CENTESSA PHARMACEUTICALS

Corporate Overview

Asset-Centric. Patient-Centric.

SEPTEMBER 2023

Disclaimer

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This presentation may contain forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Statements in this presentation that are not statements of historical fact are forward-looking statements, including, without limitation, statements related to the Company's ability to deliver impactful medicines to patients; the ability of our key executives to drive execution of the Company's portfolio of programs; our asset-centric business model and the intended advantages and benefits thereof; research and clinical development plans; the scope, progress, results and costs of developing our product candidates or any other future product candidates; the development and therapeutic potential of our product candidates, including SerpinPC, LB101, LB206, other LockBody candidates, our LockBody technology platform, ORX750 and other orexin agonist molecules; strategy; regulatory matters, including the timing and likelihood of success of obtaining approvals to initiate or continue clinical trials or market any products; enroll subjects in clinical trials; market size and opportunity for our product candidates; and our anticipated cash runway. Words such as "may," "might," "will," "could," "would," "should," "expect," "intend," "plan," "objective," "anticipate," "believe," "estimate," "predict," "potential," "continue," "ongoing," "aim," "seek," and variations of these words or similar expressions are intended to identify forward-looking statements, though not all forward-looking statements necessarily contain these identifying words. These forward-looking statements are based on the beliefs of the Company's management as well as assumptions made by and information currently available to the Company. Such statements reflect the current views of the Company with respect to future events and are subject to known and unknown risks, including, without limitation, risks related to our ability to protect and maintain our intellectual property position; business, regulatory, economic and competitive risks, uncertainties, contingencies and assumptions about the Company; risks inherent in developing products and technologies; future results from our ongoing and planned clinical trials; our ability to obtain adequate financing, including through our financing facility with Oberland, to fund our planned clinical trials and other expenses; trends in the industry; the legal and regulatory framework for the industry, including the receipt and maintenance of clearances to conduct or continue clinical testing; future expenditures risks related to our asset-centric corporate model; the risk that any one or more of our product candidates will not be successfully developed and commercialized; the risk that the results of preclinical studies or clinical studies will not be predictive of future results in connection with future studies; and risks related to the COVID-19 pandemic including the effects of the Delta, Omicron and any other variants, geo-political risks such as the Russia-Ukraine conflict and other risk factors contained in our filings with the U.S. Securities and Exchange Commission. In light of these risks and uncertainties, the events or circumstances referred to in the forward-looking statements may not occur. The actual results may vary from the anticipated results and the variations may be material. These forward-looking statements should not be taken as forecasts or promises nor should they be taken as implying any indication, assurance or guarantee that the assumptions on which such forward looking statements have been made are correct or exhaustive or, in the case of the assumptions, fully stated in this presentation. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date this presentation is given. All projections, valuations and statistical analyses are provided for information purposes only. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any forward looking statements contained herein to reflect any change in our expectations or any changes in events, conditions or circumstances on which any such statement is based, except as may be required by law. They may be based on subjective assessments and assumptions and may use one among alternative methodologies that produce different results and to the extent they are based on historical information, they should not be relied upon as an accurate prediction of future performance.

This presentation discusses product candidates that are under clinical study, and which have not yet been approved for marketing by the U.S. Food and Drug Administration or any other regulatory agency. No representation or warranty, express or implied, is made as to the safety or effectiveness of these product candidates for the use for which such product candidates are being studied. The trademarks included herein are the property of the owners thereof and are used for reference purposes only. Such use should not be construed as an endorsement of such products. Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third party sources and the Company's own internal estimates and research. While we believe these third-party sources to be reliable as of the date of this presentation, we have not independently verified, and make no representation or warranty, express or implied, as to the adequacy, fairness, accuracy or completeness of, any information obtained from third party sources. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.

