

CANbridge  
Pharmaceuticals

# Corporate Presentation

Aug 2023

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# Our Vision



To be a **Global Biopharmaceutical Company**

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Delivering **Life-changing Therapies to Patients**

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Built Upon a **Foundation in China**

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# Key Investment Highlights



Positioned to drive rapid and comprehensive product development and market access in China and globally



A comprehensive portfolio of rare disease-focused therapies with significant revenue potential



Track record of sourcing and developing innovative and validated therapies



A rare disease pioneer dedicated to addressing vast and unmet medical needs



Visionary management team with deep experience in developing and commercializing rare disease therapies globally

# Strong Investor Base

Raised total capital of **\$357m\*** since 2015



2015: Series A \$13m

2017: Series B \$54m

2019: Series C \$46m

2020: Series D \$98m

2021: Series E \$58m

2021: HKEX IPO \$88m

\*Currency: \$ USD

# Experienced Management Team

Strong global management team with deep industry experience and a track record of commercializing rare disease treatments



- **Veteran entrepreneur** with **22+ years** of experience in medical and pharmaceutical companies
- Former Founding General Manager of Genzyme China
- **Deputy Director General at CHARD, Vice Chair** of R&D Committee of **China Pharmaceutical Innovation and Research Development Association**

**Dr. James Qun Xue**  
 Founder,  
 Chairman of the Board,  
 Executive Director,  
 Chief Executive Officer




- **21 years** of biotechnology executive management experience
- Former CMO at Editas Medicine and VP at Genzyme
- Made major contributions to 4 INDs and 3 orphan drug marketing authorizations for serious and life-threatening diseases that have **generated US\$ 3.0+ billion revenue for Genzyme**

**Dr. Gerald Cox**  
 Chief Development Strategist, Interim Chief Medical Officer





- **15+ years** of extensive banking, investment, and strategy consulting experience in the healthcare sector globally
- Former Director of Healthcare Investment Banking at China Renaissance
- **Veteran public market healthcare investor** at leading firms, including Citadel and Fidelity Management

**Glenn Hassan**  
 Chief Financial Officer




- **~20 years** of business leadership experience in the biotechnology industry with **in-depth industry knowledge and extensive execution capabilities**
- Previous employment at leading biopharmaceutical companies such as Bioverativ, Ultragenyx, Synageva Biopharma and Genzyme

**Marcelo Cheresky**  
 Chief Commercial Officer


**Chris Chen**  
 Vice President of Human Resources



**Pauline Li**  
 Senior Vice President of Clinical Development and Operations



**Bettie Li**  
 Senior Director & Head of Finance Operation and Controller



**Qian Ma**  
 Head of Legal and Compliance, Joint Company Secretaries and Board Secretary



**Stella Mao**  
 Senior Director, Public Affairs



**Shirley Yue**  
 Senior Director, Procurement and Supply Chain



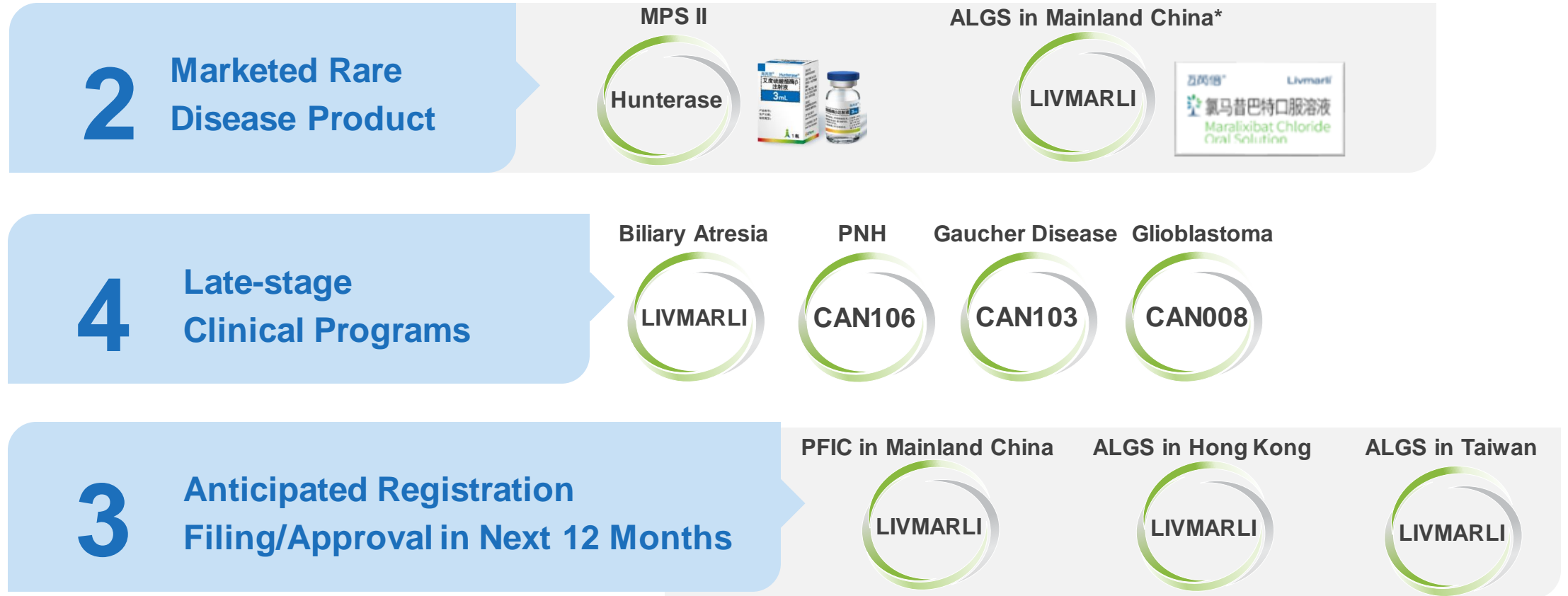
**Rebecca Zhang**  
 Senior Vice President of Regulatory Affairs



**Wei Zhang**  
 Senior Director & China Head of CMC Department

# CANbridge Today

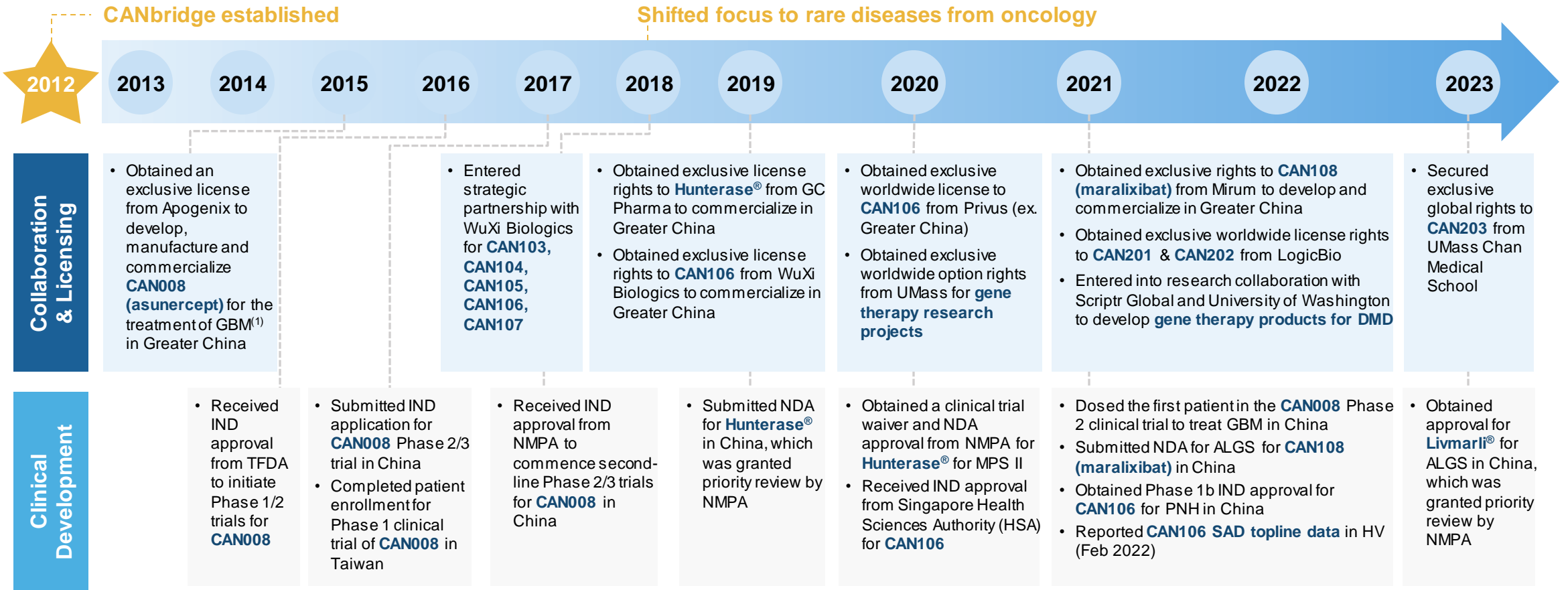
Well-positioned to Deliver Multiple Commercial and Development Milestones in Rare Diseases



To launch in 1Q 2024

# Track Record of Sourcing and Developing Innovative Therapies

- ✓ Agile execution capabilities on Hunterase® with **6 months** from licensing to NDA submission, then **14 months** to approval
- ✓ Solid clinical progress made on CAN108 with **9 months** from licensing to NDA submission, then **17 months** to approval
- ✓ Efficient clinical development on CAN103 with **16 months** from IND approval to FPI in the pivotal study



Proven track record in APAC navigating through development and regulatory landscapes in mainland China, HK, Taiwan and Singapore



# Well-established Commercialization Infrastructure

## Launched Products



**Hunterase**

- ◆ Hunterase has entered into **109** cities' commercial insurance program ("Huiminbao") as of June 30, 2023
- ◆ **72%** of Hunterase treated patients are covered by commercial insurance
- ◆ Expected **NRDL inclusion** in **2024** and **10** newly expanded target cities with commercial insurance coverage



**Livmarli**

- ◆ Expected **NRDL inclusion** in **2024** and **4** newly expanded target cities with commercial insurance coverage
- ◆ Launch of Livmarli-ALGS in China in **Q1 2024**
- ◆ Dedicated sales team of 12 professionals support early launch to cover **98 hospitals** and **300** healthcare physicians

**Expect 5 new launches in 5 years, including CAN103, CAN108-PFIC, CAN108-BA, CAN106 and CAN008**

## Established Commercial Infrastructure in Greater China



**Marcelo Cheresky**  
Chief Commercial Officer

- ◆ **20+ years** of experience in leading emerging market teams, establishing marketing and commercial operations, and regional country management
  - ◆ **Deep experience in successful launches** of multiple products globally including Eloctate, Alprolix, Thyrogen, Cerezyme, etc.
- 



**Fannie Man**  
China Commercial Head / GM of HK and Macau

- ◆ Responsible for the commercial operations in Mainland China
  - ◆ **17+ years** of commercial experience in various companies including BMS, AbbVie and GSK, where she contributed in launching numerous key oncology, hematology, hepatology and respiratory products
- 

**Commercialization team of 40+ experienced professionals**

### Broad Geographical Coverage in Mainland China

	Before NRDL	After NRDL
Covered Province #	22	30
Covered City #	~50	~180
Covered Hospital #	~300	~1,100
Covered KOL #	~1,500	~5,500
Covered Population # Mn	~550	~1,130

**Established commercial infrastructure in HK and Taiwan to drive robust sales**

# Access to GMP Manufacturing Capability for Multiple Modalities



7 CMC staff  
in China and the U.S.



Secured manufacturing capacity  
with third-party collaboration  
partners



In-house process development  
lab in the U.S.



Well-established quality control  
team in China and the U.S.



