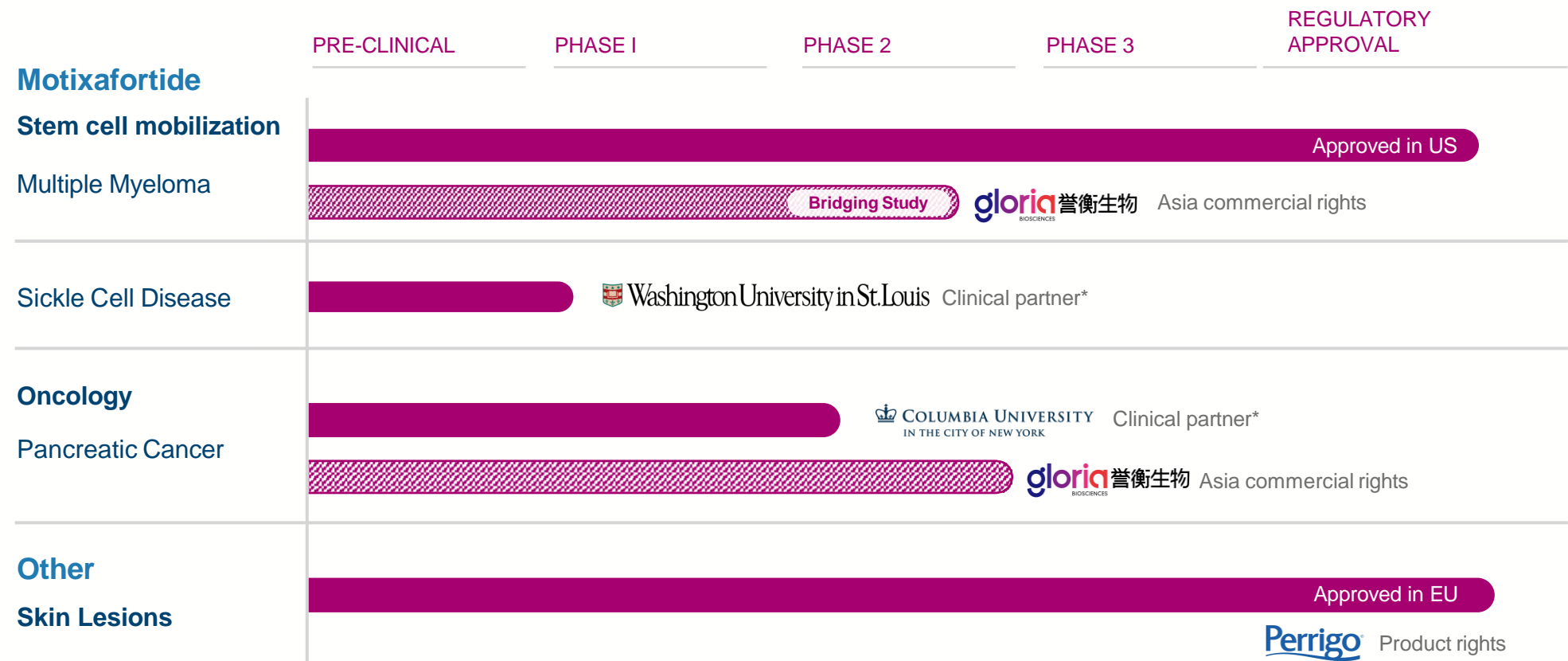


## **PDAC Program—with additional solid tumor potential—Offers Expansion Into Large Indication(s)**


- Proof-of-mechanism and concept established in completed Phase 2 study in second-line metastatic pancreatic cancer
- Encouraging single-arm pilot phase data in first-line metastatic pancreatic cancer showed significantly expanded mPFS and mORR compared to historical data
- Two randomized Phase 2b studies in first-line metastatic pancreatic cancer in combination with PD-1 inhibitors cemiplimab and zimberelimab

\*IIS with Wash U. in St. Louis

# Pipeline Targeting Multiple Indications



\*Investigator Initiated Study

 Studies in Planning

Lead asset **motixafortide** is a high affinity CXCR4 inhibitor with applications across **multiple indications** including **stem cell mobilization** and **anti-tumor therapy**





# Motixafortide in Multiple Myeloma



# Significant unmet need and opportunity in multiple myeloma (MM)

MM is the **second most common** hematologic malignancy<sup>1</sup> and autologous stem cell transplantation (ASCT) is integral to the prospect of improving survival and helping to restore the immune system

Roughly **35,000 patients<sup>2</sup>** are diagnosed with MM annually, and of those, an estimated **18,000 patients<sup>2</sup>** are eligible for an ASCT in the US



The number of ASCTs (~8,000 US) in MM have nearly **doubled since 2010<sup>3</sup>**

Mobilization and collection is a **growing challenge** in the treatment of MM patients

**Multiple apheresis sessions** can lead to:

Older patients (>60 years old)<sup>4, 5</sup>

3- and 4-drug induction therapy<sup>6,7</sup>

Up to **47%** of patients have had challenges collecting target numbers of stem cells within 1 apheresis session depending on induction regimens and mobilization strategies<sup>8,9</sup>