Discovering and developing medicines that are transformational for patients

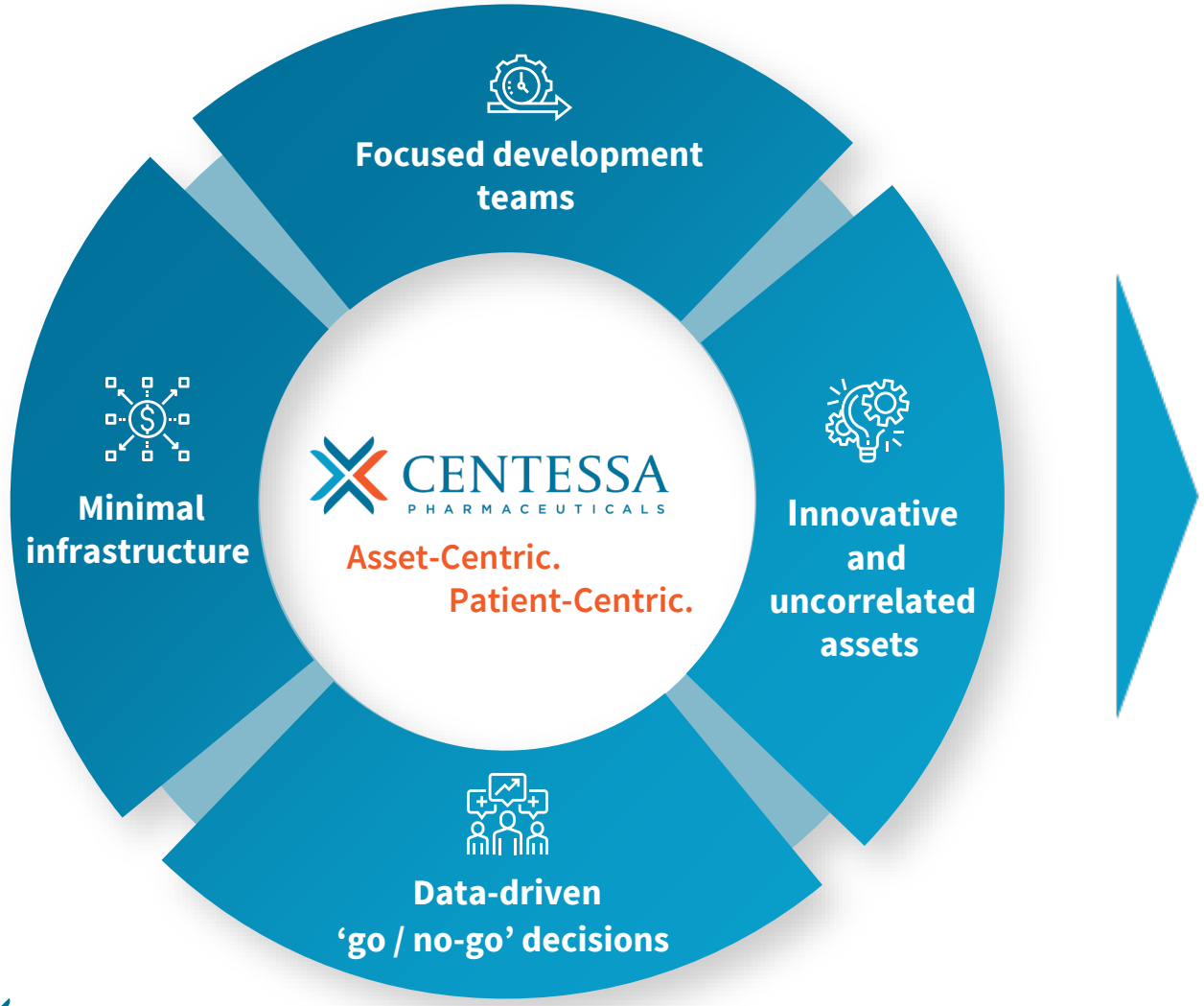
- Multiple potential blockbuster assets
- Cash runway into 2026 enables multiple clinical readouts
- World-class R&D team

Note: The Company reported $303.6 million in cash, cash equivalents and short-term investments as of June 30, 2023. In addition, the Company received approximately $15.0 million in gross proceeds through ATM sales in August 2023.

CENTESSA PHARMACEUTICALS

DIFFERENTIATION

We are a transformational pharmaceutical company fueling an innovative pipeline



MULTIPLE PATHWAYS TO SIGNIFICANT VALUE CREATION

Lead Assets	Disease	Estimated Market Size*
SerpinPC	Hemophilia B	**$2B+**[1]
PD-L1xCD47 LockBody® (LB101)	Solid Tumors	**$10B**[1]
PD-L1xCD3 LockBody® (LB206)	Solid Tumors	**$10B**[1]
ORX750	Narcolepsy (NT1) and other sleep disorders	**$2B+**[1]

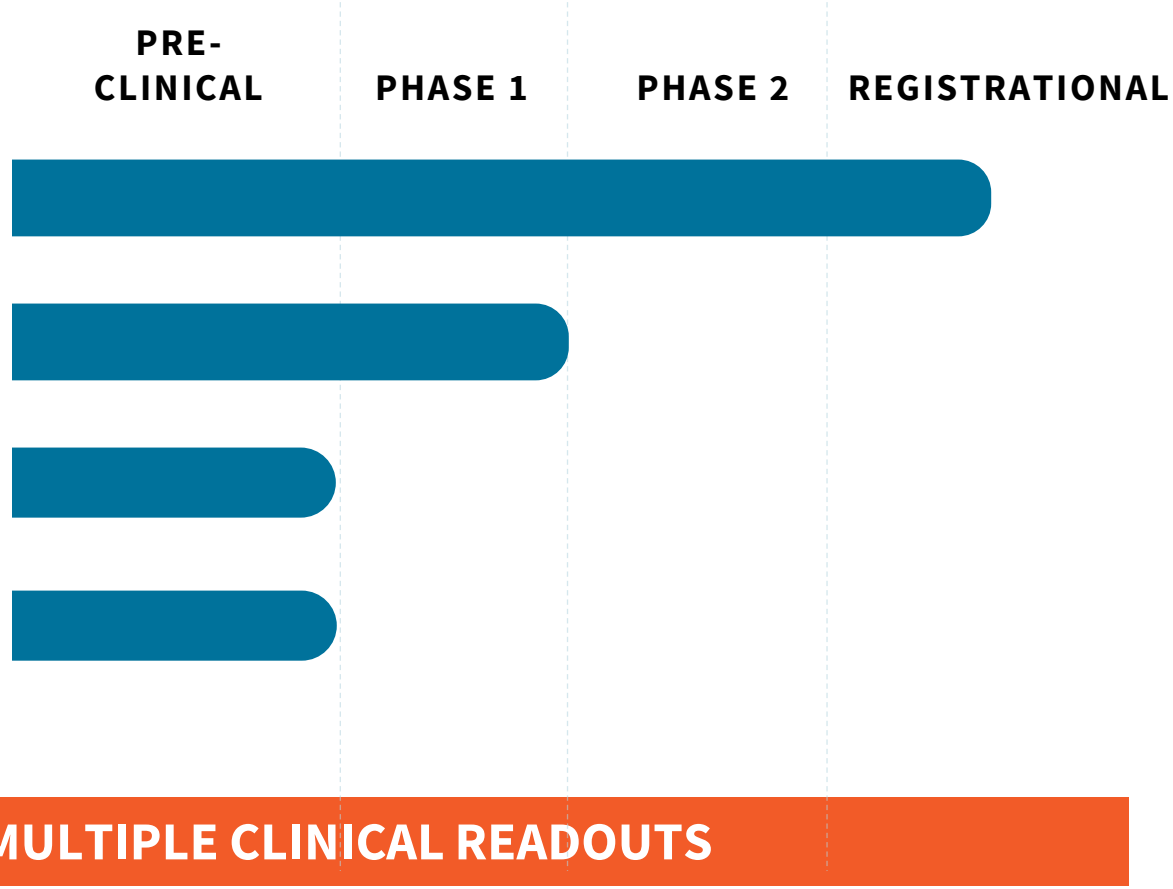
Centessa has multiple early-stage programs including additional orexin agonists and discovery-stage programs not reflected on this slide. Where applicable, Centessa plans to provide updates on preclinical programs as they advance toward clinical studies.