Abundant manufacturing capacity



**Solid partnership with Wuxi**

Preferred access to the Wuxi's global manufacturing capacity across all modalities (ERT, mAb, Gene therapy)



**US process development lab**

Total 24,500 sq. ft. (up to 90 FTEs), including AAV process lab (up to 50L scale); AAV analytical lab; Research discovery lab



# Next Generation Gene Therapy Portfolio in Development

Gene therapy holds the promise to transform treatments for LSDs and neuromuscular diseases from ameliorative to curative

## CANbridge In-house Tech Platform Pipeline



### US R&D Center. Burlington, MA

- 24,500 sq. ft. (up to 90 FTEs)
- AAV process lab (up to 50L scale)
- AAV analytical lab
- Research discovery lab
- Opened in July 2022

CANbridge Innovative Platform

Tissue-Specific Targeting Platform

PoC Exp. 2023

Protentional indication 1

Protentional indication 2

Protentional indication 3

### CANbridge Innovative AAV Platform

- Using tissue specific cell surface receptors for targeting
- AAV platform enables future development in multiple CNS/muscle-related diseases
- Patent filing in process

Upcoming milestones, SMA: Spinal Muscular Atrophy, DMD: Duchenne Muscular Dystrophy

## In-licensed Gene Therapy Programs

Candidate	Discovery	IND-Enabling	Clinical	Collaborator
CAN201	Fabry			AstraZeneca, LogicBio
CAN202	Pompe	Exp. 2024		AstraZeneca, LogicBio
CAN203	SMA	Exp. 2024		UMass Chan Medical School
Undisclosed	DMD			UW Medicine, Scriptr

### 2<sup>nd</sup> Generation Capsid and Transgene engineering, CANbridge work with:

- **LogicBio:** Novel sAAV capsid (sL65) with improved functional transduction and immunological profile compared to LK03
- **UMass:** CNS and muscle tropic new AAV
- **UW and Scriptr:** Dystrophin with improved function

# Business Overview & Opportunities

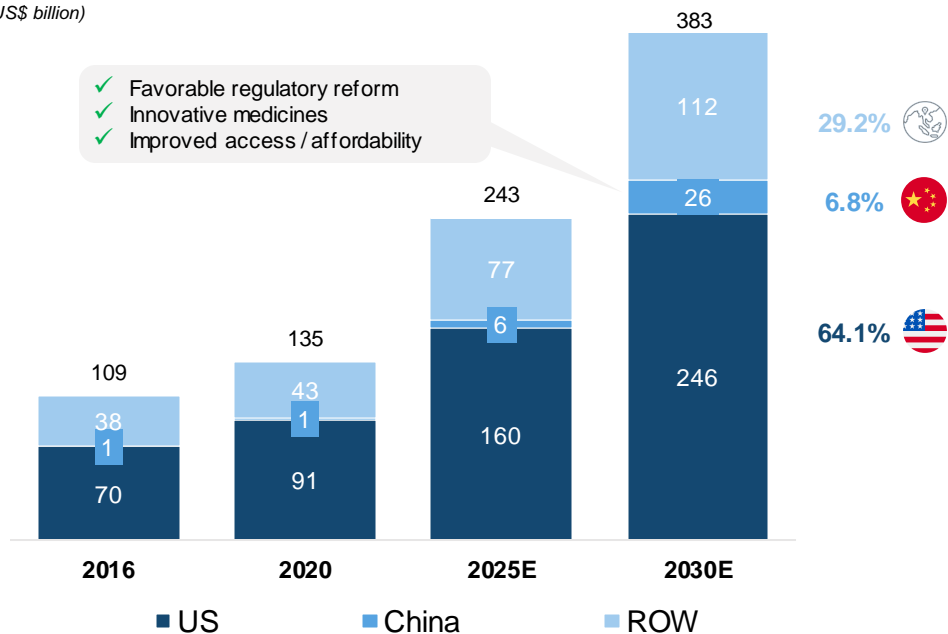
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# Proven Large Global Rare Disease Market Opportunity

## Global Rare Disease Drug Market<sup>1</sup> (By Region)

(US\$ billion)

- ✓ Favorable regulatory reform
- ✓ Innovative medicines
- ✓ Improved access / affordability



China's contribution to global rare disease market

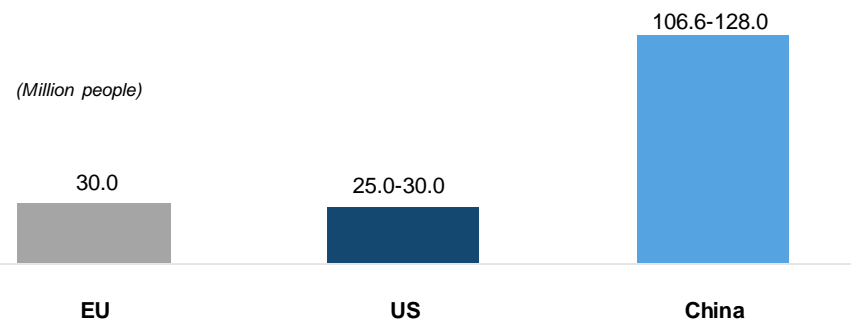
2020  
US\$ 1.3 Bn  
**<1%**



2030E  
US\$ 25.9 Bn  
**6.8%**

## Rare Disease Prevalence in U.S., EU & China (est.)

### China Rare Disease Prevalence > 100 million (est)<sup>2</sup>



## Global Competitors' Strong Rare Disease Drugs Sales



Orphan drugs achieved a combined sales of US \$173 billion globally in 2022

Source: Frost & Sullivan Analysis. Evaluate | Orphan Drug Report 2022. Notes: 1, Rare disease drugs in this market include drugs indicated for rare disease only and drugs obtaining orphan drug designation first but their indication expanded later of which generated most of their revenue, such as Humira. However, the part of revenue generated by expanded non-orphan indications was not included in this market. 2, It is an appropriately reasonable estimate that China may have a total prevalence base which exceeds 100 million patients suffering from one or more forms of rare diseases, by way of extrapolation adopting the broader definition in the U.S. or Europe.

# A Rapidly Evolving Market for Developing Rare Diseases Products

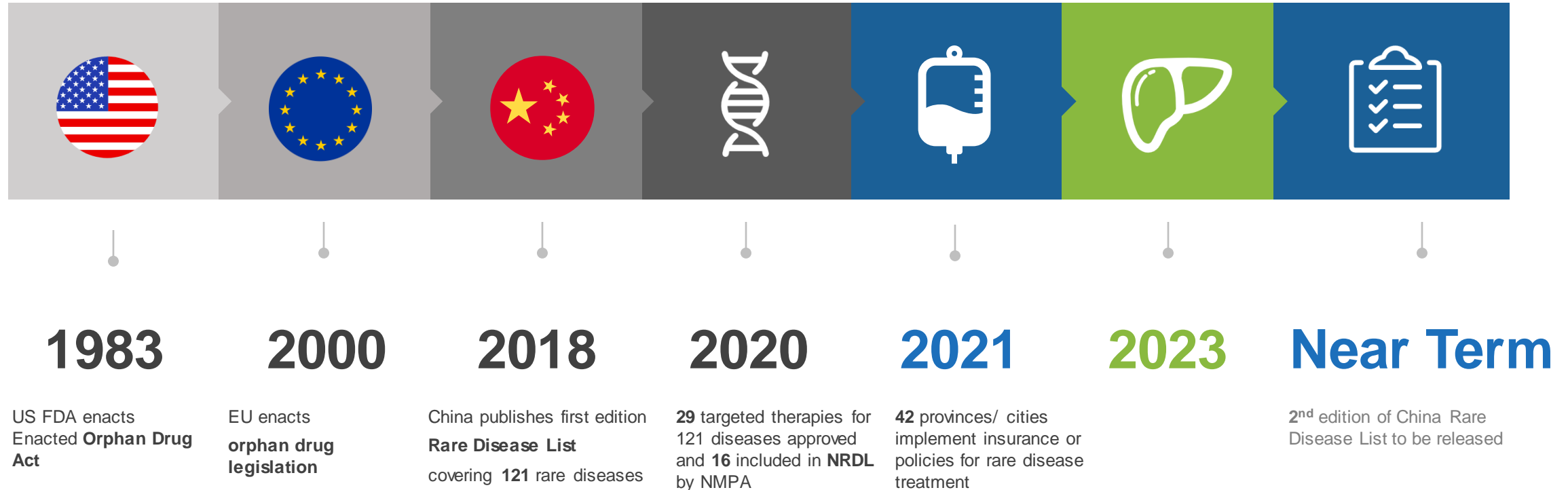
Emerging Favorable Regulatory Framework

 **CANbridge**  
Potential Commercial Path 

Hunterase launch  
in self-pay market

Livmarli NDA  
approved in China

Special rare disease funding  
Global Expansion to Further  
Improve ASP



NRDL = national reimbursement drug list

# Pipeline Targets Diseases with \$15 Billion Potential

Commercial Rights	Pipeline	Indications	Prevalence		Global Sales
China	Hunterase®	MPS II	8k		\$ >500 M
	Livmarli (CAN108)	Alagille Syndrome	10k		\$ 75 M
		PFIC	5k		\$ >25 M
		Biliary Atresia	6.5k*		\$ NA
	CAN008	GBM	55k		\$ NA
Global	CAN106	PNH	23k	124k	\$ >5 B
		aHUS	10k	32k	
		gMG	234k	1,290k	
		NMOSD	55k	171k	
	CAN 203	SMA	14k	78k	\$ 1.4 B
	CAN103	Gaucher Disease		78k	\$ >1.5 B
	CAN104 CAN201	Fabry Disease		1,789k	\$ ~2 B
	CAN202	Pompe Disease		170k	\$ >1 B
	CAN107	XLH		117k	\$ ~1 B
	CAN105	Hemophilia A		340k	\$ ~4 B

2022 Global Sales (US\$)  
 2022 Global / China Prevalence

Abbreviations: GBM – Glioblastoma Multiforme; MPS II – Mucopolysaccharidosis type II; ALGS – Alagille Syndrome; PFIC – Progressive Familial Intrahepatic Cholestasis; PNH – Paroxysmal nocturnal hemoglobinuria; aHUS – Atypical Hemolytic Uremic Syndrome; gMG – Generalized Myasthenia Gravis; NMOSD – Neuromyelitis Optica Spectrum Disorders; XLH – X-linked hypophosphatemia; PD – Pompe Disease. Source: Frost & Sullivan and CANbridge Analysis, NCBI research, Endocrine Journal research, World Federation of Hemophilia research

Notes: CAN008 currently has no commercialized comparable product.

Note: targeted patient pool

# Our Comprehensive and Diversified Pipeline

CANbridge holds global rights to 8 out of 14 assets, spanning biologics, small molecules, and gene therapy, targeting most prevalent rare diseases and oncology indications, with proven mechanisms and significant market potential

	Candidate	Mechanism	Discovery	IND-enabling	Ph 1	Ph 2/3	NDA	Marketed	Dev Strategy	Partner	Commercial Rights
Rare Onc.	<b>CAN008</b> (Asunercept)	CD95-Fc fusion protein	Glioblastoma Multiforme						In China for China	apogenix	Greater China
	<b>Hunterase®</b> (Idursulfase beta)	ERT IDS	Hunter Syndrome (Mucopolysaccharidosis Type II)							GCPharma	Greater China
Rare Disease	<b>Livmarli®</b> (CAN 108)	IBAT inhibitor	Alagille Syndrome						In China for China	mirum	Greater China
			Progressive Familial Intrahepatic Cholestasis								
				Biliary Atresia							
	CAN 106	Anti-C5 mAb	Paroxysmal Nocturnal Hemoglobinuria						In China for Global	WuXi Biologics / Privus	Global
	CAN 103	ERT GBA	Gaucher Disease							WuXi Biologics	Global
	CAN 107	Anti-FGF23 mAb	XLH						In China for China	WuXi Biologics / Privus	Global
	CAN 104	ERT GLA	Fabry Disease							WuXi Biologics	Global
	CAN 105	Anti-Factor IXa/X bsAb	Hemophilia A						WuXi Biologics	Greater China	
	CAN 201	AAV sL65 GLA	Fabry Disease						Global for Global	AstraZeneca / LogicBio	Global
	CAN 202	AAV sL65 GAA	Pompe Disease							AstraZeneca / LogicBio	Global
CAN 203	AAV SMN1	SMA						UMass Chan MEDICAL SCHOOL		Global	
Undisclosed	AAV	DMD						UW Medicine / Scriptr		Global	
Other Onc.	<b>Caphosol™</b>	Calcium phosphate rinse	Oral Mucositis							EUSA Pharma	China
	<b>Nerlynx®</b> (Neratinib)	Tyrosine kinase inhibitor	HER2+ Breast Cancer							Pierre Fabre	Hong Kong, Taiwan, Macau

Clinical trials performed by license partner
 Biologic
 Small Molecule
 Gene Therapy
 Medical Device



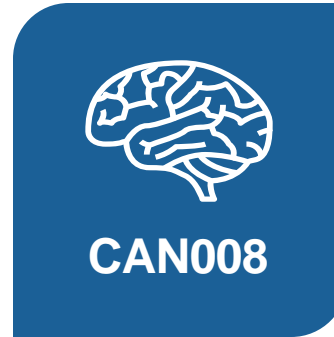
# Recent Business Highlights



- Received China NMPA approval for marketing in May 2023
- Completed patient enrollment in Phase 2 EMBARK study in BA in China in May 2023



- Reported positive proof-of-concept data from Phase 1b trial in PNH patients in June 2023



- IDMC<sup>1</sup> conducted a mid-study analysis of the Phase 2 trial in Chinese patients with newly diagnosed GBM. The recommendation was to proceed with the current trial design without any changes.
- Long-term data from phase 1/2 trial presented in ESMO in Mar 2023 showed 67% five-year OS rate vs. 8.2% in institutional database; 17.95 months median PFS vs. 5.8 months PFS in historical group



- Initiated dosing in Phase 2 trial in adult and adolescent Gaucher disease in January 2023



- Presented ICV data that demonstrated improved lifespan and motor function in mice at 2023 ASGCT

1: independent data monitoring committee

# Pipeline Portfolio Update

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# Hunterase:

The First and the  
Only Approved  
Enzyme Replacement  
Therapy for MPS II  
in China

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# Hunterase® – Early Commercialization In Non-reimbursed Market

Identification of new patients accelerates, and commercial insurance coverage expands

## Overview of MPS II



MPS II is a **rare, disabling** and **life-threatening** genetic disease



In **East Asian** countries, MPS II is the most common form of MPS disorders



Chinese government has included MPS II on the “**National Rare Disease List**” as a disease group to target



Life expectancy of patients with severe MPS II (**60%-80%** of cases) is significantly reduced



Death occurs generally before the age of **25**

## Hunterase Commercial Updates



MPS II Patient Identification

### Total 739 identified patients

- **72** patients newly identified in 2023
- **263** patients newly identified in 2022
- **195** identified in 2021 since launch in May 2021
- **209** registered by patient group



Reimbursement Campaign

- **Hunterase has entered into 109 cities'** commercial insurance program (“Huiminbao”) as of end of June 2023, covering a population of 586 million in China
- **72%** of Hunterase treated patients are covered by commercial insurance
- Reimbursement rate ranges from **20% to 90%**



In China for China

In China for Global

In Global for Global

# Livmarli<sup>®</sup> (CAN108):

Near-term Launch  
in Rare Cholestatic Liver  
Diseases in China

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# Livmarli – IBAT Inhibitor for Rare Cholestatic Liver Diseases