More adverse events



Higher costs

**Inconvenience** for patients and transplant center administrators<sup>10</sup>

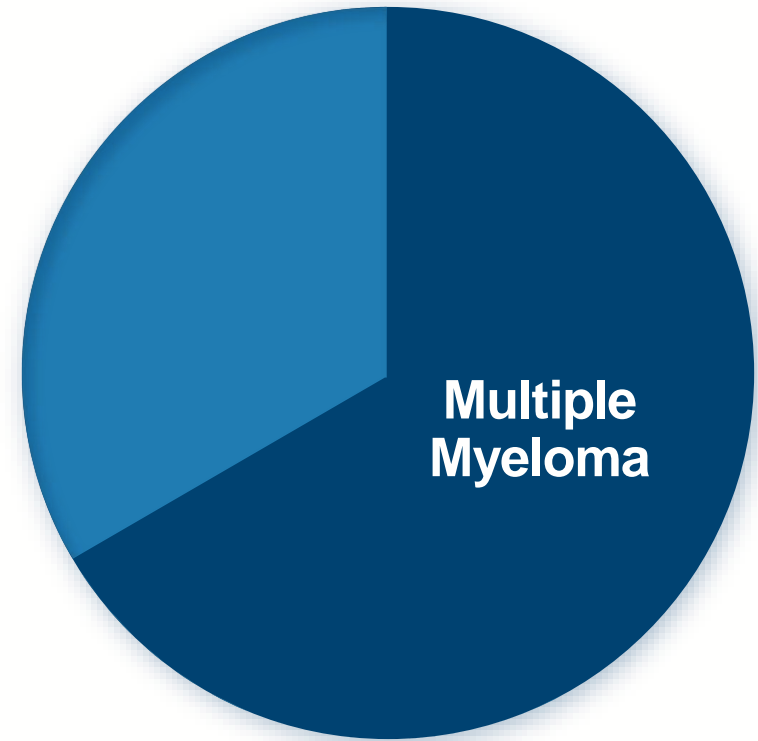


1. Anderson, K.C. (2011). Multiple Myeloma: A Clinical Overview. *Oncology*, 25(12); 2. National Cancer Institute. Cancer Stat Facts: Myeloma. Bethesda, MD. Accessed August 22, 2023.; 3. CIMBTR; 4. Giralt S, et al. *Biol Blood Marrow Transplant*. 2014;20(3):295-308. doi:10.1016/j.bbmt.2013.10.013; 5. Hagen PA, Stiff P. *Biol Blood Marrow Transplant*. 2019;25(3):e98-e107. doi:10.1016/j.bbmt.2018.12.002; 6. Hulin C, et al. *Haematologica*. 2021;106(8):2257-2260. doi:10.3324/haematol.2020.261842; 7. Chhabra S, et al. *Transplant Cell Ther*. 2023;29(3):174.e1-174.e10. doi:10.1016/j.jtct.2022.11.029; 8. Edmison J, et al. Poster presented at: 64th American Society of Hematology Annual Meeting and Exposition; December 10-13, 2022; New Orleans, LA.; 9. DiPersio JF, et al. *Blood*. 2009; 113(23):5720-6; 10. Shaughnessy P, et al. *Biol Blood Marrow Transplant*. 2013;19(9):1301-1309.

# ASCT remains preferred first-line treatment for MM

- The **3-year survival** probability after ASCT is >80% (95% CI: 80, 82)<sup>4</sup>
- **Time to relapse is about 50% longer for those who receive ASCT + chemotherapy** than those who receive chemotherapy alone<sup>5</sup>
- **Other treatment options for patients who are ineligible for ASCT (i.e., CAR-T) present significant barriers**, including high cost<sup>6</sup> and high incidence of serious adverse effects (e.g., CRS, neurological symptoms)<sup>7</sup>

**MM accounts for nearly two-thirds of all ASCTs performed<sup>4,8</sup>**



1. Dhakal B, et al. *Transplant Cell Ther.* 2022;28(6):284-293. 2. Thalambedu N, et al. *Blood.* 2022;140(1):13210-13211. 3. Cowan AJ, et al. *Biol Blood Marrow Transplant.* 2020;26(12):2372-2377. 4. Bolon YT, et al. CIBMTR summary slides, 2022. Accessed July 3, 2023. <https://cibmtr.org/CIBMTR/Resources/Summary-Slides-Reports> 5. Richardson PG, et al. *N Engl J Med.* 2022;387(2):132-147. 6. Cliff ERS, et al. *Am Soc Clin Oncol Educ Book.* 2023;43:e397912. 7. Lei W, et al. *Cancers.* 2021;13(15):3912. 8. D'Souza A, et al. *Biol Blood Marrow Transplant.* 2020;26(8):e177-e182.


# Adequate mobilization of CD34+ stem cells is important for successful ASCT

## Consensus Recommendations on Stem Cell Targets


Organization	Recommendation
ASTCT Consensus Recommendations <sup>1</sup>	<b>Minimum Dose</b> $2 \times 10^6$ CD34+ cells/kg*
	<b>Recommended Collection Target</b> $3-5 \times 10^6$ CD34+ cells/kg†
	<b>Higher Target</b> Double the target if multiple transplants are planned
IMWG Consensus Statement <sup>2</sup>	<b>Minimum Dose</b> $2 \times 10^6$ CD34+ cells/kg
	<b>Recommended Collection Target</b> $4-6 \times 10^6$ CD34+ cells/kg‡
	<b>Higher Target</b> Minimum of $4 \times 10^6$ CD34+ cells/kg with a target of $8-10 \times 10^6$ CD34+ cells/kg to allow for 2 transplants if needed

A minimum dose of  $>3-5 \times 10^6$  CD34+ cells/kg was associated with faster recovery of both platelets and neutrophils.<sup>3</sup>


## Risk factors for poor mobilization\*




Previous treatment with **lenalidomide**<sup>1</sup> or **daratumumab**<sup>4</sup>