1.Evaluate Pharma 2021 and internal estimates

INNOVATIVE PIPELINE

Potential first-in-class/ best-in-class medicines for patients

ASSET	DISEASE	MECHANISM
SerpinPC	Hemophilia B	Activated Protein C Inhibitor
LB101	Solid Tumors	PD-L1xCD47 LockBody
LB206	Solid Tumors	PD-L1xCD3 LockBody
ORX750	Narcolepsy Type 1 (NT1) and other sleep disorders	Orexin Receptor-2 (OX2R) Agonist



CASH RUNWAY INTO 2026 ENABLES MULTIPLE CLINICAL READOUTS

CENTESSA PHARMACEUTICALS

Centessa has multiple early-stage programs including additional orexin agonists and discovery-stage programs not reflected on this slide.

LEADERSHIP

Team with deep R&D experience and focused on execution

SAURABH SAHA MD PhD

Chief Executive Officer

Bristol Myers Squibb · NOVARTIS · Delinia · ATLAS VENTURE · McKinsey&Company

ANTOINE YVER MD MSc

EVP & Chairman of Development

Daiichi-Sankyo · CHUGAI · Johnson&Johnson · als · AstraZeneca · Schering-Plough · MERCK · RHÔNE-POULENC · Aventis

DAVID GRAINGER PhD

Chief Innovation Officer

medicxi · RxCelerate · totalscientific · Index Ventures

IQBAL HUSSAIN

General Counsel

ReedSmith · SLAUGHTER AND MAY · ROPES&GRAY · Johnson&Johnson

GREG WEINHOFF MD MBA

Chief Financial Officer

ARVELLE THERAPEUTICS · CHL HEALTHCARE PARTNERS · Morgan Stanley · Amicus Therapeutics · AXOVANT

TIA BUSH

Chief Technology & Quality Officer

AMGEN

DAVID CHAO PhD

Chief Administrative Officer

BIOMED VALLEY DISCOVERIES · nectagen · STOWERS INSTITUTE FOR MEDICAL RESEARCH · McKinsey&Company · NOVARTIS

KAREN ANDERSON

Chief People Officer

Baxter · BAYER · Alnylam · Biogen · mimecast

KRISTEN SHEPPARD ESQ

SVP, Investor Relations & Corp. Comm.

Dicerna · STAGE · Akebia THERAPEUTICS · EQUALLOGIC · CABLETRON SYSTEMS · enterasys Secure Networks