A novel, oral, minimally-absorbed agent designed to selectively inhibit IBAT in the ileum and treat rare cholestatic liver diseases, including ALGS, PFIC and BA

## Recent Highlights

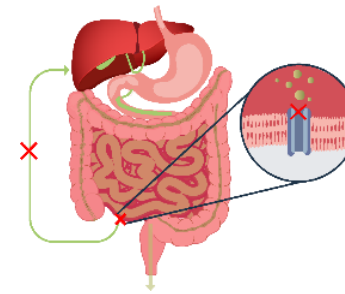
- Received China NMPA marketing approval for **ALGS** in 1H 2023
- Filed Hong Kong/Taiwan FDA for **ALGS**, with estimated approval by the end of 2023
- Mirum realized **\$75.1 million** in LIVMARLI (maralixibat) net product sales in the first full fiscal year of its U.S. launch
- Mirum dosed first patient in Phase 2 BA China study and reported positive topline **Phase 3 PFIC data and** label expansion for ALGS to include infants of 3 months+

## Disease Overview

- **Alagille Syndrome (ALGS):** a rare genetic disorder that can affect multiple organ systems of the body, including the liver, heart, skeleton, eyes and kidneys. No procedure to cure ALGS completely
- **Progressive Familial Intrahepatic Cholestasis (PFIC):** a rare genetic liver disorder in which liver cells don't release bile properly, causing bile accumulation in the cells. Surgical treatment includes external or internal biliary diversions
- **Biliary Atresia (BA):** a rare disease of the liver and bile ducts that occurs in infants. Currently no cure for BA available. Treatments include liver transplant and Kasai procedure

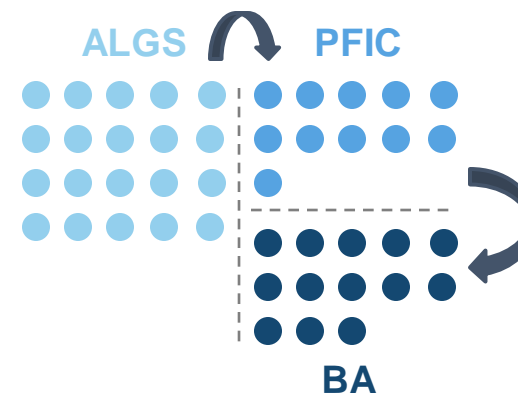
Source: Frost & Sullivan Analysis. Abbreviations: IBAT, ileal sodium-dependent bile acid transporter

## Mechanism of Action



1. IBAT is primarily responsible for recycling bile acids from the intestine ileum back to the liver
2. Elevated bile acids damage the liver and lead to cholestatic liver disease
3. Livmarli is designed to inhibit IBAT in the ileum and result in more bile acids being excreted in the feces, leading to lower levels of bile acids systemically, thereby reducing bile acid mediated effects and liver damage

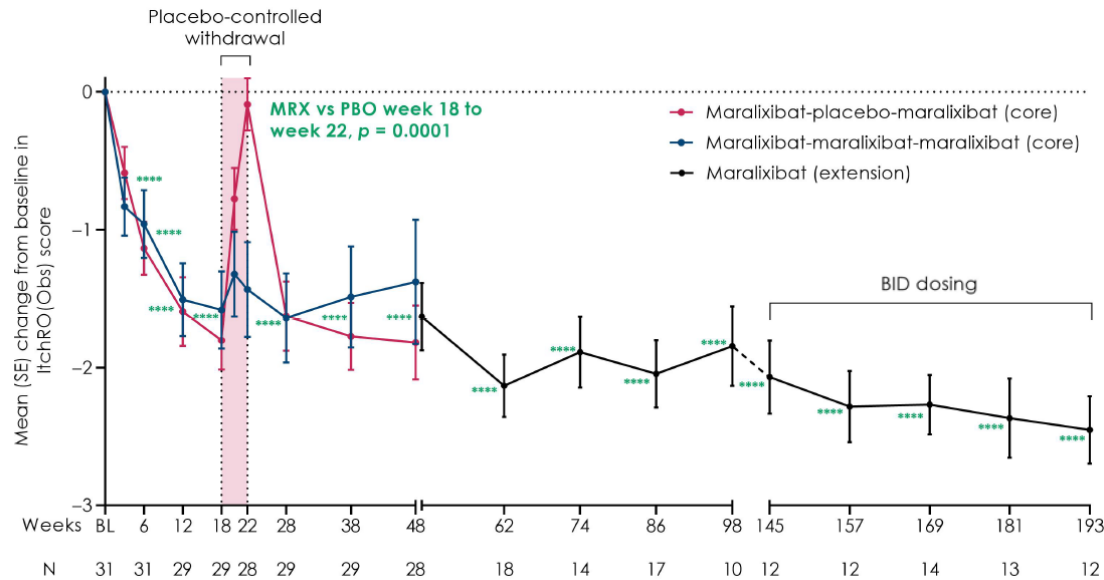
## Epidemiology



More ~22,000 targeted patients with ALGS, PFIC, BA in China

● Represent 500 patients

# Statistically Significant, Clinically Meaningful, and Sustained Improvement in Pruritis



Change from baseline, \*\*\*\*  $p \leq 0.0001$  (overall population)

- ◆ **Robust results from the pivotal LUM001-304 study, meeting the efficacy endpoint, improvement in pruritus, and long-term treatment benefit**
- ◆ **The results of the 4 supportive studies support the pivotal study efficacy results and effective dose**
  - The effect of maralixibat treatment on all efficacy parameters was maintained after Week 48 up to Week 240.

## Safety Data of LIVMARLI in ALGS Includes 5 Years of Follow-up

Events observed over 5% patients	Number of events per 100 person-years
Diarrhea	41.6
Abdominal pain	38.6
Vomiting	19.8
Nausea	2.9
Fat-soluble vitamin deficiency	11.1
Transaminase increased	6.9
GI bleeding	3.8
Bone fractures	3.3

- ◆ **Population Exposure Status:** Maralixibat has been studied in > 1600 subjects, including more than 180 pediatric or adult subjects with cholestatic liver disease. Of 119 children with cholestatic liver disease treated for up to 5 years, 86 had ALGS.
- ◆ **Common Adverse Events:** In the ALGS pool, events of diarrhea and abdominal pain were the most frequently reported AE in subjects exposed to maralixibat and placebo.
- ◆ **Serious Adverse Events:** in the ALGS pooled population, no subjects in the majority of maralixibat clinical studies experienced SAE and no deaths were reported.

Adapted from Mirum Investor Communication

# Long-term Data Emerging Suggests Improvement in Event-Free Survival and Growth

**Maralixibat-treated patients with Alagille syndrome (ALGS) demonstrate improved event-free survival in a natural history comparison with patients from the GALA database: Application of real-world evidence analytics**

**Bettina E. Hansen, PhD<sup>1,2</sup>**  
and **Binita M. Kamath, MBBChir<sup>3</sup>** on behalf of The GALA Study Group

<sup>1</sup>Department of Epidemiology and Biostatistics, Erasmus MC, Rotterdam, The Netherlands  
<sup>2</sup>Toronto Center for Liver Disease, University Health Network and the Institute of Health Policy, Management and Evaluation, The University of Toronto, Toronto, Canada  
<sup>3</sup>The Hospital for Sick Children and the University of Toronto, Division of Gastroenterology, Hepatology, and Nutrition, Toronto, Canada

**Bettina E. Hansen<sup>1,2</sup>**, Shannon M. Vandert, Pamela Vig, Will Garner, Li-Ting Li, Nuiyee She, Jian-Shie Wang, Melissa A. Gilbert, Ines Jankowska, Piotr Cudkowicz, Dorota Golec-Mioduska, Emmanuel M. Gonzalez, Emmanuel Jacquemin, Jérôme Bouligand, Nancy B. Spinner, Kathleen M. Loomes, David A. Piccoli, Lorenzo D'Antiga, Emanuele Nascato, Estelle Sokal, Tangy Demant, Noelle H. Ebel, Jeffrey A. Feinstein, Rima Fawaz, Shila Nastaio, Florence Lacaille, Dominique Delbray, Henrik Anvil, Björn Fischer, Susan Saw, Michael Storrman, Saul J. Kagan, Rene Romero, Kyung-Min Kim, Woo-Yun Baek, Wanda Haidich, Jelena Stankovic, Anur J. Roberts, Helen M. Evans, M. Kyle Jensen, Marianne Kayan, Shikha S. Sundaram, Alexander Chudek, Palanisamy Karthikeyan, Suzanne Dawson, Maria Camila Sanchez, Maria Lorena Cevallos, Hienhiep V. Vanhieu, Wan-Seok Lee, James E. Squires, Christine Heptinstall, Channaman Arundodharamani, Ryan T. Fischer, Catherine Larson-Heath, Neil Kizer-Glasberg, Cigdem Arkan, Henry C. Lin, Jessa Quintero Bernabeu, Serena Alam, Dorothea Kelly, Eliza Carvalho, Cristine Targa Ferreira, Giuseppe Indolfi, Ruben E. Quizon-Rojas, Pinar Balci, Peter Luigi Galati, Dennis O'Neil, Pamela L. Valentinis, Devi M. Sena, John Schar, Maria Nagaflo, Arsal Dardari, Sabina Wlecek, Gabriella Vekiba, Raquel Borges Pinto, Victoria M. Wolters, Maria Luígeria Tamará, Andréanne N. Zizzo, Jennifer Garcia, Kathleen Schwarz, Maria Beretta, Thomas Damgaard Sandahl, Carolina Jimenez-Rivera, Nanda Sarkar, James Brendel, Quah Muiwen, Nathalia Rock, Cristina Molera-Busoms, Wilroon Kamnitski, Eberhard Lutz, Ermelinda Santos-Silva, Hilarion Stordet, Luis Rujandi, Uloma Shah, Richard J. Thompson, **Binita M. Kamath<sup>3</sup>**

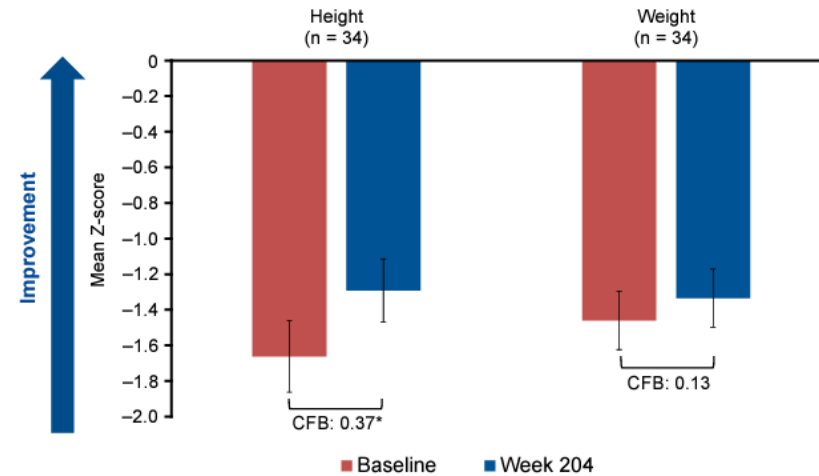
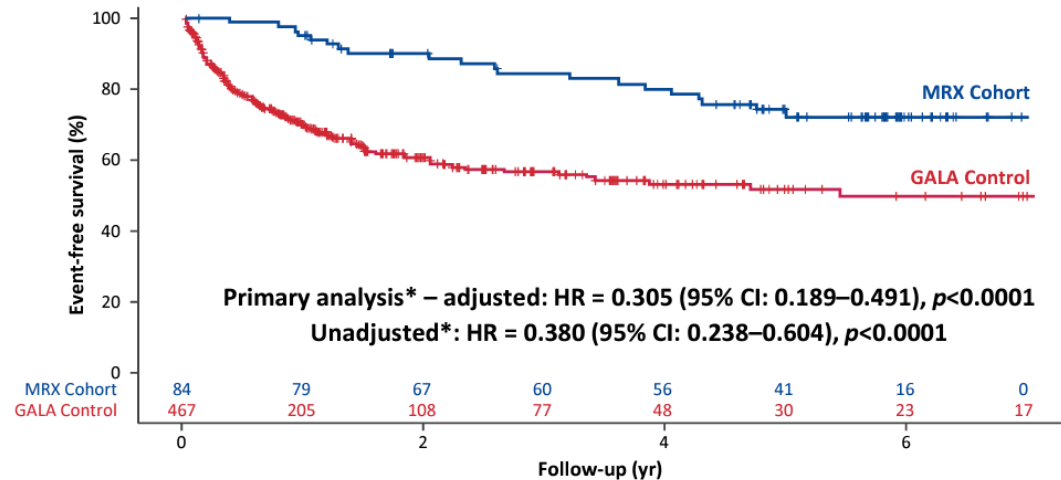
- Cohort of 84 patients treated with maralixibat compared with an external matched control cohort of 469 patients from the GALA\* Database
- Events defined as: liver transplantation; biliary diversion surgery; liver decompensation event; or death.