Previous radiation therapy<sup>1</sup>



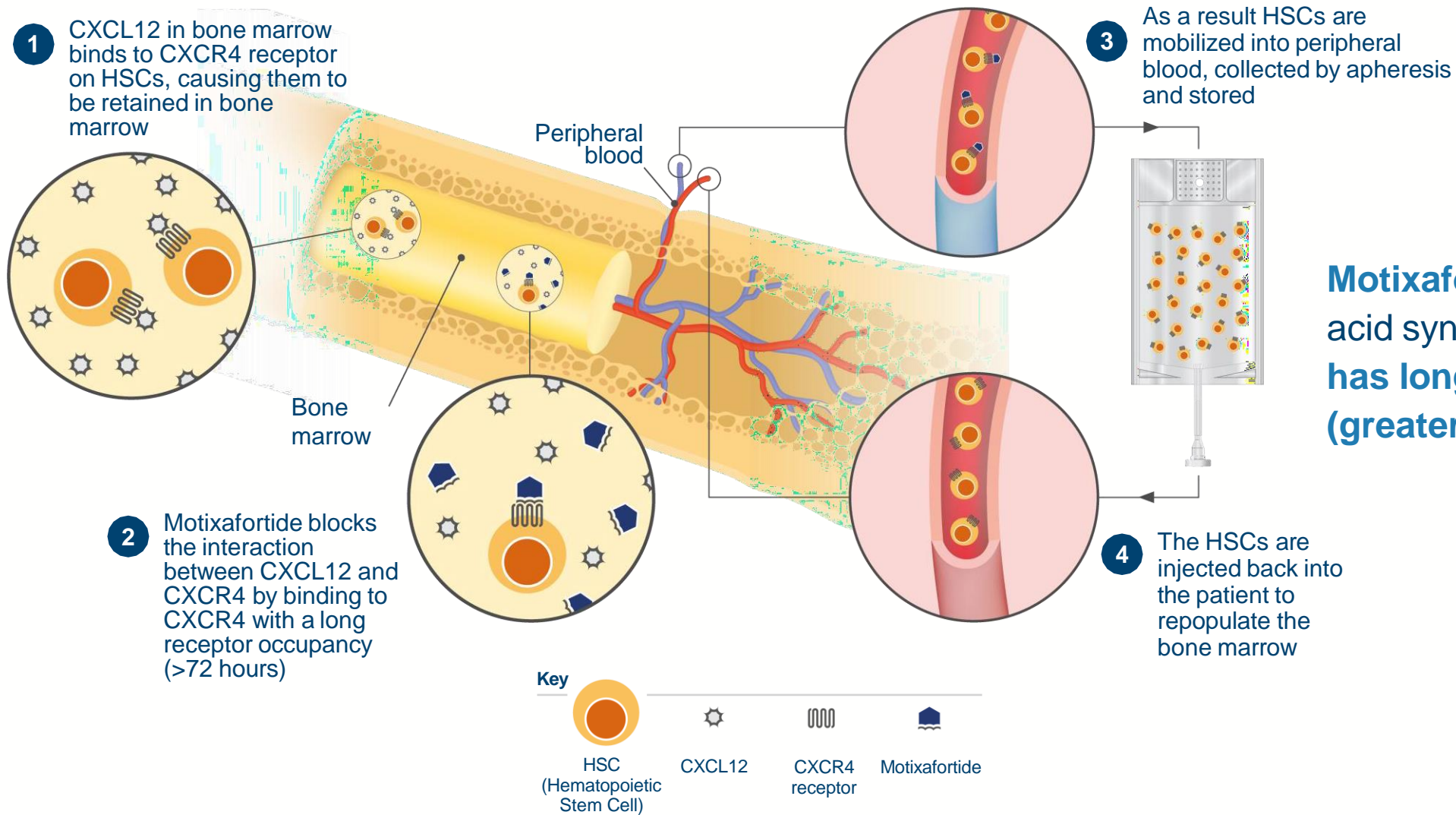
Advanced age<sup>1</sup>



Low pre-apheresis peripheral blood CD34+ cell counts<sup>1</sup>

1. Giralt S, et al. *Biol Blood Marrow Transplant.* 2014;20(3):295-308. 2. Giralt S, et al. *Leukemia.* 2009;23(10):1904-1912. 3. Tricot G, et al. *Blood.* 1995;85(2):588-596; 4. Hulin C, et al. *Haematologica.* 2021;106(8):2257-2260.

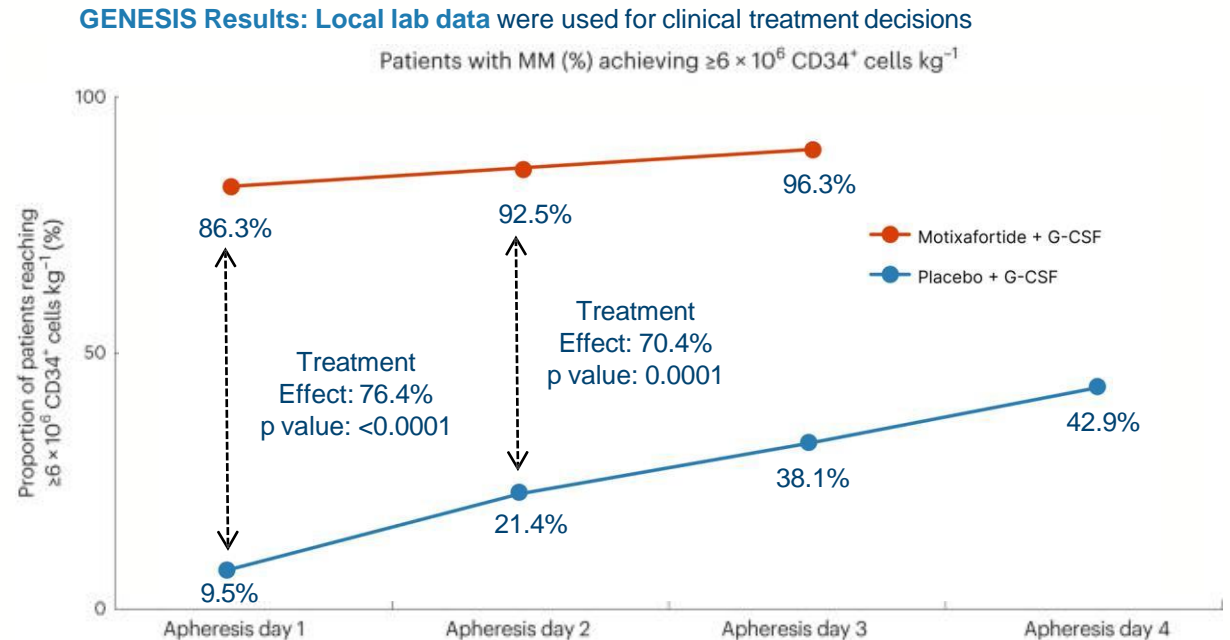
# Best-in-class stem cell mobilization (SCM) agent



**Motixafortide** is a 14- amino acid synthetic cyclic peptide that **has long receptor occupancy (greater than 72 hours)**

# GENESIS phase 3 clinical trial results

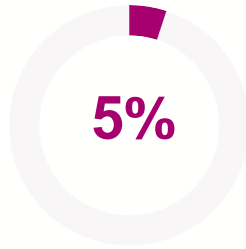
- Majority of patients successfully collected **target goal of  $\geq 6$  million stem cells** after only 1 dose<sup>1</sup>
- Trial included **patients representative of current multiple myeloma population** undergoing autologous HSCT<sup>2</sup>
- Motixafortide plus G-CSF had a **favorable safety-profile and was generally well tolerated**<sup>1</sup>
- Motixafortide plus G-CSF resulted in a significant **reduction in healthcare resource utilization**<sup>2</sup>



1. Data on file; 2. Crees, Z.D., et al., (2023). Motixafortide and G-CSF to Mobilize Hematopoietic Stem Cells for Autologous Transplantation in Multiple Myeloma..

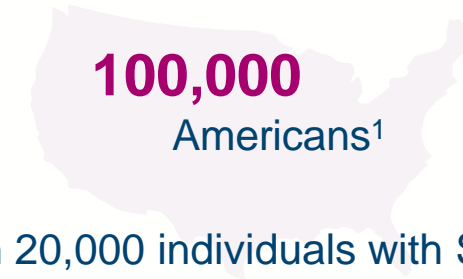
# Significant unmet need and opportunity in sickle cell disease (SCD)

SCD is one of the most common inherited genetic disorders globally,<sup>1</sup> and approximately



**of the world's population** carries trait genes for hemoglobin disorders (including SCD)<sup>2</sup>

SCD affects approximately



Greater than 20,000 individuals with SCD may be supported by gene therapy

Effective HSC-based gene therapies depend upon the collection of **significant quantities of stem cells** to engineer the treatments that enable the potential genetic reversal of SCD



Common mobilization agent G-CSF is contraindicated in SCD and therefore there is a **need for mobilization regimens that reliably yield optimal numbers of HSCs** for gene therapy