HARRIS ROTMAN PhD

SVP, Regulatory Affairs

SANOFI · Shire · Wyeth · endo · SwanBio THERAPEUTICS

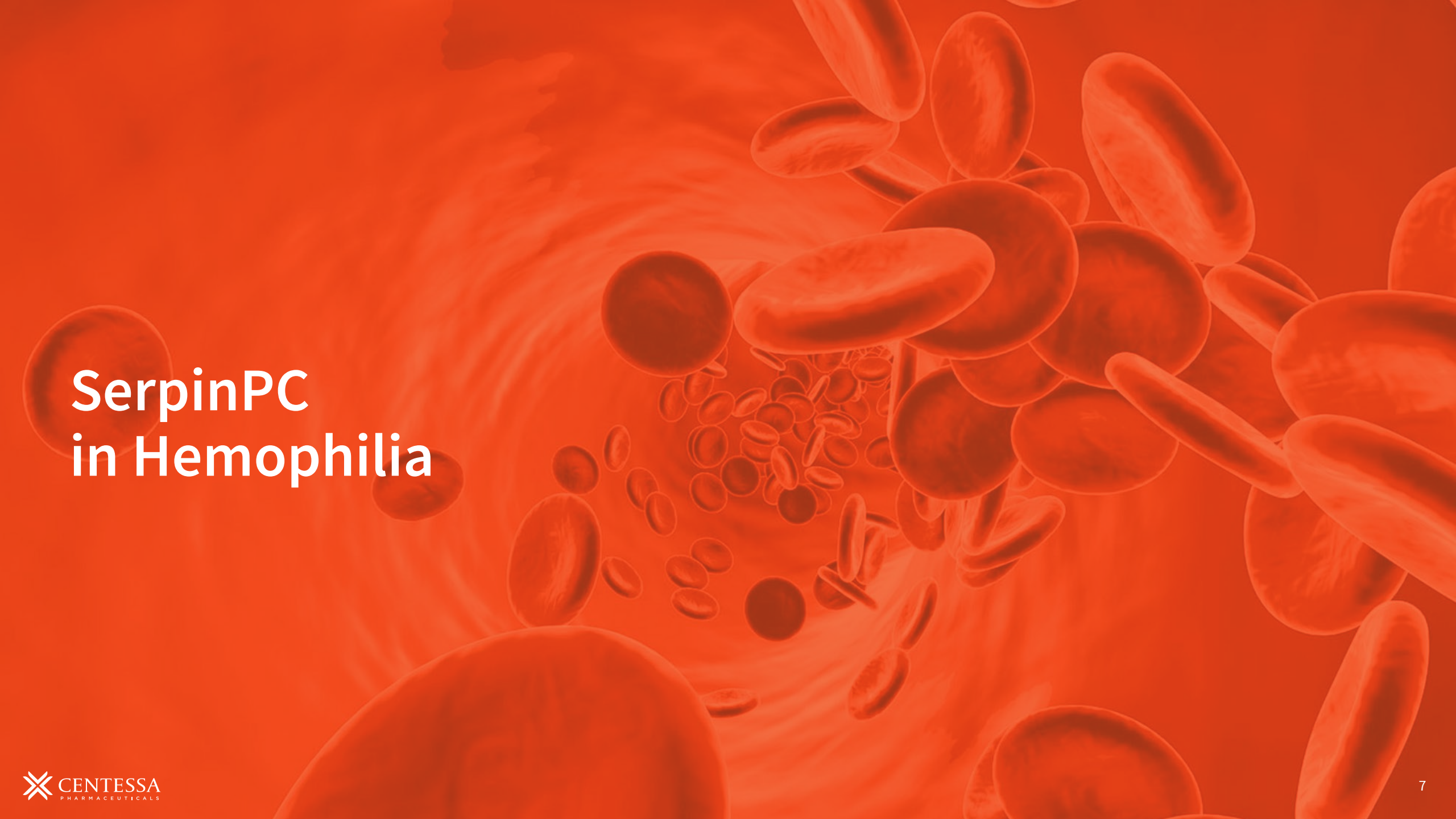
PATRICK YUE MD

SVP, Clinical Development

GBT · GILEAD · PORTOLA

CENTESSA PHARMACEUTICALS

SerpinPC in Hemophilia



CENTESSA PHARMACEUTICALS

SerpinPC: Novel, subcutaneously administered biologic inhibitor of APC

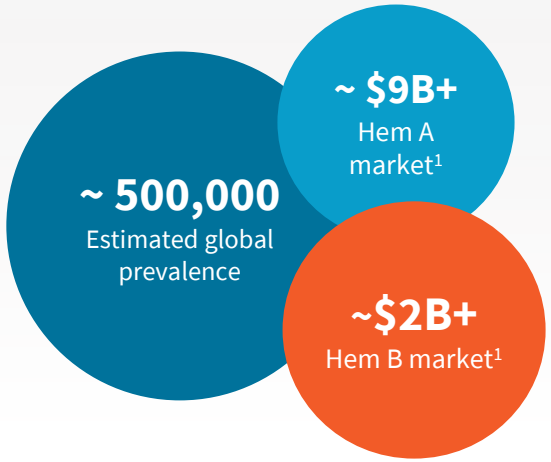
In registrational studies for the treatment of hemophilia B

HEMOPHILIA B UNMET NEED

Inconvenient, frequent and invasive IV dosing required with standard of care factor prophylaxis

Data for potentially competitive agents has shown potential risk of thrombosis

High proportion of patients outside U.S. and Europe are not treated



Novel MoA;
Showed significant **reduction in bleeding**[2]

Shown to have a **favorable safety and well tolerated profile**[2]; **No thrombosis** observed[2]