**Maralixibat improves growth in patients with Alagille syndrome: A 4-year analysis**

**Binita M Kamath,<sup>1</sup> Douglas B Mogul,<sup>2</sup> Marshall Baek,<sup>2</sup> Tiago Nunes,<sup>3</sup> Pamela Vig<sup>2</sup>**

<sup>1</sup>Division of Gastroenterology, Hepatology & Nutrition, Hospital for Sick Children and University of Toronto, Toronto, ON, Canada.  
<sup>2</sup>Mirum Pharmaceuticals, Inc., Foster City, CA, USA; <sup>3</sup>Mirum Pharmaceuticals, Inc., Basel, Switzerland

- Patients with ALGS typically suffer significant growth deficiency
- Mean height Z-score significantly increased from Baseline to Week 204 in ALGS patients treated with maralixibat



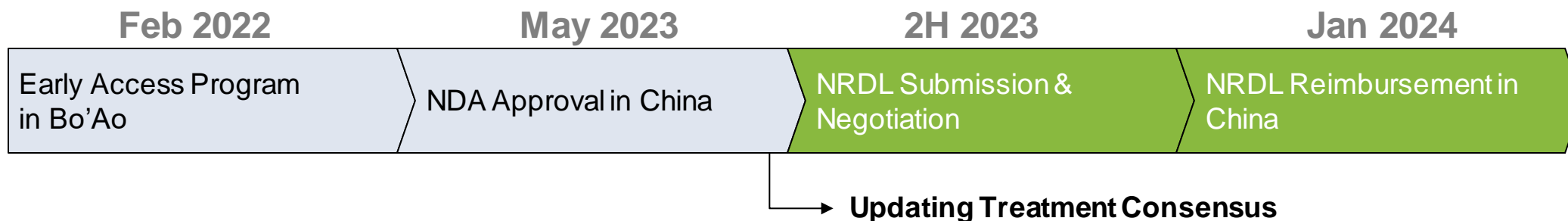
\*p=0.0004.  
CFB, change from baseline.

Adapted from posters and presentations at 2022 ESPGHAN Annual Meeting. GALA: Global Alagille Alliance



# Commercial Launch of LIVMARLI in Reimbursed Market in Jan 2024

China market potential: \$100-150 million in ALGS and \$200-250 million for three indications combined



10,000 potential ALGS patients in China

**~450**

Current diagnosed patients

**~350**

Current addressable patients

**CANbridge Sales Team of 12 dedicated to support early launch in 2024 to cover :**

Target Hospitals: **98**

Target Healthcare Physicians: **300**

Anticipated approval and launch in Taiwan and Hong Kong between 2H 2023 and 1 Q 2024

NRDL = national reimbursement drug list

# LIVMARLI Key Launch Initiatives

## LIVMARLI as New Standard of Care

- Leverage maralixibat efficacy in pruritus relief and sBA reduction
- Explore long-term clinical outcome, such as transplant avoidance or delay

## Disease Awareness

- Increase physician attention to pruritus and the impact on patients' quality of life
- Build a full recognition on the significance between pruritus relief/sBA reduction and long-term event-free survival enhancement

## Patient Diagnosis and Identification

- Boost patient registration in key provinces
- Expand Center of Excellence and referral network

Abbreviation: sBA, serumbile acids



In China for China

In China for Global

In Global for Global

# CAN106

Clinically De-risked, Near  
Commercialization, Targeting  
Multiple Indications with  
Significant Market Potential

---



# CAN106 – Long-acting Anti-C5 Therapy for Complement Disorders

Novel, long-acting monoclonal antibody for the treatment of complement-mediated diseases, including PNH, myasthenia gravis (MG) and various other complement-mediated diseases that are targeted by anti-C5 antibodies.

## Recent Highlights



Completed first-in-human study conducted in Singapore in 2021 and **positive top-line data** reported



**IND Approval** for the treatment of PNH in China in Jul. 2021



**Orphan Drug Designation granted by FDA** for treatment of myasthenia gravis in Nov. 2022



**Positive Phase 1b data in PNH** patients reported in Jun. 2023

## Disease Overview

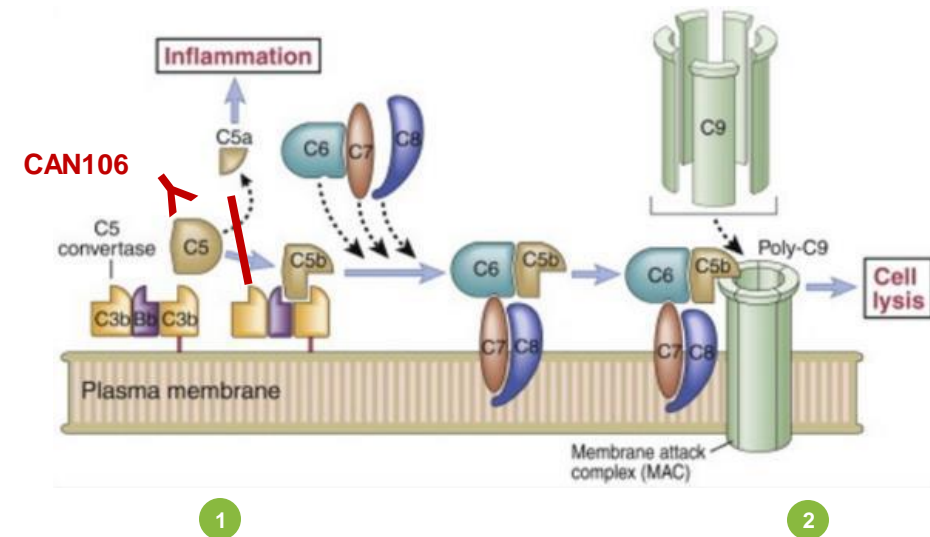
### Paroxysmal nocturnal hemoglobinuria (PNH)

belongs to a group of fatal and rare disorders that occur when the complement system is dysregulated. In patients with PNH, the proteins that normally protect their red blood cells are not present, leaving these denuded cells susceptible to complement attack, which results in their destruction (hemolysis).

This leads to severe anemia, thromboembolism, gastrointestinal pain and dysfunction, fatigue, cardiac failure, pulmonary hypertension, renal impairment, and eventually, death.

PNH is an acquired genetic condition that can occur at any age across genders and race, but most commonly presents in adults in their 30s to 40s and continues for the life of the patient.

## Mechanism of Action



CAN106 binds to the  $\alpha$  chain of C5, which prevents C5 from being cleaved into C5a and C5b by C5 convertase, thus preventing MAC formation and cell lysis

CAN106 preserves the generation of C3b, which is essential for the clearance of circulating immune complexes and the normal phagocytosis of bacterial and fungal pathogens

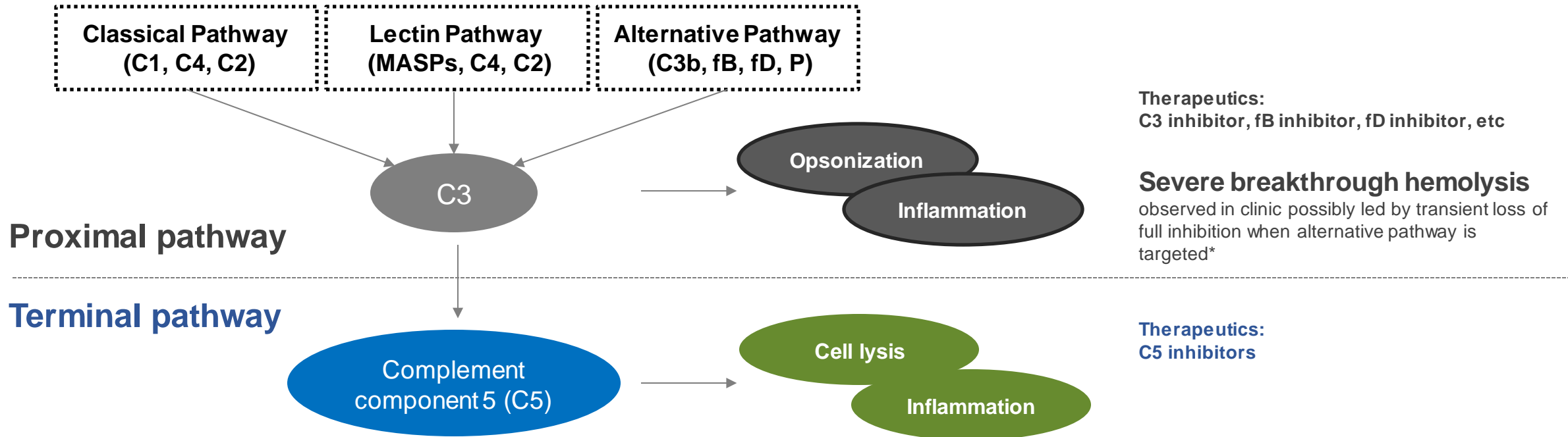


# C5 Inhibition Remains the Current Standard of Care for PNH

Recent studies raise concerns about potential risks associated with proximal inhibitors in anti-complement treatment.

- Enhanced complement inhibition leads to heightened breakthrough hemolysis risk upon inhibition loss, due to increased susceptible PNH clones.
- Enzymatic activities upstream of the terminal pathway contribute to amplified breakthrough hemolysis risk with proximal inhibition.
- Loss of inhibition at the proximal level triggers exacerbated intra- and extra-vascular hemolysis severity, contrasting with terminal level inhibition loss.

## Illustration of Complement Pathways



PNH = Paroxysmal nocturnal hemoglobinuria \*Risitano AM, et al. Immunological Review s. 2022

# CANbridge Reported Positive Preliminary Results From Phase 1b/2 Trial In PNH Patients

## Safety & Tolerability

- CAN106 was well-tolerated and safe. 6 subjects (37.5%), up until the data cutoff, experienced 18 drug-related AEs, with all AEs being mild and moderate. No drug-related SAE, and no drug-related AE led to discontinuation.
- Two breakthrough hemolysis events (Grade 2) were observed in 2 subjects in Cohort 3, due to COVID-19 infection and were assessed as unrelated to study drug.

## PK & PD

- CAN106 exposure ( $C_{max}$  and AUC) was dose-proportional over the studied dose range (20 mg/kg to 80 mg/kg).
- Free C5 inhibition was dose-dependent with complete and sustained inhibition (< 0.5 ug/ml) achieved by all subjects in Cohort 3.
- Free C5 inhibition was achieved with every four-week dosing.

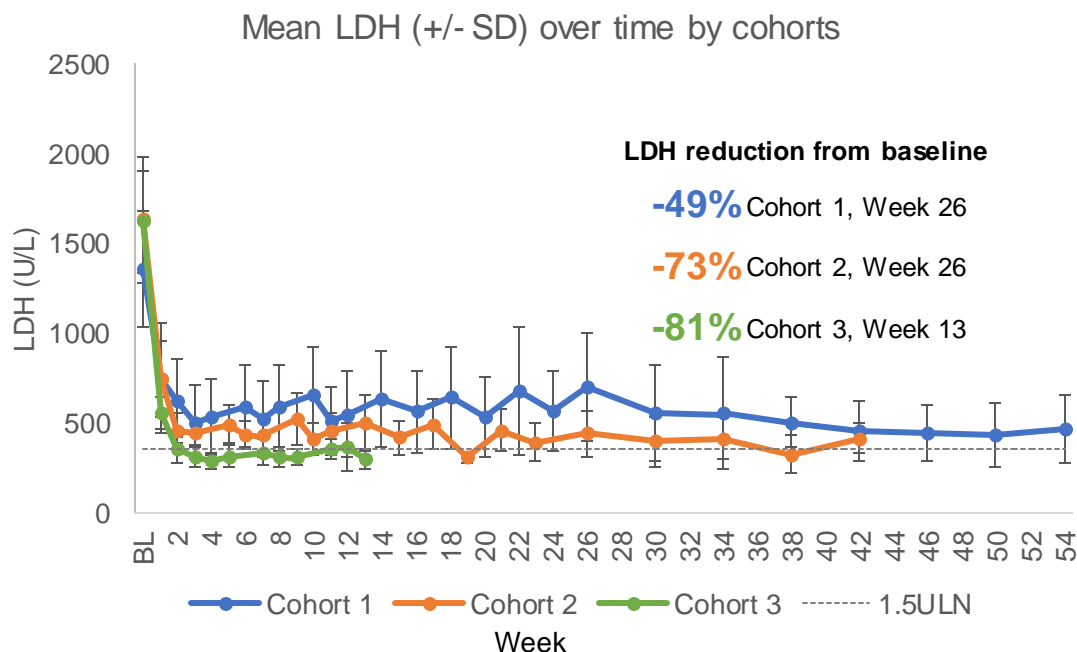
## Clinical Efficacy

- LDH levels were reduced in a dose-dependent manner: -49% in Cohort 1, -73% in Cohort 2, and -81% Cohort 3.
- Hemoglobin levels increased across all cohorts: 1.8 g/dL (Week 26) and 3.8 g/dL (Week 54) in Cohort 1; 2.0 g/dL (Week 26) and 2.4 g/dL (Week 42) in Cohort 2, and 1.0 g/dL (Week 13) in Cohort 3.
- % of subjects with Hgb >7 g/dL at baseline → last visit: 50% → 100% in Cohort 1, 50% → 75% in Cohort 2, 88% → 88% in Cohort 3
- % of subjects with Hgb >9 g/dL at baseline → last visit: 0% → 100% in Cohort 1, 25% → 50% in Cohort 2, 25% → 50% in Cohort 3