1. ASH – Sickle Cell Disease; 2. Africa Health Organization Fact Sheet

# CD34+ HSC minimum collection goals for approved SCD gene therapies

Gene therapy manufacturing requires large amounts of HSCs

## LYFGENIA<sup>1</sup>

**15 million** CD34+ cells/kg for manufacturing

**1.5 million** additional CD34+ cells/kg for backup

- In registration trial, **minimum HSCs collected in most patients with 1 or 2 cycles of mobilization and apheresis**, which typically required two consecutive collection days per cycle
- For patients requiring a second cycle, **mobilization cycles must be separated by at least 14 days**

## CASGEVY<sup>2</sup>

**20 million** CD34+ cells/kg for manufacturing

**2 million** additional CD34+ cells/kg for backup

- In registration trial, the mean (SD) and median (min, max) number of **mobilization and apheresis cycles required for manufacturing and backup were 2.3 (1.41) and 2 (1,6) respectively**. Six patients (10%) were unable to achieve the minimum dose
- For patients requiring a second cycle, **mobilization cycles must be separated by at least 14 days**

1. LYFGENIA prescribing information December 2023; 2. CASGEVY prescribing information December 2023.

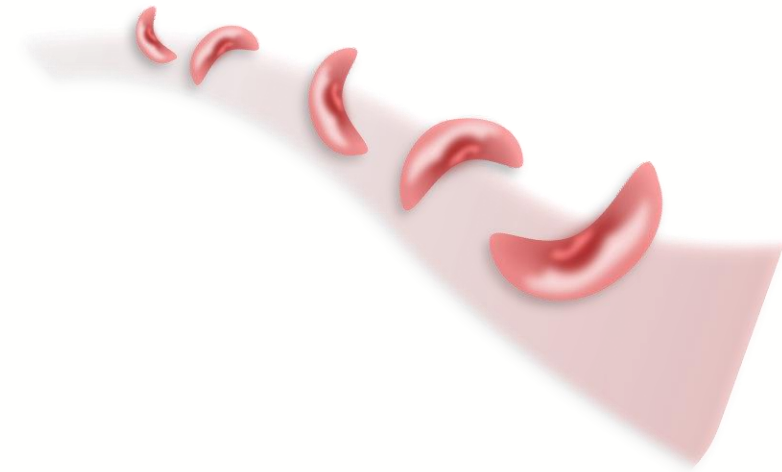


# Phase 1 pilot study evaluating HSC mobilization in SCD patients recruiting

Potential to increase patient access, improve patient journey, and decrease patient/caregiver burden



- BioLineRx and Washington University School of Medicine are **advancing a Phase 1 Sickle Cell Disease clinical trial** that will evaluate the safety and feasibility of motixafortide as monotherapy and in combination with natalizumab (VLA-4 inhibitor) to mobilize HSCs for gene therapies in patients with SCD
- FPD in December 2023; data anticipated in 2H of 2024





# Motixafortide in Cancer Immunotherapy – Pancreatic Ductal Adenocarcinoma (PDAC) and Other Solid Tumors

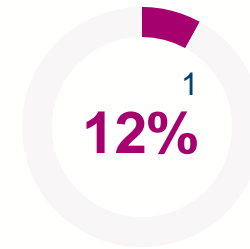
# Significant unmet need and opportunity in PDAC

PDAC is associated with **poor patient outcomes** because efficacious therapies do not yet exist

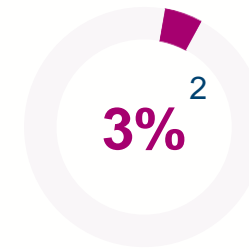



– the highest mortality rate among solid tumor malignancies – and globally, nearly a **half million** people were diagnosed in 2020 alone<sup>2</sup>

For all stages, the five-year **survival rate** in the US is only

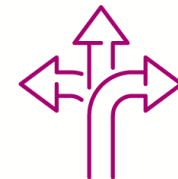


For **metastatic** PDAC (>50% of diagnosed cases), the five-year survival rate in the US is only



PDAC incidence is growing, and it is estimated that there will be **815,000 cases**  by 2040<sup>3</sup>

Newer treatments like immunotherapy do not address all unmet needs, demonstrating a clear need to co-target **alternative pathways**



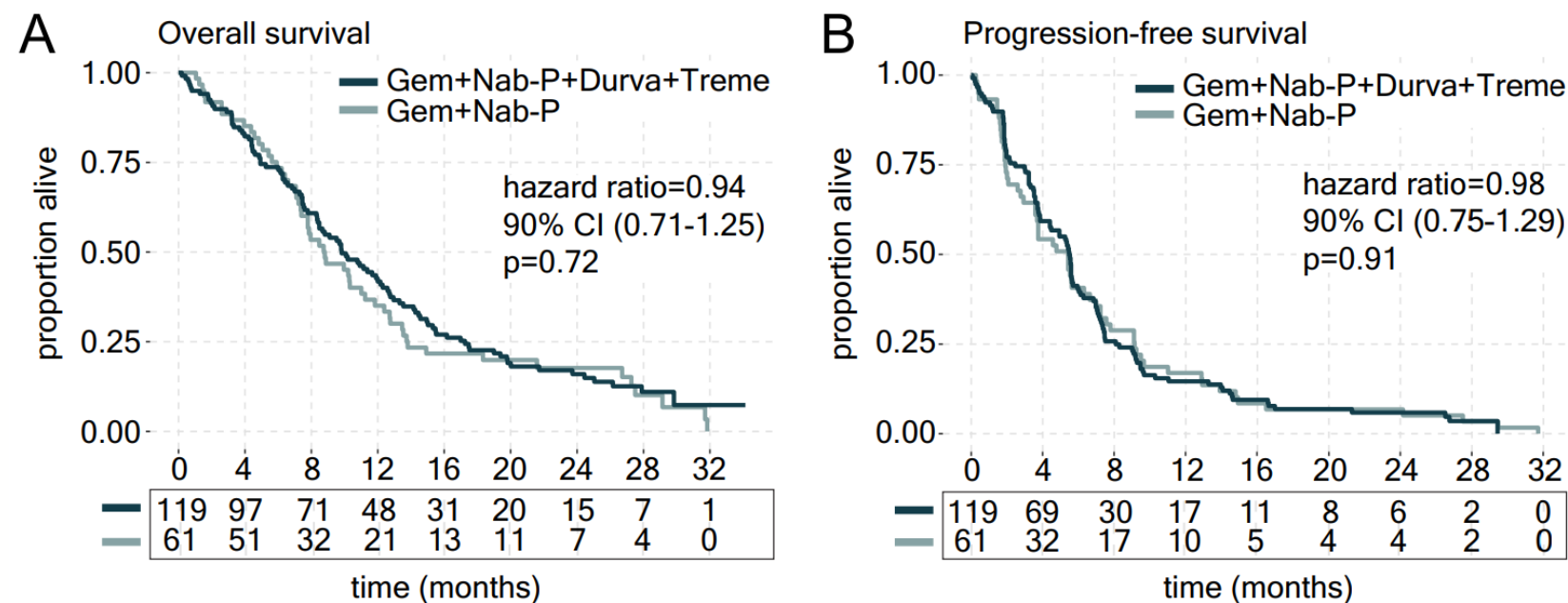
1. Pancreatic Cancer Action Network; 2. Cancer Net – Pancreatic Cancer Statistics; 3. The Global Cancer Observatory