Designed as **convenient subcutaneous injection**

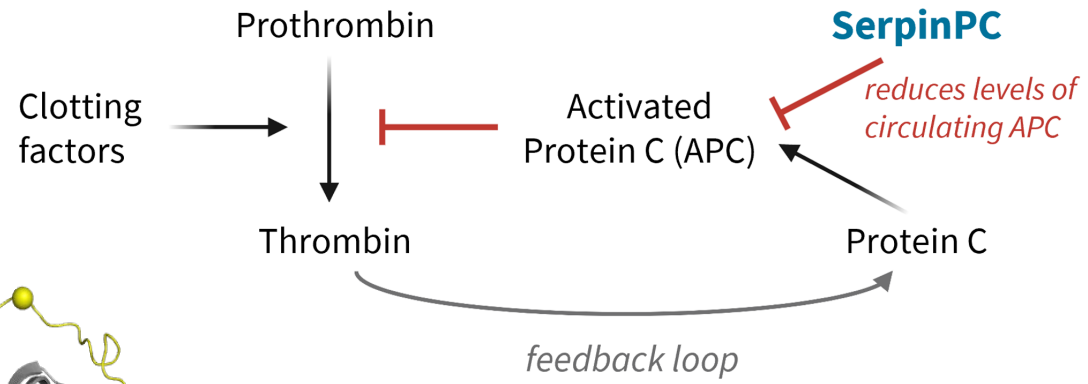
SerpinPC is an investigational serine protease inhibitor (SERPIN) engineered to specifically inhibit activated protein C (APC), that has not been approved by the FDA or any other regulatory authority. MoA is mechanism of action.

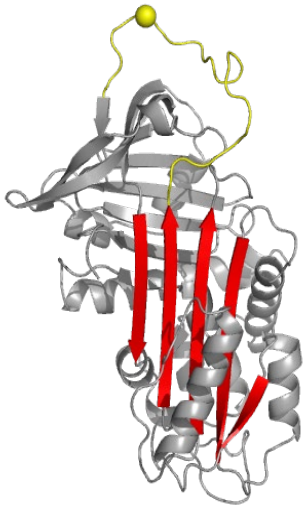
1. Evaluate Pharma 2021. 2. Ongoing Phase 2a Study (AP-0101) being conducted in Georgia and Moldova to evaluate safety, tolerability, pharmacokinetics and efficacy of SerpinPC in a population of severe hemophilia A and B subjects not on previous prophylaxis and with a history of frequent bleeding.

CENTESSA PHARMACEUTICALS

SerpinPC: Designed to exploit novel pharmacology to prevent and reduce bleeding

Primary APC is the target of SerpinPC





3D-model of SerpinPC

Modified a1 anti-trypsin with 3 substitution mutations to confer selective inhibition of activated protein C (APC)

SerpinPC

- Human genetic target validation
- Engineered to specifically inhibit APC
- Inhibition of APC increases thrombin
- Feedback loop designed to prevent excess thrombin generation