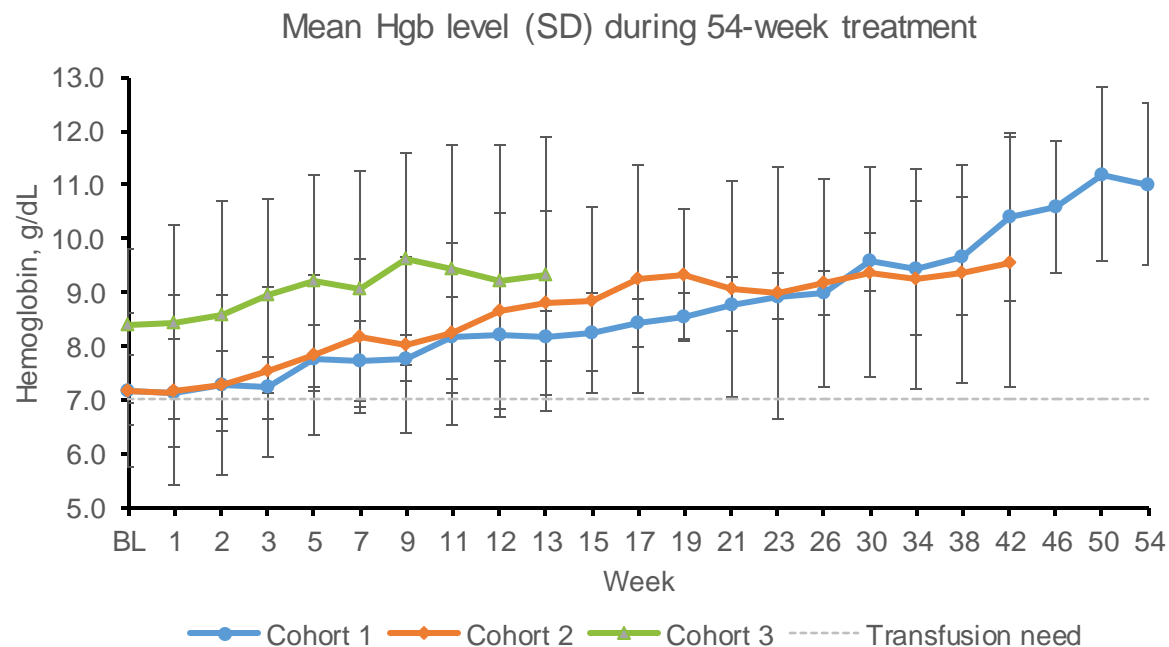


# Dose-dependent, Rapid and Substantial Effects on LDH and Hgb

Cohort 3: LDH, a biomarker of hemolysis, was reduced by 81% at Week 13. All subjects showed rapid and sustained LDH reduction, with 88% (7/8) subjects in Cohort 3 achieving LDH < 1.5 x ULN at least once after Week 3



Cohort	Maintenance Dose	Extension Dose (after Week 26)
1	20 mg/kg q4w	40 mg/kg q4w
2	40 mg/kg q4w	
3	80 mg/kg q4w	80 mg/kg q4w



## Hgb levels improved across all cohorts.

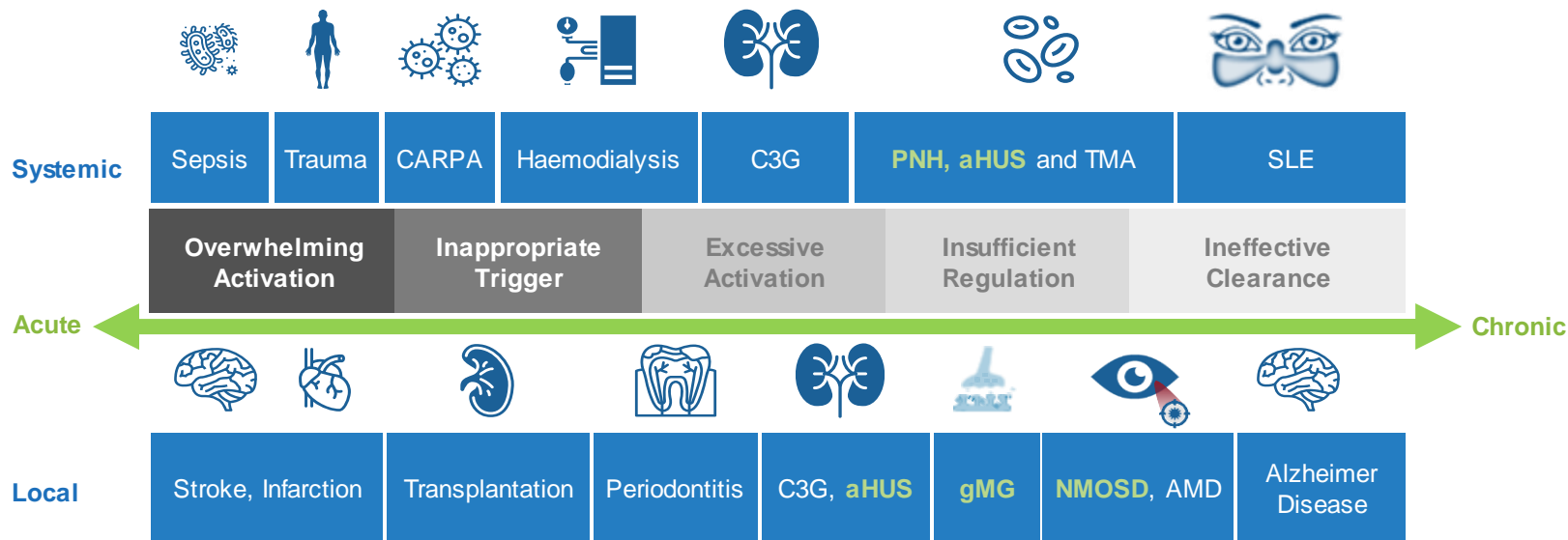
- Cohort 1: Mean Hgb increase from baseline of 1.8 g/dL at Week 26 and 3.8 g/dL at Week 54.
- Cohort 2: Mean Hgb increase from baseline of 2.0 g/dL at Week 26 and 2.4 g/dL at Week 42.
- Cohort 3: Mean Hgb increase from baseline of 1.0 g/dL at Week 13.
- Two subjects in Cohort 3 at Week 13 achieved Hgb  $\geq$  12 g/dL in the absence of transfusion.

LDH=lactate dehydrogenase. Target range for hemolysis inhibition is LDH is < 1.5 x ULN = 351 U/L; Two breakthrough hemolysis events caused by COVID-19 were reported at Week 12 in Cohort 3, leading to transient elevations in LDH (> 2 x ULN) that recovered by Week 13.

# CAN106 – Potential for Other Complement Disorders

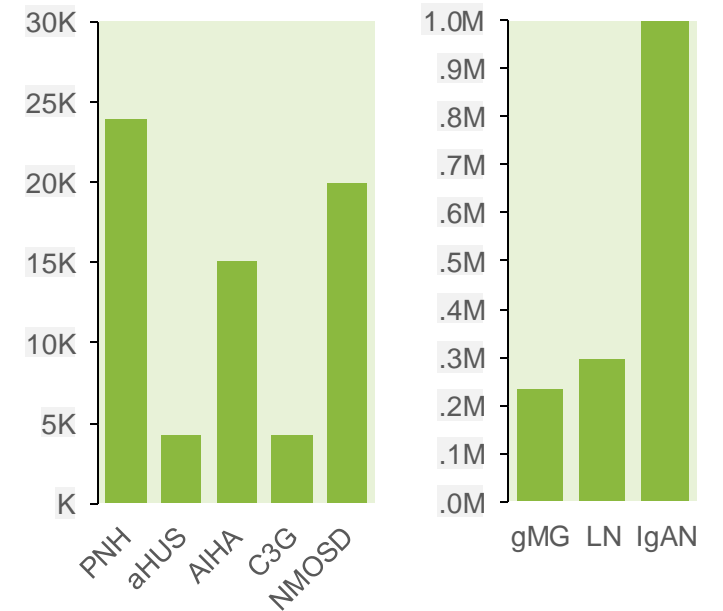
Potential “Pipeline in a Product”. Initial development efforts focused on PNH treatment. Estimated global market revenue projections of >\$9B in 2025<sup>1</sup>

## Potential Indications for Complement Therapeutics



Indications that have been approved for complement therapeutics

## Estimated Addressable Patient Population in China<sup>2</sup>










Abbreviation: PNH, paroxysmal nocturnal hemoglobinuria. Notes: 1. According to Alexion Investor Day 2020 new s release published on October 6, 2020. 2, Risitanton and Rotoli, 2008 & Chinese KOL interview ; China aHUS Diagnosis and Treatment Consensus, 2017; China MG Diagnosis and Treatment Guideline, 2015 & Howard et al, 2017; Zanella and Barcellini, 2014 & Berentsen and Sundic, 2015; Mahmoud et al, 2016; CANbridge research








# CAN106 – Differentiated Follow-On Indication Strategy

CAN106’s multi-indication potential, coupled with the limited access to the current available anti-C5 therapies in most parts of the world, allows for versatile indication expansion and go-to-market strategies to maximize its global commercial value

Soliris & Ultomiris Approval and Reimbursement Status <sup>1</sup>								
Soliris	PNH	✓	✓	✓	✓	✓	✓	✓
	aHUS	✓	✓	✓	✓	✓	✓	✓
	gMG	✓	○	✓	○	○	○	✓
	NMOSD	✓	○	✓	✓	○	○	✓
Ultomiris	PNH	✓	✓	✓	✓	✓	✓	✓
	aHUS	✓	✓	✓	✓	✓	✓	✓
	gMG	✓	X	○	○	○	○	✓
	NMOSD	X	X	○	○	○	○	○

Diagnosed Prevalence for Select Complement-mediated Disorders <sup>2</sup>			
			
PNH	~5K	~8K	~1K
aHUS	~2K	~3K	~450
gMG	~66K	~102K	~13K
NMOSD	~13K	~6K	~4K

**Key:** ✓ Approved, Reimbursed   ○ Approved, Not Reimbursed   X Not Approved

- Despite broad approval of existing C5 inhibitors, **patient access to Alexion’s therapies** approved in gMG and NMOSD is still **limited, particularly in European and Rest-of-World markets**
- Access to anti-C5 therapies in developing countries is even **more limited or non-existent**
- Future CAN106 clinical development and commercialization plans can be **optimized to prioritize development in de-risked, high-value complement-mediated disorders in markets underserved by Soliris and Ultomiris**
- **Additional indications** where anti-C5 therapies are not approved yet are **available for exploration and expansion**

1. ClearView Healthcare Partners Analysis; Japan gMG reimbursement status inferred from previous reimbursement activities 2. CANbridge Internal Analysis



# CAN106 – Complement Advisory Board

Board will offer guidance on the CAN106 global development program, as well as explore the potential for CAN106 in other indications



**Anthony Amato,  
MD**

- Brigham and Women's Hospital Distinguished Chair in Neurology
- Chief of the Neuromuscular Division and Director of the Clinical Neurophysiology Laboratory at Brigham and Women's Hospital
- Professor of Neurology at Harvard Medical School



**Gerald Cox, MD,  
PhD**

- Chief Development Strategist & Interim Chief Medical Officer
- Clinical geneticist and pediatrician at Boston Children's Hospital
- Former Chief Medical Officer at Editas Medicine
- Vice President, Rare Disease Clinical Development at Sanofi



**Jean Francis,  
MD**

- Medical Director of Kidney Transplant Program at Boston Medical Center and Boston Univ Sch of Med
- Medical Director of Combined Pancreas Transplant Program at Boston Medical Center and Brigham and Brigham & Women's Hospital
- Associate Professor of Medicine at Boston Univ Sch of Med



**Richard Polisson,  
MD, MHSc**

- Clinical Development Consultant
- Former CMO at Artax Biopharma
- Senior VP and Head of Transl Med at Sanofi-Genzyme R&D Center
- Clin Dir of Arthritis Unit and Chair of Mallinckrodt Clin Res Unit Scientific Adv Comm at Massachusetts General Hospital
- Associate Professor of Medicine at Harvard Medical School



**Sushrut Waikar,  
MD, MPH**

- Chief of Nephrology at Boston Medical Center
- Norman G. Levinsky Professor of Medicine at Boston University School of Medicine
- Former Constantine L. Hampers, MD Distinguished Chair in Renal Medicine at Brigham and Women's Hospital



**Brian Weinschenker, MD**

- Professor of Neurology at University of Virginia
- Former Professor of Neurology at Mayo Clinic

Neuromuscular Disorders

Rare Disease Drug Development

Organ Transplant, PNH, Thrombotic Microangiopathy

Rare Disease Drug Development, Rheumatologic Diseases

Renal Diseases, Non-invasive Biomarkers of Renal Injury and Fibrosis

NMOSD and Other CNS Demyelinating Diseases





# CAN008:

Development in  
Newly Diagnosed GBM



# CAN008 – CD95-Fc Fusion Protein for Glioblastoma Multiforme (GBM)

CAN008 is in clinical development as a first-line therapy for GBM in China

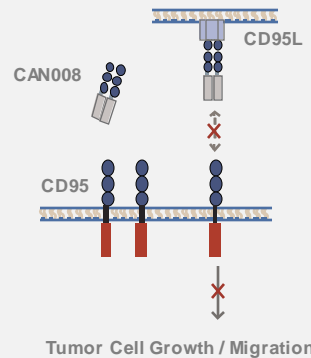
## Recent Highlights

- An independent data monitoring committee completed an interim analysis and review of the ongoing Phase 2 study of CAN008 and **recommended the study continue without any changes to the current trial design in July 2023.**
- Currently in Phase 2 registrational trial in newly diagnosed GBM in China. Patient enrollment (N = 117) completed in March 2023
- Long-term data from phase 1/2 trial presented in ESMO in Mar 2023 shows
  - 67% five-year OS** rate compared to 8.2% in institutional database
  - 83% OS** at two years vs. 34.3% OS from institutional database
  - 17.95 months median PFS** vs. 5.8 months PFS in historical group

## GBM Overview

- A rare oncologic disease with **lower incidence** than other cancer types
- Median age of diagnosis is 64 years, and it is slightly more common (1.59 times) in men as compared to women
- The **most common and malignant** type of glioma in adults. About 45% of gliomas are glioblastoma multiforme
- Estimated **5-year survival of 5.5%** globally and below 5% in China
- Treatment options: surgical resection, adjuvant chemotherapy with TMZ, tumor treating field (TTF), bevacizumab (Avastin)