# Need in first-line metastatic PDAC

First Line Treatment	mOS (mos)	mPFS (mos)	cORR (%)
Gemcitabine <sup>2,3</sup>	5.6-6.7		7-9.4%
5FU <sup>1</sup>	4.4	1	0%
Gem / Abrax <sup>3</sup> (Van Hoff study)	8.5	5.5	23%
Gem / Abrax <sup>4</sup> (NAPOLI 3 study)	9.2	5.6	36.2%
NALIRIFOX <sup>4</sup> (NAPOLI 3 study)	11.1	7.4	41.8%
mFOLFIRINOX <sup>2</sup>	11.1	6.4	31.6%

mPFS values in graphic; mPFS varies between studies due to study design, inclusion/exclusion criteria and patient demographics. 5-FU=5-flurouracil.  
1. Burris HA et al. J Clin Oncol. 1997; 2. Conroy T et al, NEJM 2011; 3. Von Hoff et al. NEJM 2013/ 4 NAPOLI-3 Study ASCO 2023

# Effectiveness of immunotherapy in PDAC remains limited



- Immune checkpoint inhibitors have demonstrated significant efficacy in multiple solid tumor types, **but effectiveness of ICI in mPDAC remains limited<sup>1</sup>**
- **No survival benefit found** among the unselected patient population **in phase 2 randomized trial with 180 patients** comparing combination immunotherapy and standard-of-care chemotherapy vs standard-of-care chemotherapy alone<sup>2</sup>

**CCTG PA.7 Phase 2 Trial (2022):** durvalumab (PD-L1) and tremelimumab (CTLA-4) with gemcitabine and nab-paclitaxel vs. gemcitabine and nab-paclitaxel alone in PDAC patients receiving first line therapy

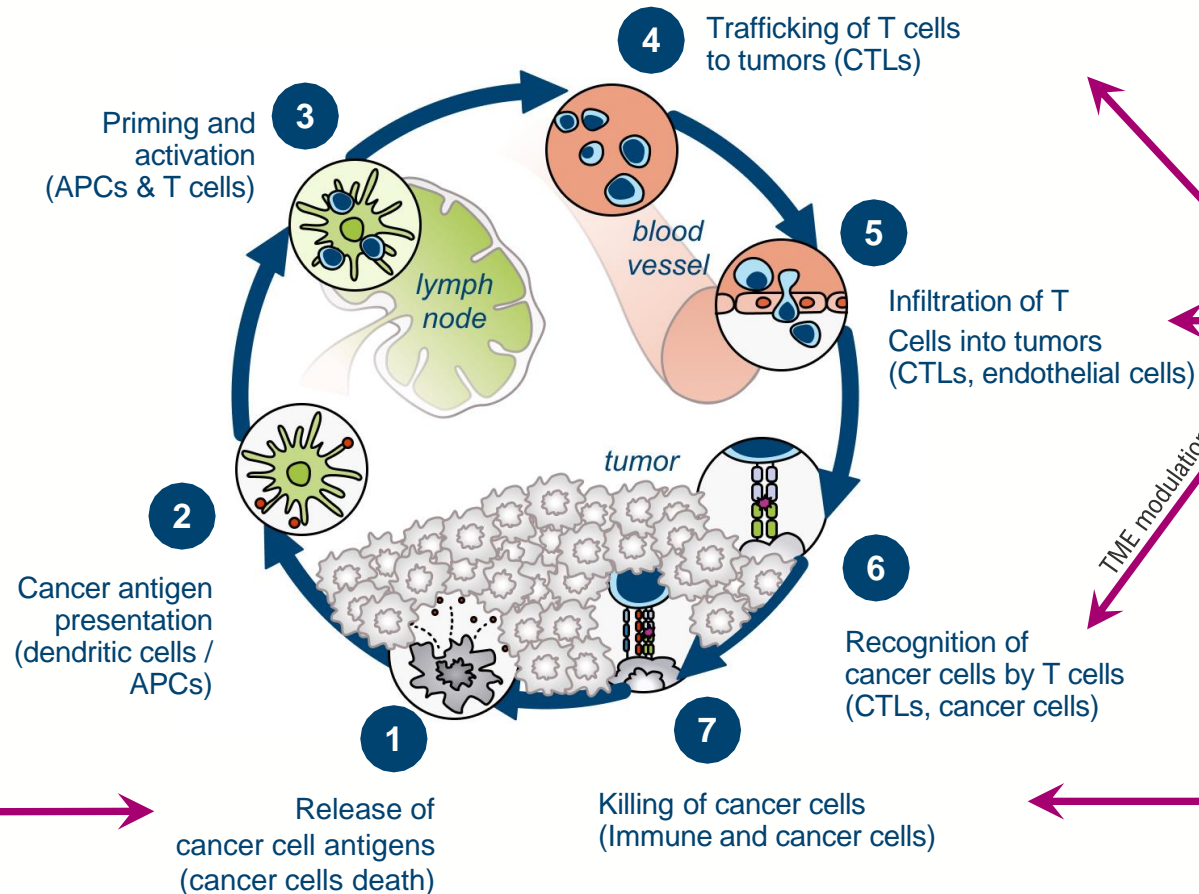
1. O'Reilly, EM JAMA Oncol. 2019; Wainberg ZA Clin. Cancer Res. 2020; Renauf DJ Nat Commun. 2022; 2. Renauf DJ Nat Commun. 2022; 13: 5020.