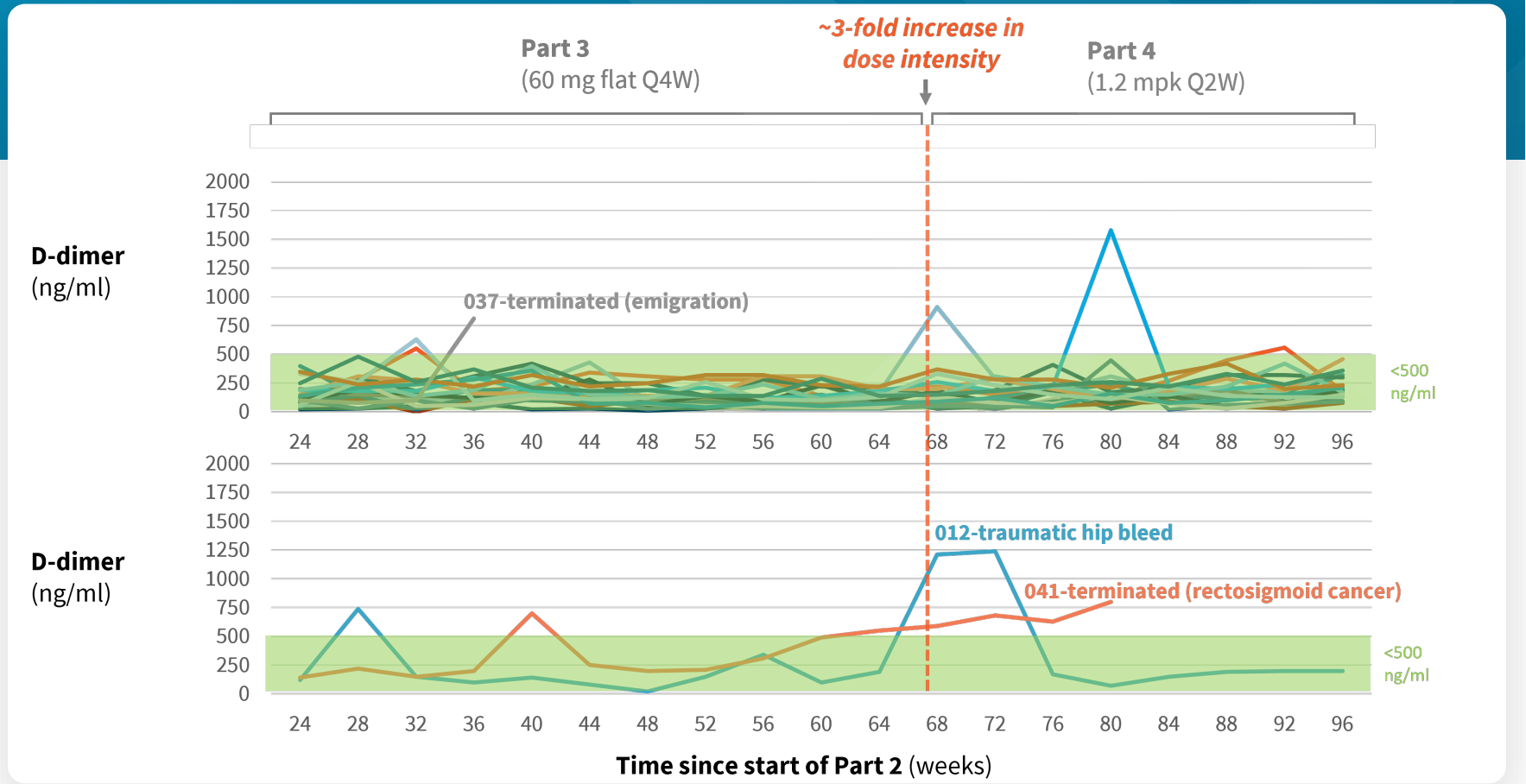
SerpinPC Phase 2a Study

Robust and highly differentiating clinical data

With total exposure of over 40 patient-years across multiple dosing regimens, Phase 2a data showed:

Favorable Safety Profile[1,2]

No observations of thrombosis or treatment-related, non-transient elevations in D-dimer[1,2]



The top graph shows the D-dimer results in the 17 subjects who had results < 500 and the 5 subjects who had non-consecutive results > 500. The bottom graph shows the results in the 2 subjects who had two or more consecutive results > 500. The blue line represents a subject who suffered a large traumatic hematoma (hip bleed), and the orange line represents a subject diagnosed with cancer, neither of which were determined to be treatment-related elevations.

1. Phase 2a study data from Part 3 and Part 4 were presented in oral presentations at ASH and EAHAD in December 2022 and February 2023, respectively. 2. There were no thromboembolic events and no treatment-related sustained elevations of D-dimer observed across the Phase 2a study, to date. D-dimer is a sensitive measure of excessive thrombin generation.

SerpinPC Phase 2a Study

Robust and highly differentiating clinical data

With total exposure of over 40 patient-years across multiple dosing regimens, Phase 2a data showed:

Favorable Tolerability Profile[1]

No observations of treatment-related, adverse events[1]

	Part 3 (n=22)		Part 4 (n=21)	
Treatment Emergent Adverse Events	**Subjects with event** No. (%)	**Treatment-related***	**Subjects with event** No. (%)	**Treatment-related***
Elevated ALT	3 (14%)	0	3 (14%)	0
Elevated gamma-GT	0	NA	2 (10%)	0
COVID-19 infection	2 (9%)	0	1	0
Hepatic fibrosis	1	0	1	0
Chronic hepatitis C	0	NA	1	0
Fever	0	NA	1	0
Urinary tract infection	0	NA	1	0
Fracture	1	0	1	0
Radiculopathy	1	0	1	0
Elevated creatinine phosphokinase	1	0	0	NA
Anemia	1	0	1	0
Elevated sodium	0	NA	1	0
Rectosigmoid cancer	0	NA	1	0
Low neutrophil count	1	0	0	NA

* Determined by Safety Review Group

CENTESSA PHARMACEUTICALS

1. Phase 2a study data from Part 3 and Part 4 were presented in oral presentations at ASH and EAHAD in December 2022 and February 2023, respectively. SerpinPC administered subcutaneously at 60 mg flat Q4W (Part 3) and 1.2 mpk Q2W (Part 4).

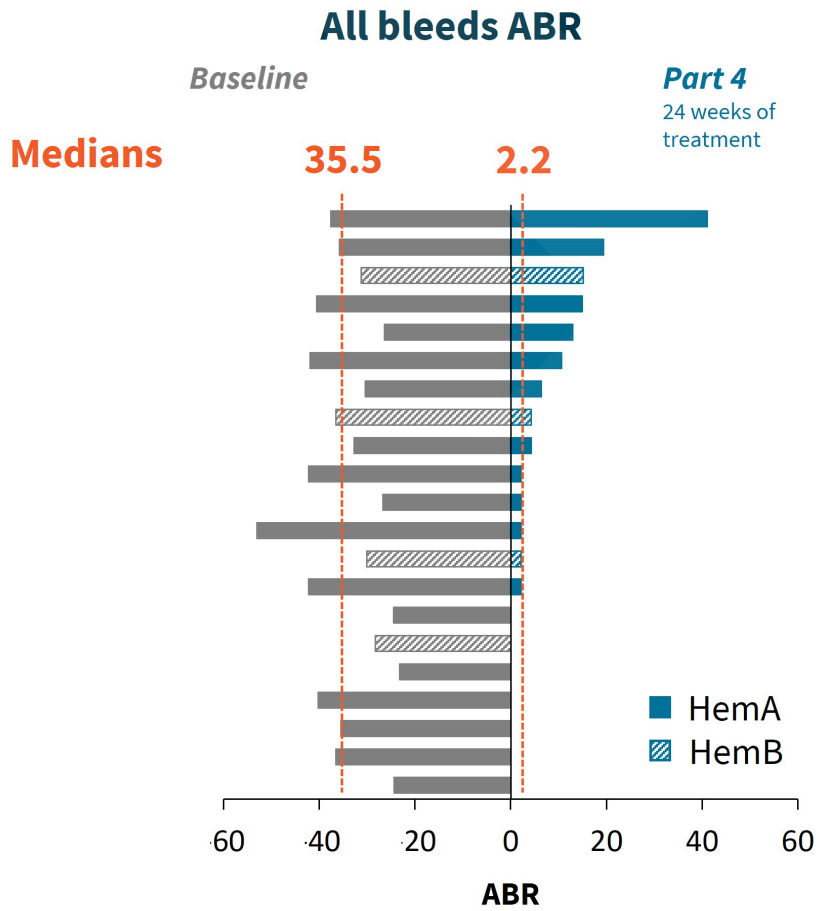
SerpinPC Phase 2a Study

Robust and highly differentiating clinical data

With total exposure of over 40 patient-years across multiple dosing regimens, Phase 2a data showed:

Reduction in Bleeding[1]

SerpinPC reduced median all-bleeds ABR by **93%** at highest dose tested



Part 4 Dosing: 1.2 mpk of SerpinPC administered subcutaneously once every 2 weeks for 24 weeks

ABR is annualized bleeding rate.

1. Phase 2a study data from Part 4 presented at ASH and EAHAD in December 2022 and February 2023, respectively.

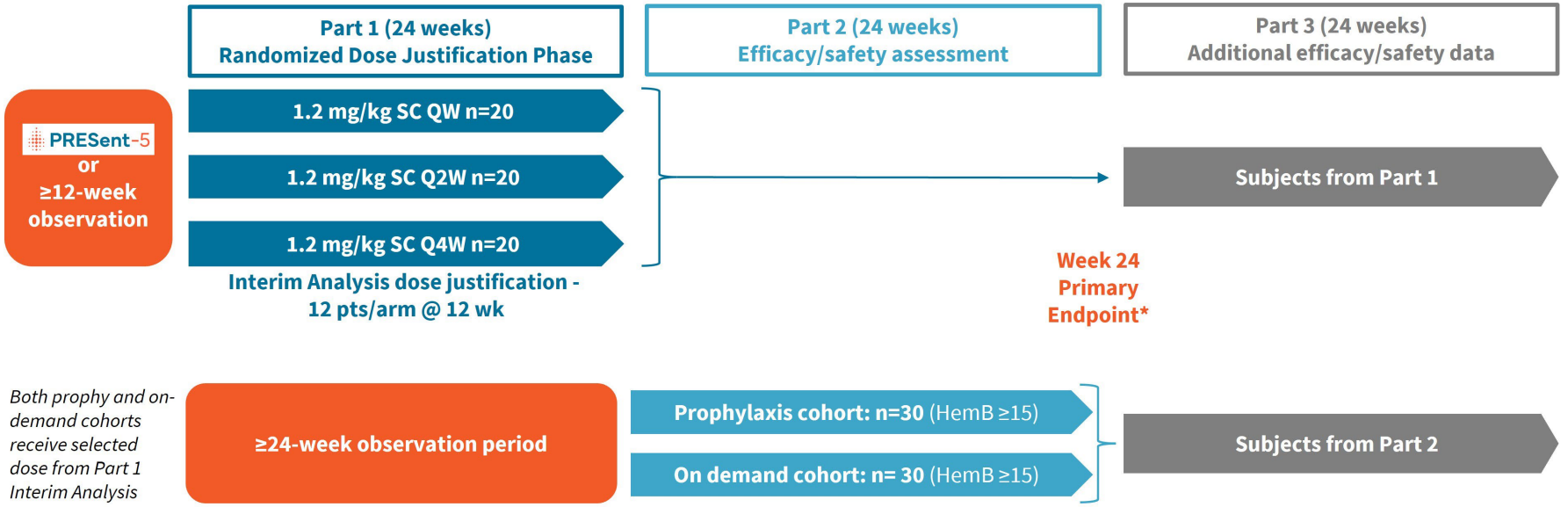
SerpinPC

In registrational studies for hemophilia B, with or without inhibitors

- Granted Fast Track designation by the FDA in May 2023
- Granted Orphan Drug Designation by the FDA in Sept. 2022

PRESent-2

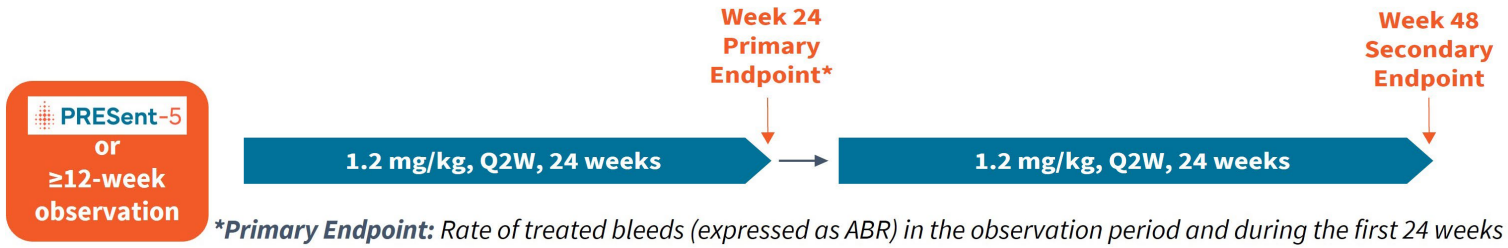
Hemophilia B without inhibitors (n=120) *Study to also include hemophilia A subjects to support safety database*