## Mechanism of Action

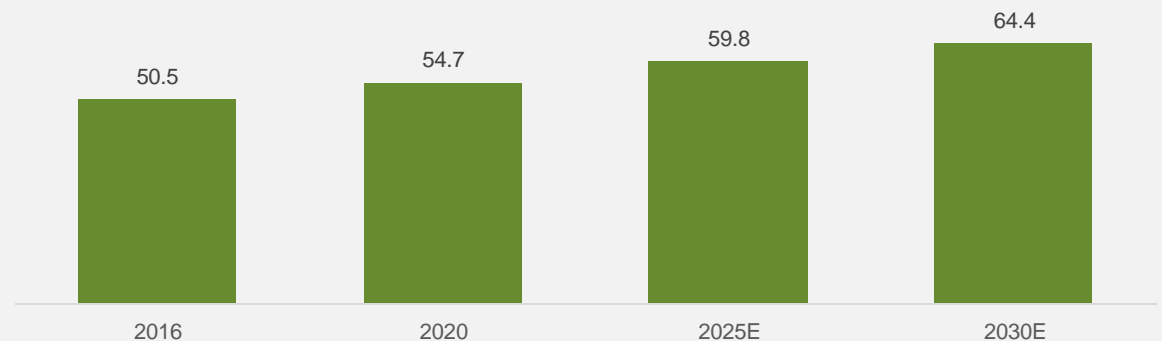


- CD95L binds to its receptor, CD95, on the cell surface and induces the oligomerization of CD95, which triggers an intracellular signaling cascade that stimulates tumor cell growth and migration
- CAN008 acts as a soluble receptor that specifically binds to CD95L and blocks the endogenous CD95 / CD95L signaling pathway in tumor cells. CAN008 also blocks CD95 / CD95L engagement on T cells, which prevents T cell apoptosis and restores immune function
- As the oligomerization of CD95 is blocked and signal transduction is inhibited, the growth and migration of tumor cells are suppressed

## Epidemiology

Annual Incidence of GBM in China

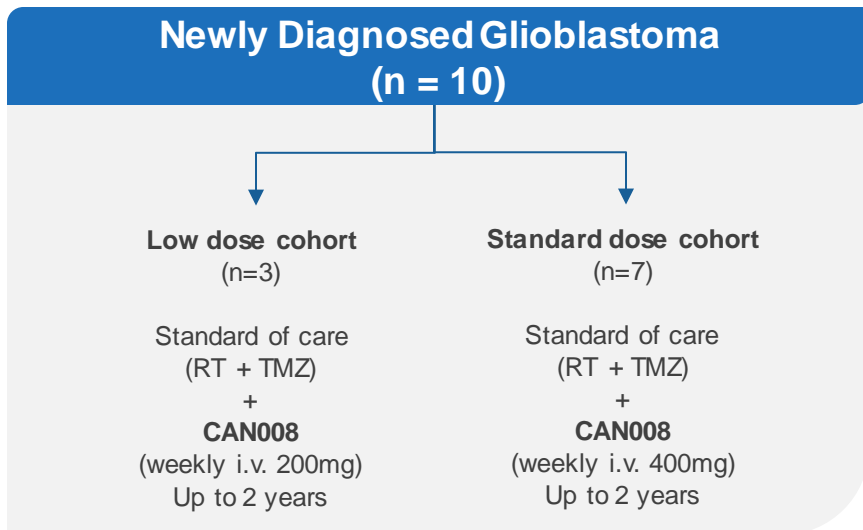
Unit: Thousand



Source: Frost & Sullivan Analysis. Notes: GBM, glioblastoma multiforme; TMZ, temozolomide

# CAN008 – Phase 1 in Newly Diagnosed GBM

CAN008 shows clear signs for clinical efficacy in newly diagnosed GBM patients

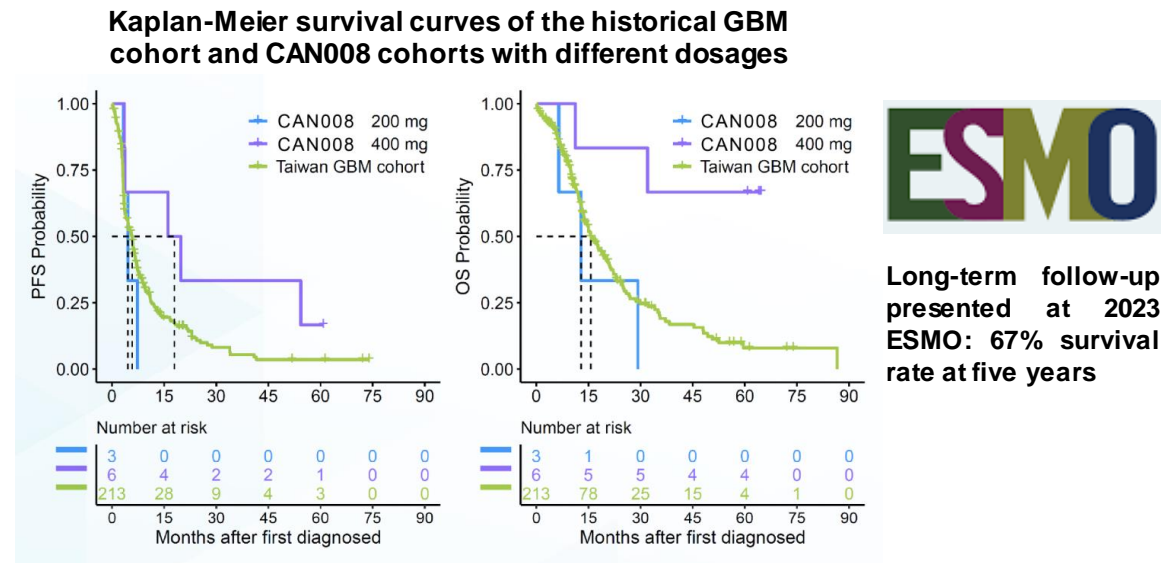


### Safety

- **No specific safety issues** when CAN008 (200 or 400 mg) was combined with RT and TMZ.
- **No subjects discontinued** due to treatment-emergent adverse events.
- No patients experienced dose-limiting toxicity (DLT).
- Maximum administered dose of **400 mg IV once weekly** recommended as the RP2D.

### Efficacy

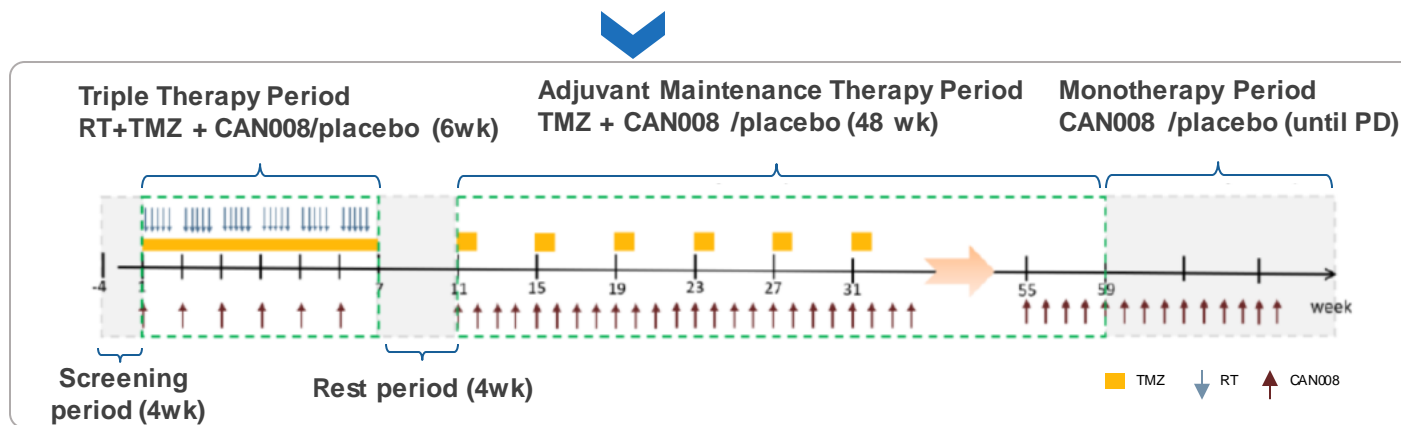
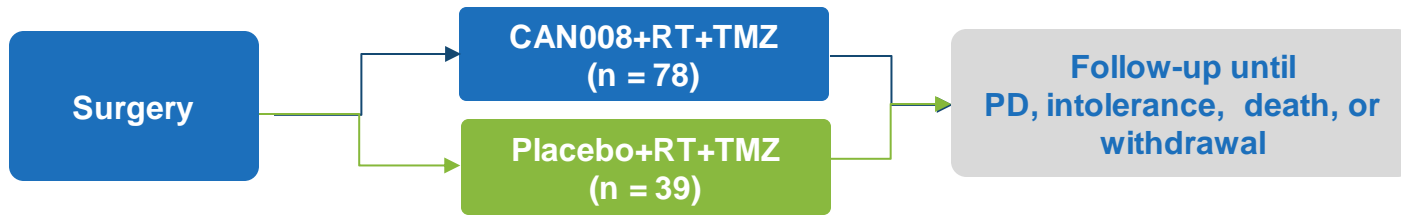
PFS rates	200 mg cohort	400 mg cohort
PFS-3 months	33.33%	71.42%
PFS-6 months	33.33%	57.14%
PFS-9 months	0% (all progressed)	57.14%
PFS-12 months	-	57.14%
Median PFS	2.37 months	N/A <sup>(1)</sup>



Source: Wei K-C et al, Sci Rep 2021;11:24067

# CAN008 – Ongoing Phase 2 Registrational Trial in Newly Diagnosed GBM

Phase 2 Multi-center, randomized, double-blind, placebo-controlled study



### Primary endpoint

- Progression-free survival (PFS)

### Interim Readout

- Progression of 37 cases

### Key Development Timeline

Enrollment completion  
in Q1 2023

Phase 2 interim analysis  
in H2 2023

Phase 2 top-line data  
in early 2024

Next Catalyst

# Next-gen Gene Therapy Pipeline



---

# Proprietary Gene Therapy Technology Platform & Powerful Discovery Engine

We continue to invest in gene therapy as our next-generation technology development and expand our in-house R&D activity to generate promising leads for treatment of rare diseases

## Research Collaborations with World-Renowned Investigators and Academic Institutions

*Collaborations in Neuromuscular Disorders*

 <b>UMass Chan</b> MEDICAL SCHOOL	<b>Investigators:</b> <ul style="list-style-type: none"><li>• Dr. Guangping Gao</li><li>• Dr. Miguel Esteves</li></ul>
 <b>UW Medicine</b> UW SCHOOL OF MEDICINE	<b>Investigator:</b> <ul style="list-style-type: none"><li>• Dr. Jeff Chamberlain</li></ul>

*Potentially best-in-class SMA GT (Global rights secured)*

*Novel tissue-tropic AAV capsid discovery*

*Potentially best-in-class DMD GT*

## In-House AAV Gene Therapy Platform and Process Development Facility



*Platform technology with guided AAV tissue targeting, such as CNS or muscles*



*AAV process development lab and pilot plants in Greater Boston*

## Strategic Collaborations with Innovative Industry Partners



*Licensed worldwide rights to **liver-tropic capsid** for AAV gene therapy products to treat Fabry and Pompe diseases*

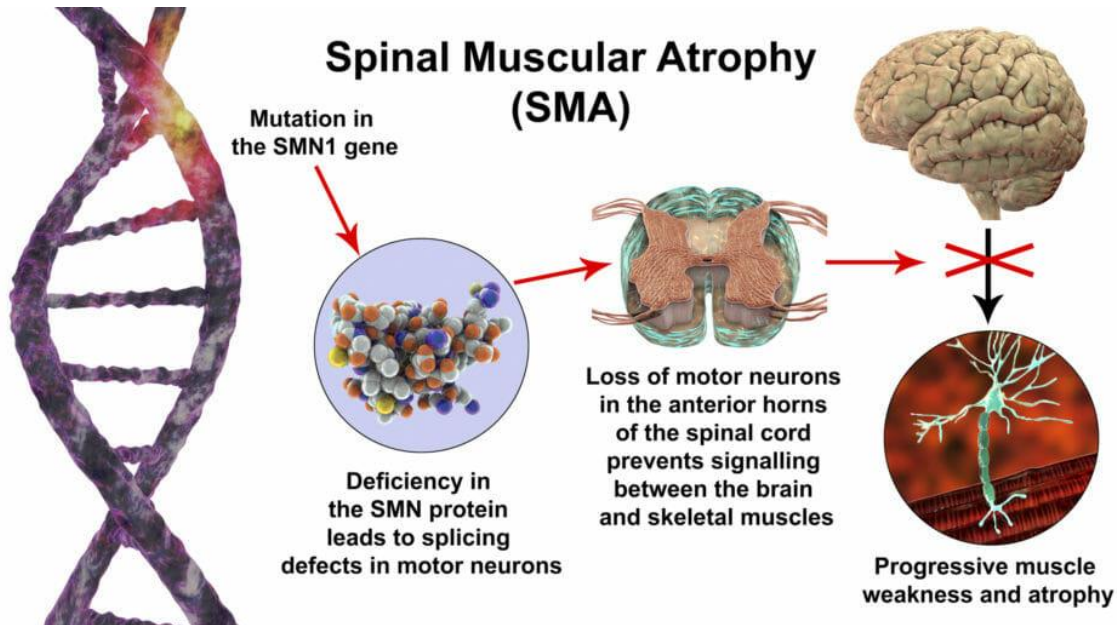


*Exclusive worldwide rights to **proprietary RNA Assembly Technology** to develop next-gen GT for dystrophinopathies*



# CAN203 – Second Generation Gene Therapy for Spinal Muscular Atrophy

## SMA Pathophysiology Illustration



Source: Cowen Equity Research and SMA Foundation.