# Rationale for motixafortide triple combination therapy

**Solid tumors with low immune system visibility require a multi-pronged approach**

## Chemotherapy

- Chemotherapy induces tumor death, reducing tumor burden
- Chemotherapy induces immunogenic cell death, leading to activation & expansion of new tumor-reactive T-cell clones



## Motixafortide + Checkpoint Inhibitor

- Motixafortide facilitates T cell trafficking and infiltration into tumor core; TME modulation

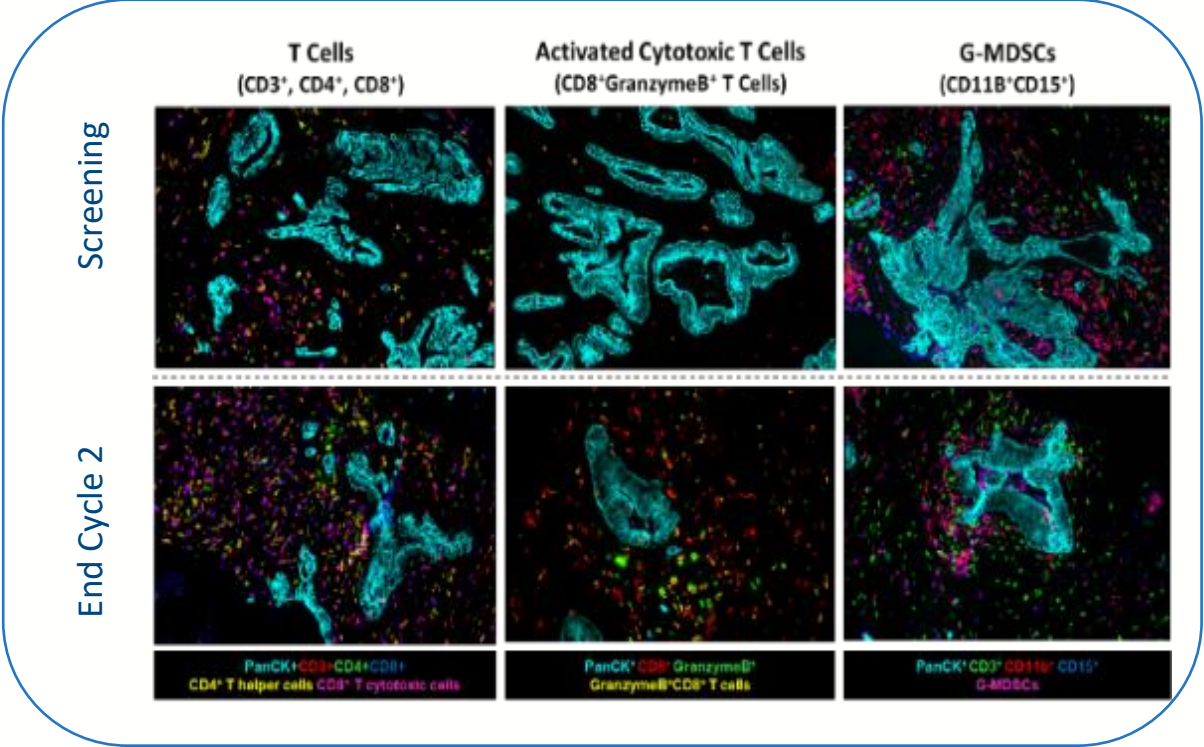
## Checkpoint Inhibitor

- PD-1 maintains and restores activity of T cells within tumor

Adapted from Chen, D. et al. Immunity Review 2013

# Proof of mechanism & concept from COMBAT phase 2 PDAC study (second line)

**Cohort 1:** Dual combination of motixafortide + pembrolizumab



\*Representative MultiOmyx™ data taken from SD patient with long treatment duration (11 combo cycles ~34 weeks). Data shown before treatment vs. after ~7w of treatment (end of cycle 2)

- **Increased** activated cytotoxic T cells
- **Decreased** suppressor cells in tumor microenvironment
- **Reduction** in tumor cell numbers

**Cohort 2:** Triple combination of motixafortide + pembrolizumab + chemo (Onivyde, 5FU, Leucovorin)

	COMBAT	HISTORICAL DATA#
mOS	6.5 months	4.7 months <sup>1</sup>
mPFS	4.0 months	2.7-3.1 months <sup>2,3</sup>
cORR	13.2%	7.7% <sup>3</sup>
DCR	63.2%	29-52% <sup>2,4</sup>

- COMBAT results suggest **motixafortide + PD-1 inhibitor + chemotherapy** benefit in second-line PDAC setting
- **Improvements were seen across all study endpoints**, including overall survival, progression-free survival, and overall response rate in patients with very advanced disease
- **Favorable safety** and **generally well tolerated**

<sup>1</sup> Macarulla Mercade et al, Pancreas 2020; <sup>2</sup> Petrelli et al Eu J Cancer 2017; <sup>3</sup> Onivyde SMPC; <sup>4</sup> Wang Gillam Eu J cancer 2019