## CAN203

- Second-gen gene therapy to potentially treat SMA type 1-3 (from infants to adult patients)
- Endogenous promoter: regulated, targeted tissue expression to avoid unwanted toxicity in liver and heart
- Codon optimized: enhanced tissue expression
- May achieve safer, more cost-effective treatment with lower doses compared to standard of care gene therapy
- Presented additional preclinical data at the premier academic conference 2022 and 2023 ASGCT.

## Epidemiology

- Autosomal recessive genetic inheritance
- 1 in 6,000 to 1 in 10,000 children born with SMA
- Affects all racial and ethnic groups
- One of the most common rare diseases

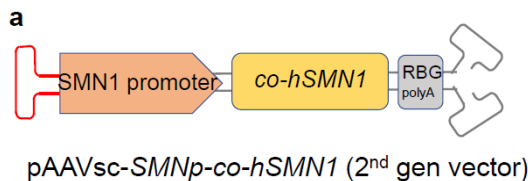
## Unmet Need

- Patients with SMA over the age of two cannot be treated with the 1st-gen gene therapy Zolgensma®
- Black box warning of serious liver injury associated with Zolgensma®
- Limited access due to high price

# CAN203 - Preclinical Data Presented at 2022 and 2023 ASGCT

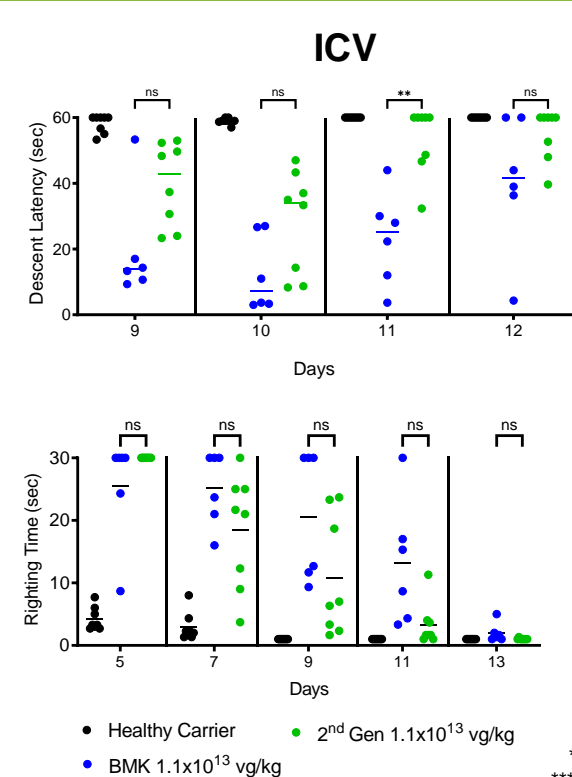
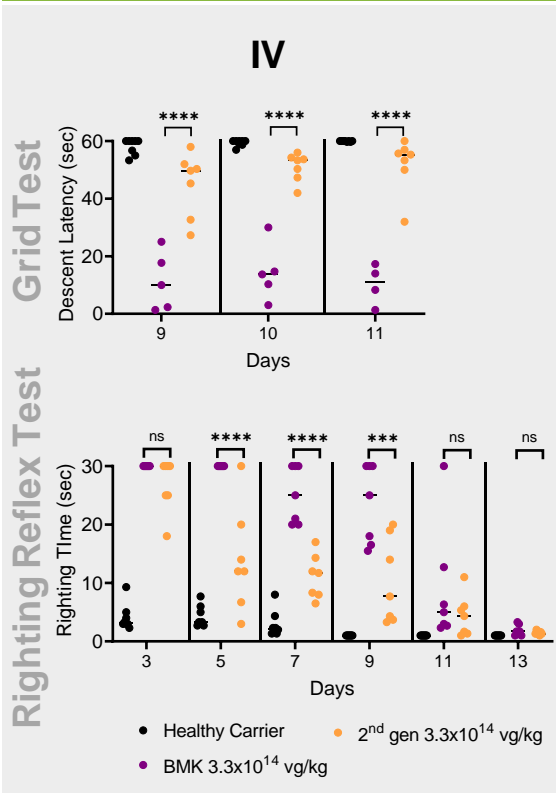
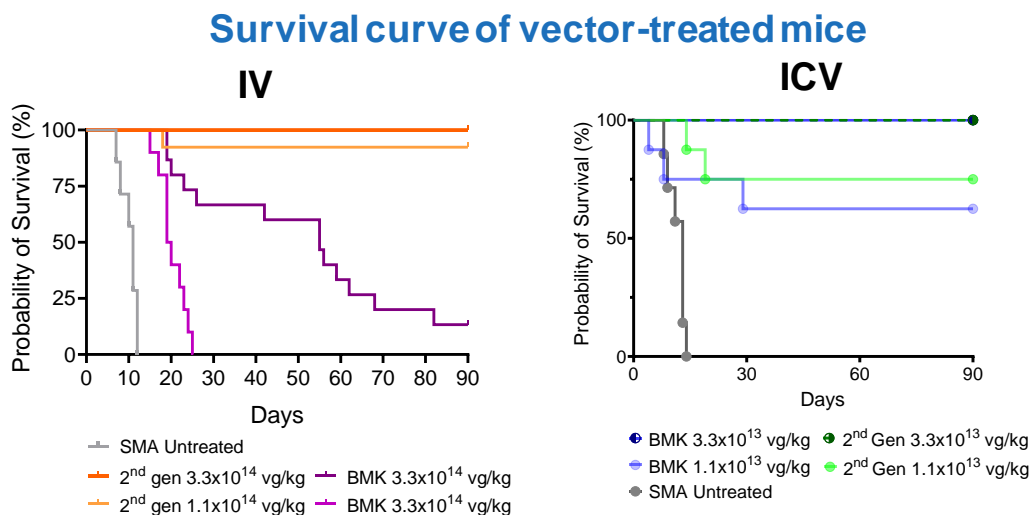
Head-to-head comparison between the 2nd-generation vector (CAN203) and the reference vector (designed similar to Zolgensma®): both IV\* and ICV\* injections demonstrate therapeutic advantages

**2<sup>nd</sup> gen vector: Endogenous SMN1 promoter isolated and inserted upstream of the codon-optimized hSMN1**



Unlike the 1<sup>st</sup> gen benchmark vector that utilizes a ubiquitous promoter leading to non-specific high-level SMN expression across tissues, the 2<sup>nd</sup> gen vector (CAN203) utilizes an endogenous SMN1 promoter, enabling tissue-specific regulation of SMN protein expression.

**2<sup>nd</sup> gen vector conferred significantly better restoration of motor function than the benchmark vector in SMA mice**



\* P < 0.05  
 \*\* P < 0.01  
 \*\*\* P < 0.001  
 \*\*\*\* P < 0.0001

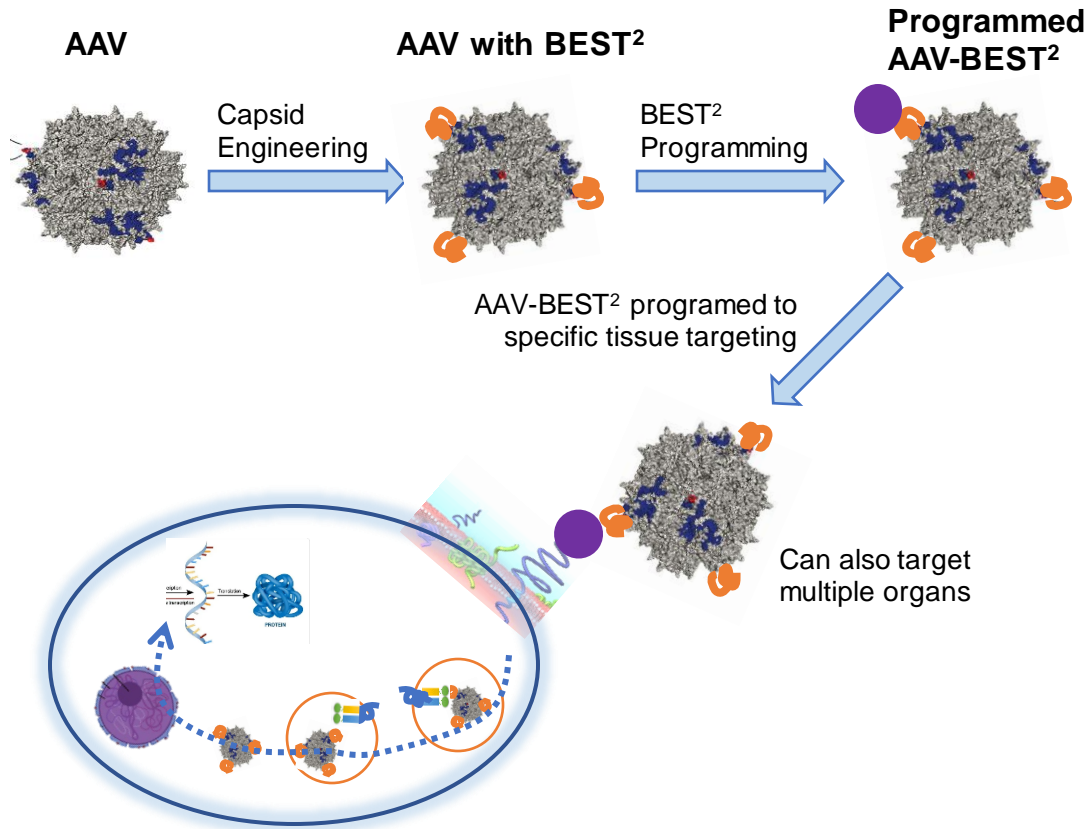
**In vivo data demonstrates the superiority of the 2nd-generation vector in extending lifespan, improving motor function, and eliminating liver toxicity (data not shown)**

IV: intravenous; ICV: Intracerebroventricular

# CANbridge Innovative AAV Capsid Platform: BEST<sup>2</sup>AAV

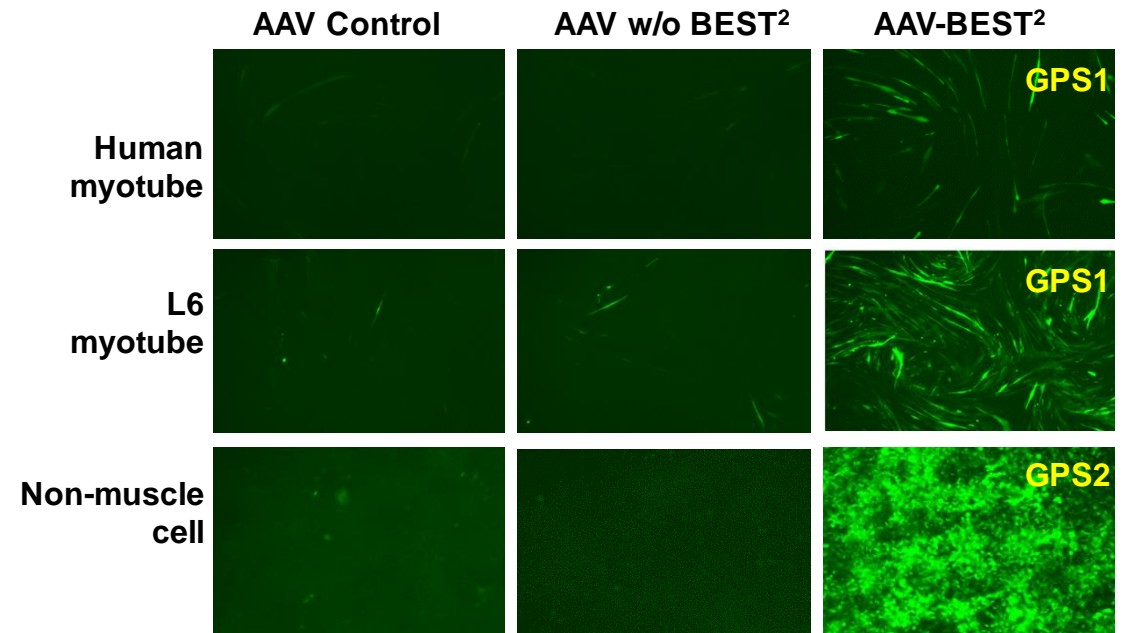
Addressing limitations of current AAV technology

## CANbridge BEST<sup>2</sup> Tissue Specific Delivery Platform



Note: Tabebordbar M et al, Cell 2021

## PoC of BEST<sup>2</sup>AAV *in vitro* in Myotubes and Non-Muscle Cells



### Additional Data

- BEST<sup>2</sup> demonstrated superior transduction to AAV, with similar transduction to MyoAAV\*
- MIG inhibited transduction of myotubes by AAV9 and MyoAAV, but not by BEST<sup>2</sup>

# Comparison of CANbridge BEST<sup>2</sup> with Other Novel Capsid Approaches

## Natural Cap Discovery

### Pros

- 100s identified
- Nature made from evolution

### Cons

- Serendipitous
- Broad tissue tropism
- NAb/CTLs
- Unknown species translatability

## Rational Design

- Based on understanding of receptor biology
- More predictable species translatability
- May alter NAb
- Lack of full understanding of receptor biology
- Hard to engineer into AAV

## Directed Evolution

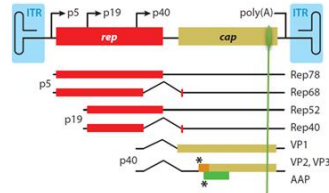
- High throughput
- Inclusive of all possible combinations nature can't do
- Time consuming on panning Unknown species translatability
- Costly validation on transability and manufacturability
- **Different tissues may need different AAVs**