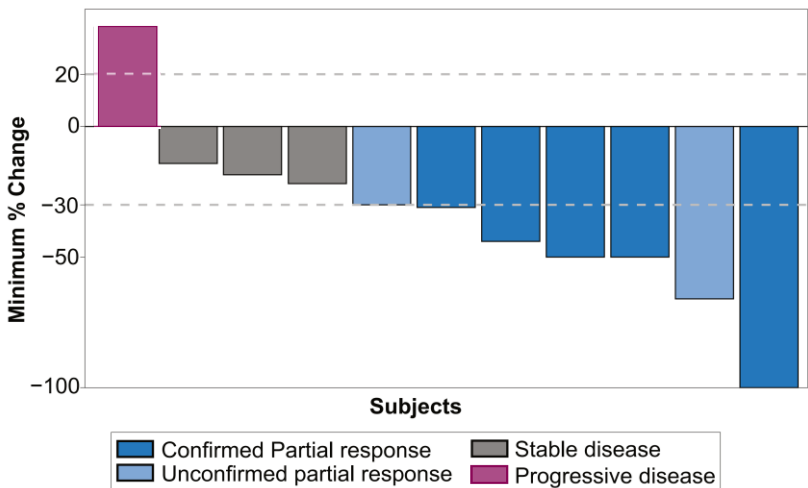




# Chemo4MetPanc phase 2 clinical trial pilot phase at AACR (first line)

## Pilot Clinical Findings

Radiological Response<sup>1</sup>



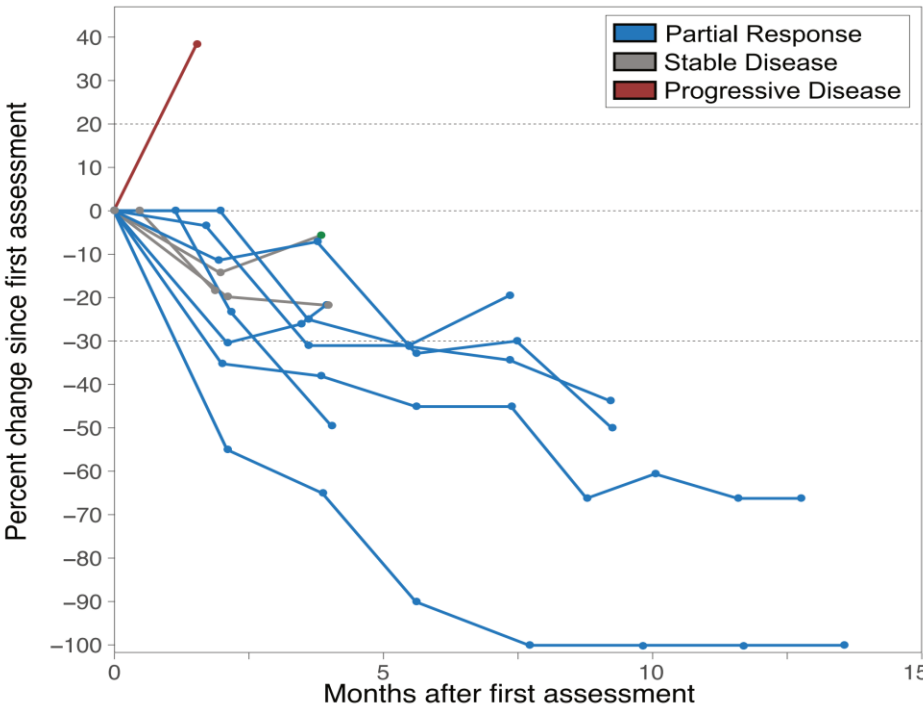
\*N = 11 (%)

Disease Progression	1 (9%)
Stable Disease	3 (27%)
**Partial Response	7 (64%)
**Disease Control Rate	(91%)

\*90% of patients had liver metastasis at baseline

\*\*Compares favorably to historical PR (23%) and DCR (48%) with gemcitabine and nab-paclitaxel alone

Radiological Response Duration<sup>1</sup>



1. Manji, GA AACR Pancreatic Cancer 2023 (Censor Date – July 20, 2023)

# Chemo4MetPanc phase 2 clinical trial pilot phase at AACR (first line)

## Pilot Phase Conclusions



Gemcitabine, nab-paclitaxel, motixafortide and cemiplimab resulted in

Overall Response Rate **64%**

Median Progression Free Survival **9.6 months**

One patient experienced

**resolution of hepatic (liver)**

**metastatic** lesion as of July 20, 2023.

The combination demonstrated a **tolerable safety profile**

No unexpected Grade 4 or 5 treatment related adverse events

**Correlative analysis on paired tumor** biopsies on all patients are ongoing

The encouraging preliminary efficacy prompted a change in clinical trial design to a **randomized phase 2 trial (Chemo4MetPanc; NCT NCT04543071)**

Manji, GA AACR Pancreatic Cancer 2023 (Censor Date – July 20, 2023)

# Chemo4MetPanc phase 2 clinical trial design and endpoints (first line)

## Randomized Trial Recruiting

### Participating Sites

- Columbia University (Dr. Manji – Lead PI)
- Brown University
- University of California - San Francisco
- Medical College of Wisconsin
- Northwell Health

### Primary Endpoint

median PFS

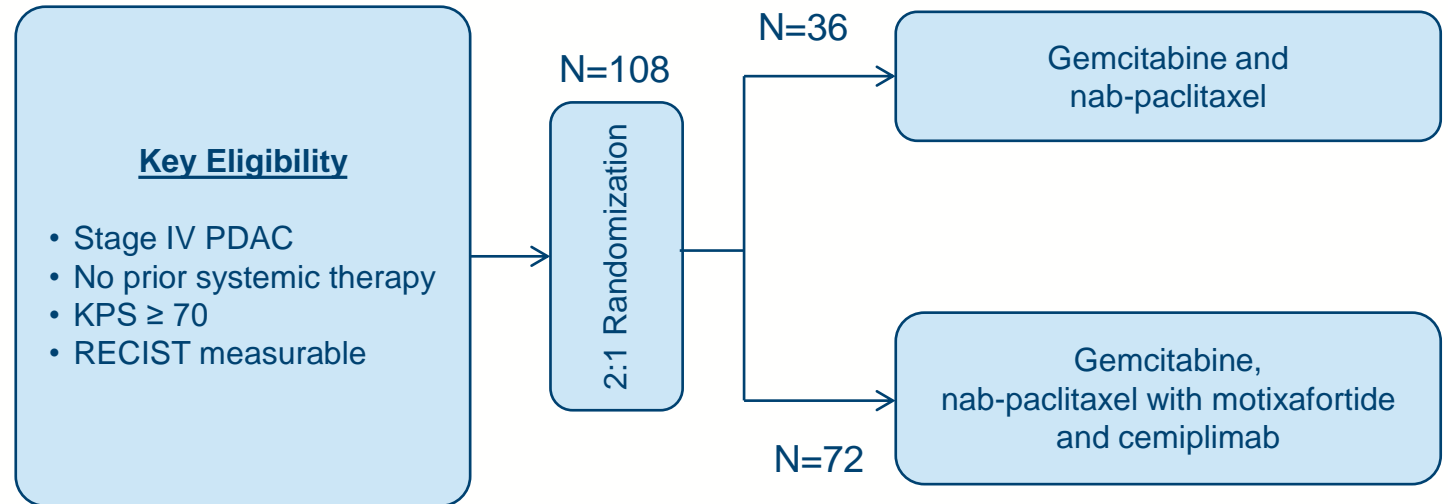
### Secondary Endpoints

OS, RR

### Correlates

mIF, snRNAseq, cytokine

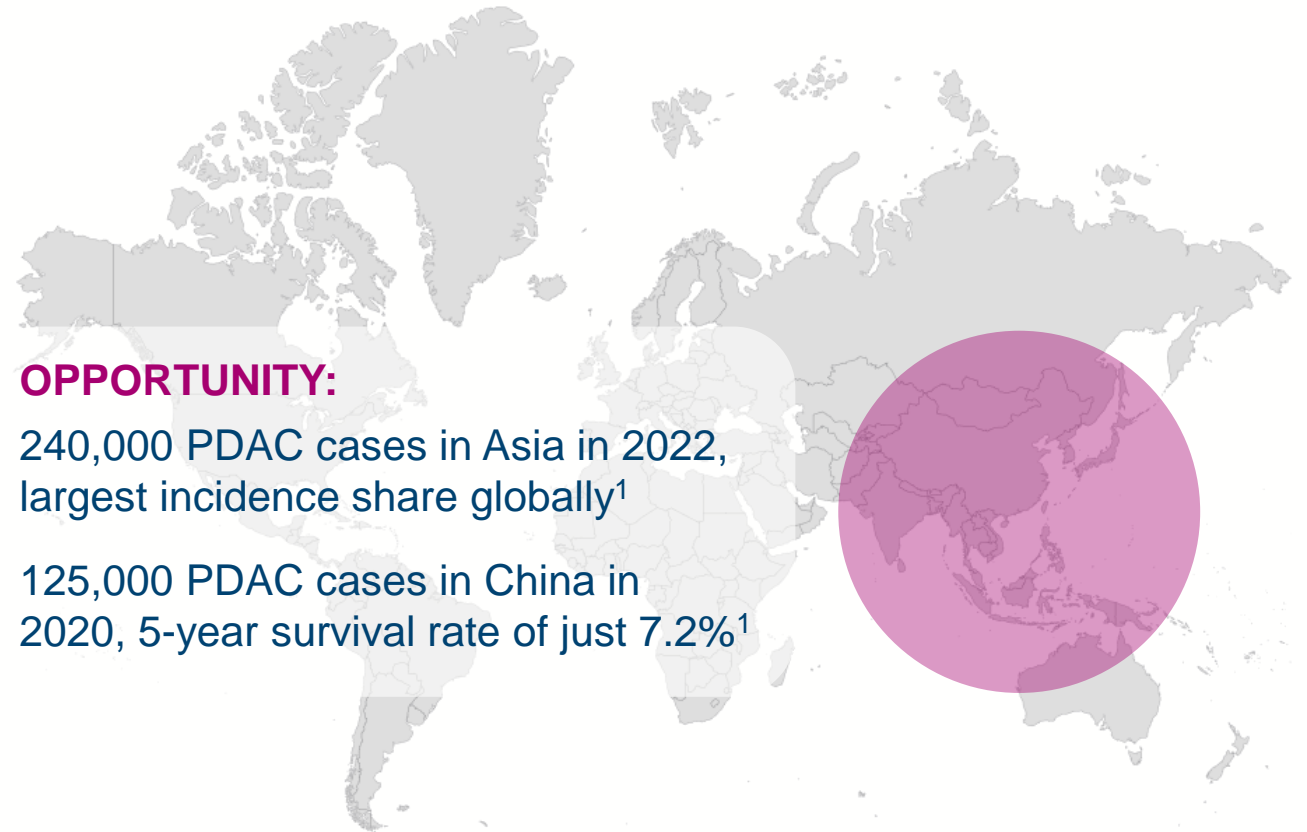
### Study Design



# Additional randomized study in first-line PDAC in China



- GloriaBio will execute a randomized first-line PDAC trial in China evaluating motixafortide in combination with PD-1 inhibitor \*zimberelimab and standard of care combination chemotherapy
- Zimberelimab is a fully human anti-PD-1 monoclonal antibody. GloriaBio is developing and commercializing zimberelimab in Greater China, including mainland China, Hong Kong, Macao and Taiwan, where zimberelimab is approved for R/R classical Hodgkin's lymphoma and recurrent or metastatic cervical cancer



1. Datamonitor Healthcare; the National Central Cancer Registry of China (NCCR); United Nations, 2022; China CDC Weekly, 2022, 4(24): 527-531

\*Arcus Biosciences, and development partner Gilead Sciences, have the exclusive rights to develop and commercialize zimberelimab throughout the world except in Greater China and certain territories



# Summary and Upcoming Milestones

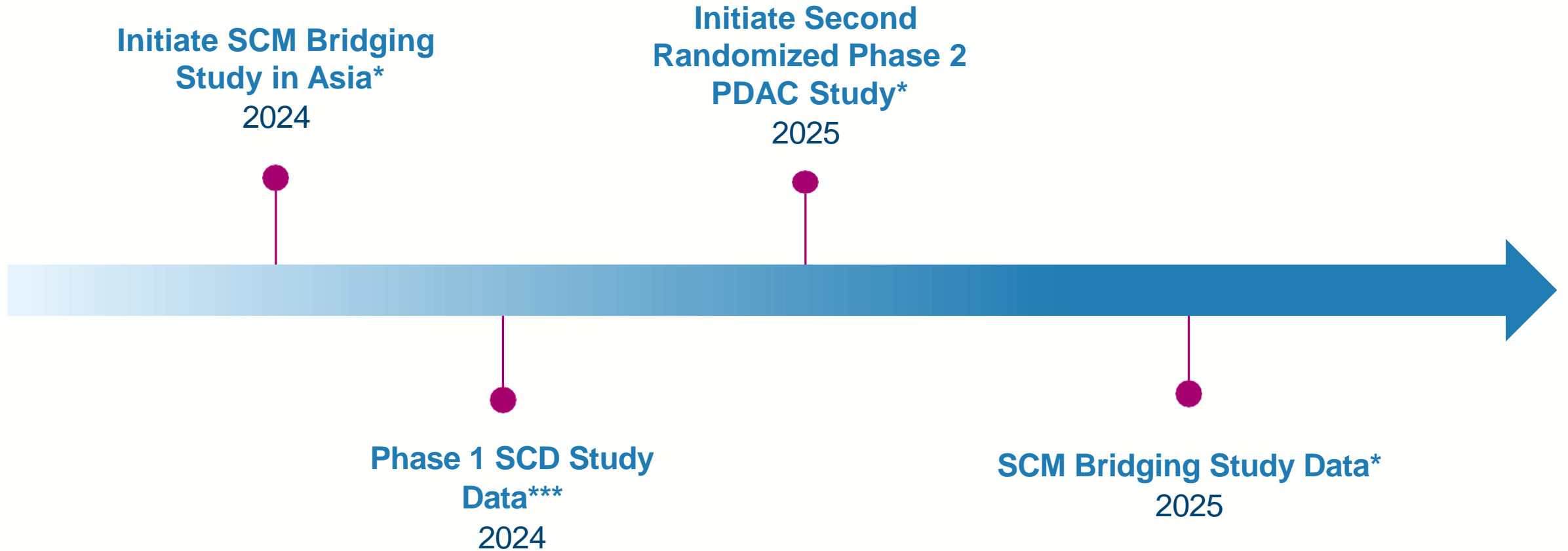
# Focused vision for growth

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- Maximize value of APHEXDA™ in stem cell mobilization
  - Accelerate development of motixafortide in combination with PD-1 inhibitors in pancreatic cancer and additional select solid tumors
  - Leverage US commercial infrastructure
  - Broaden pipeline via in-licensing of selected assets
-



# Expected major pipeline milestones over next 18 months



\*Clinical development with GloriaBio

\*\*IIS with Columbia University

\*\*\*IIS with Wash U. in St. Louis

# Fully integrated, commercial stage biopharmaceutical company



Commercial stage company with **multiple value enhancing opportunities**



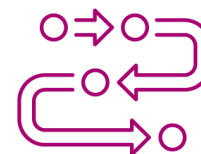
Innovative clinical development programs supporting **indications with significant unmet need**



**Strong financial position** coupled with disciplined execution



Presence in **global biopharmaceutical hubs**



Proven **end-to-end expertise**



Thank You