## In-Silico Design

- As for Directed evolution
- Powerful AI learning capsid biology to guide rational library design
- As for Directed evolution
- **Different tissues may need different AAVs**

```

441      451      461      471      481      491
MNFLLDQLLYLRSRINTPS...SELQFSQAGASDIRIQSRNWLPGPCYRQQRVSRKTSADNNN
071      081      091      101      111      121
RTINFVAREQYGVSVSNL...KATAQVNTIQQLFQSNVWQDRVYLLQGFIAWLEHIDGHEF
701      711      721
IQYTSNYSKSVWVDFTVDTNGVYSEFRPIGTRYLTRNL
    
```



## CANbridge AAV-BEST<sup>2</sup>

- Small edits to avoid impact on CMC developability
- Liver de-targeted AAV to avoid peripheral sinkers
- One AAV fits all, only need to replace the "GOI"
- Simplify manufacturing process development with one AAV
- Programmable "GPS-like" for a specific tissue or tissues
  - Single or multi-tissue delivery capability
- Bypass NAb → increases the number of patients eligible to AAV gene therapy
- Two targets on the same tissue can be used by two different BEST<sup>2</sup> to further avoid NAb for repeated dosing

# Gene Therapies to Treat LSDs

Gene therapy holds the promise to transform treatments for lsd such as Fabry disease / Pompe disease from chronic to curative

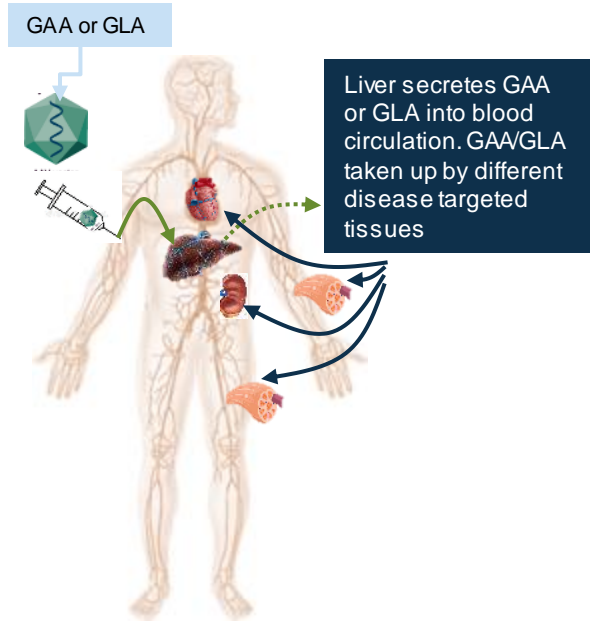
## Application to Lysosomal Storage Diseases (LSDs)



LSDs are a group of over **70 diseases** that are characterized by lysosomal dysfunction, most of which are inherited as autosomal recessive traits, including Gaucher disease, Fabry disease and Pompe disease



Clinical trials are in progress on possible treatments for some of these diseases, but there is currently **no approved treatment** for many LSDs



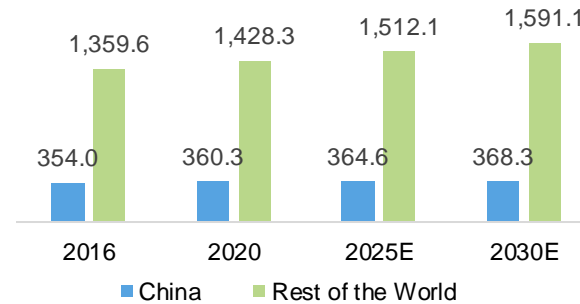
### Introduction

### Prevalence (in Thousand)

### Treatment Approaches

#### CAN201 - Fabry disease (FD)

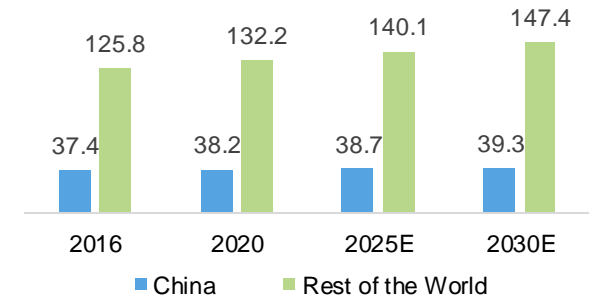
One of the most common LSDs, usually starts in childhood



Symptomatic Treatment	ERT
Substrate reduction therapy	Chaperone therapy

#### CAN202 - Pompe disease (PD)

One of the most common LSDs, onset of symptoms from childhood to adulthood



Symptomatic treatment	ERT
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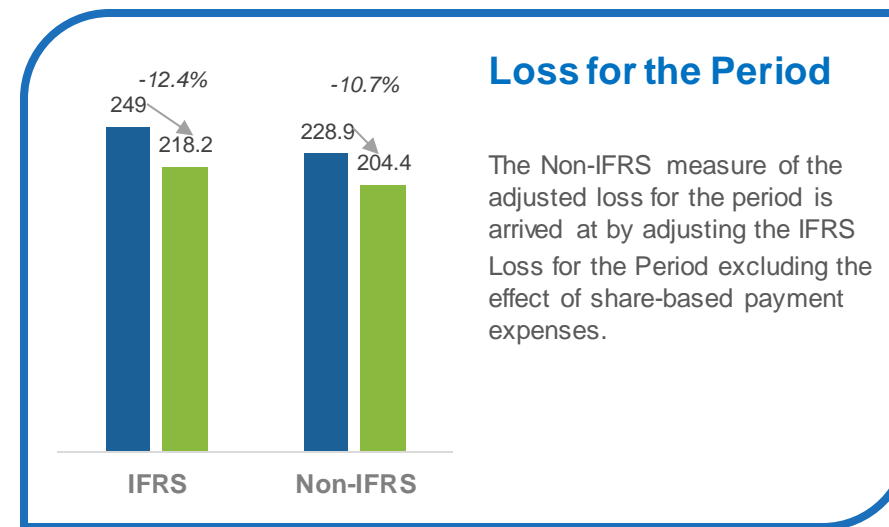
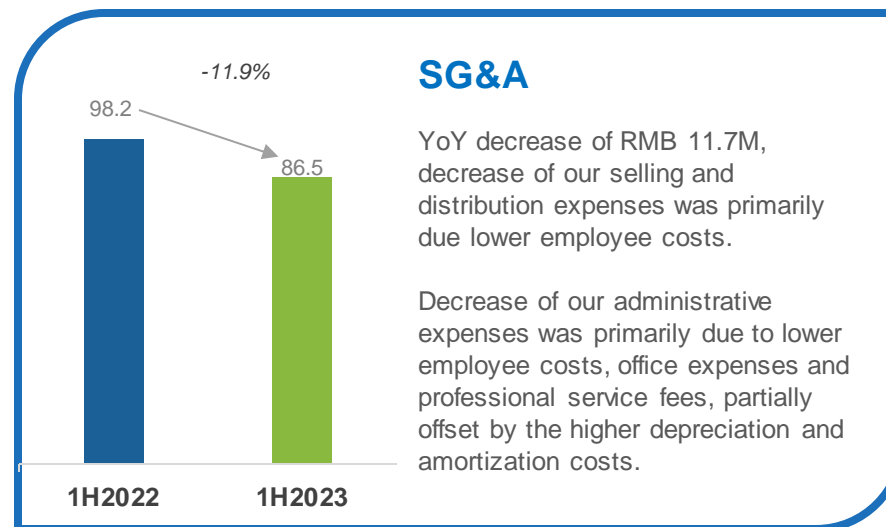
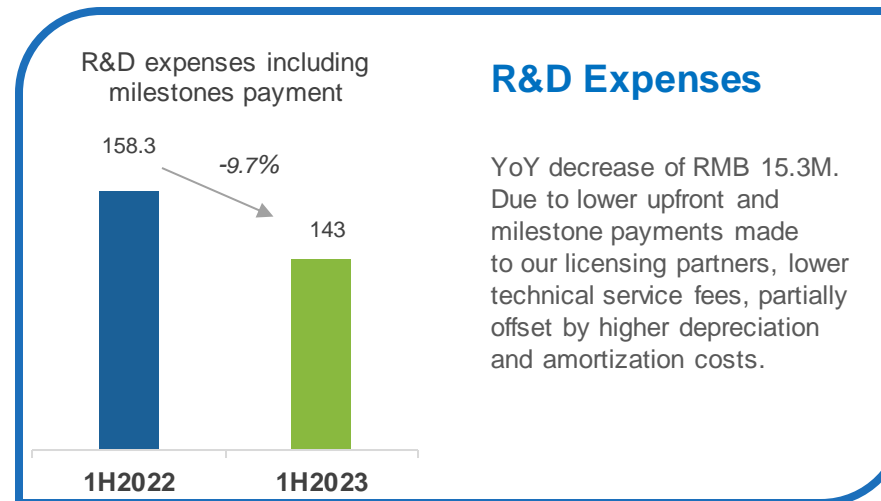
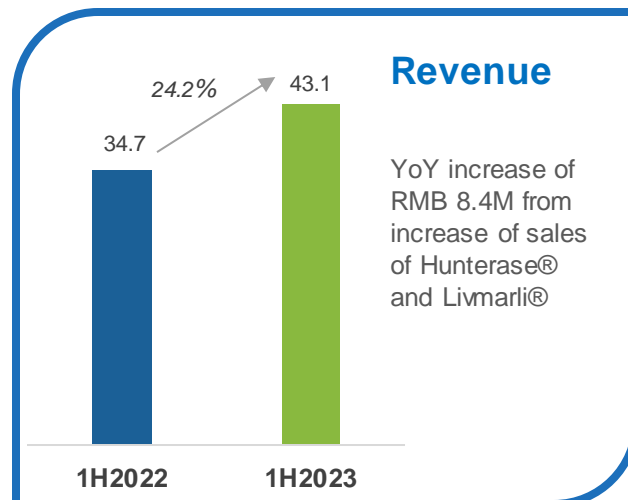
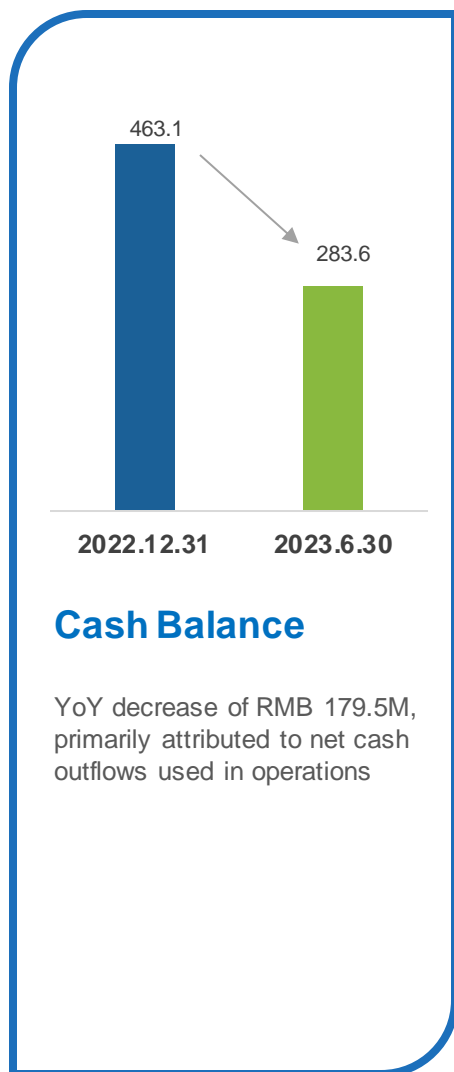
**Gene therapy** is considered an innovative and promising treatment and is currently at clinical stages

# Financial Review

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# 1H 2023 Financial Highlights

RMB Million



# Outlook

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# Past and Upcoming Milestones

Two products planned for NRDL negotiation in 2023 and Multiple NDA filings expected by 4Q2024

	Livmarli	Hunterase	CAN106	CAN008	CAN103	CAN203
1H 2023	Approved for marketing in mainland China	Identified 739 patients, expanded to 109 cities, covering 586m population	Released positive Phase 1b data	Phase 2 Enrollment completed in Q1 IDMC <sup>1</sup> completed an interim analysis and review of Phase 2 study and recommended the study continue without any changes	Initiated Part B in the Phase 1/2 Clinical trial	Data Presented at ASGCT <sup>2</sup> shows CAN203 is able to achieve superior potency, efficacy and safety in mice with SMA compared to the benchmark vector
Upcoming	<p><b>H2 2023</b> – NRDL negotiation</p> <p><b>H2 2023</b> – ALGS Approval in TW/HK</p> <p><b>H2 2023</b> – BA Interim readout</p> <p><b>H2 2024</b> – PFIC Approval in mainland China/Taiwan</p>	<p><b>H2 2023</b> – NRDL negotiation</p> <p><b>2023/24</b> – Keep enhancing commercial insurance entrance to more cities</p>	<p><b>H2 2023</b> – Phase 2 patient enrollment</p> <p><b>2025</b> – Potential NDA filing in 1H2025</p>	<p><b>1H 2024</b> – Topline data from the Phase 2 clinical trial</p> <p><b>2024</b> – Potential NDA filing in 2024</p>	<p><b>End of 2024</b> – Plan to file NDA</p>	<p>Continue to advance 2nd gen SMA gene therapy to IND</p>

1 : IDMC, Independent Data Monitoring Committee,

2 : ASGCT, American Society of Gene and Cell Therapy Annual Meeting

# Q&A

CANBRIDGE-B  
01228. HK

[www.canbridgepharma.com](http://www.canbridgepharma.com)

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# THANK YOU



Contact

[IR@canbridgepharma.com](mailto:IR@canbridgepharma.com)

CANBRIDGE-B  
01228. HK

[www.canbridgepharma.com](http://www.canbridgepharma.com)



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