***Primary Endpoint:** Rate of treated bleeds (expressed as ABR) in the observation period and during the first 24 weeks with SerpinPC*

PRESent-3

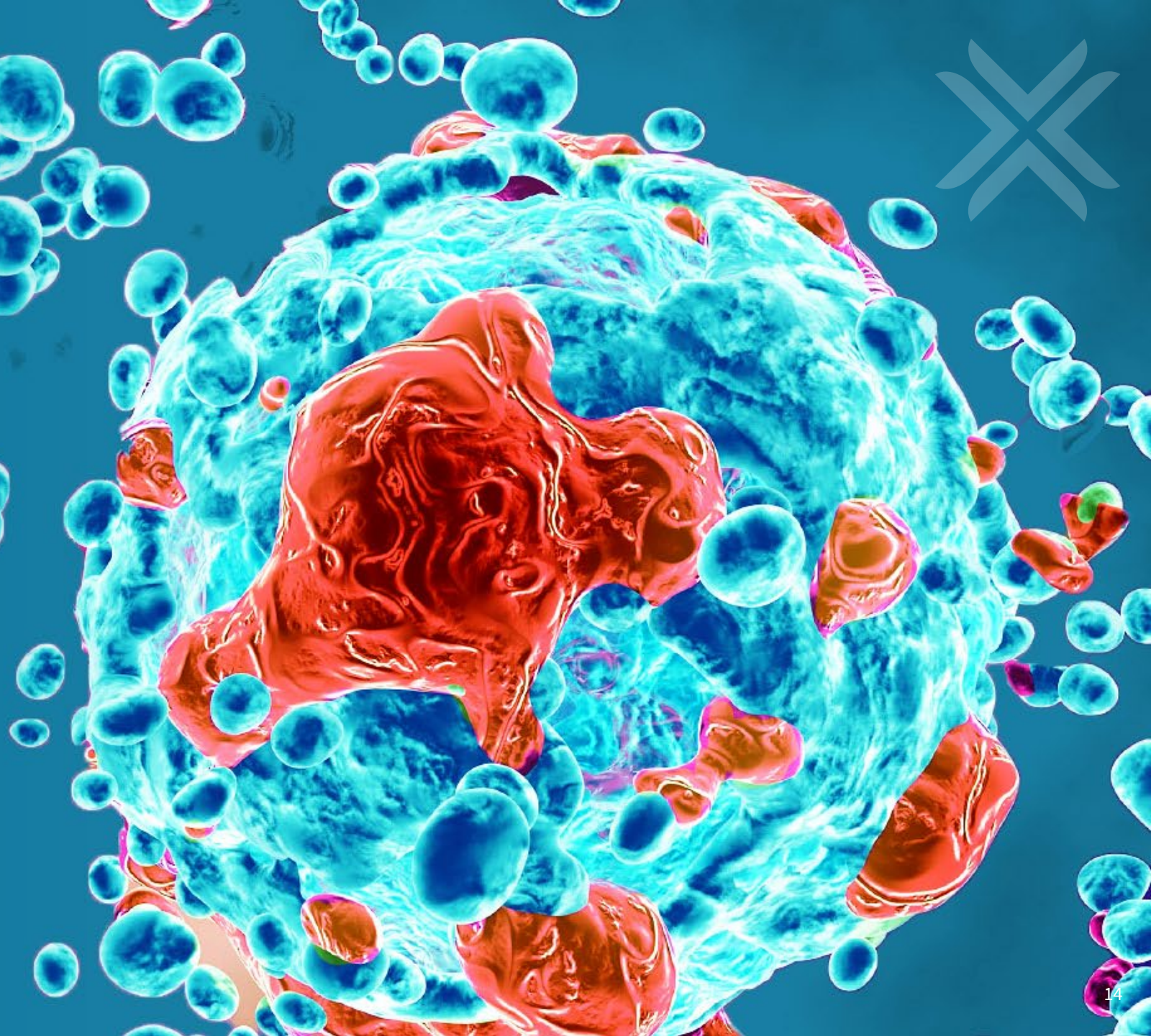
Hemophilia B with inhibitors (n≥12)



***Primary Endpoint:** Rate of treated bleeds (expressed as ABR) in the observation period and during the first 24 weeks with SerpinPC*

SerpinPC has not been approved by the FDA or any other regulatory authority.

LB101 and LB206 in Solid Tumors

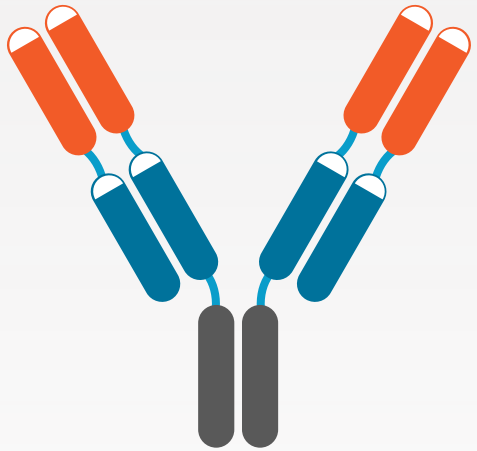


LockBody Technology Platform: Aims to redefine immuno-oncology treatment

Phase 1/2a trial of first LockBody candidate (LB101) is ongoing

LockBody®

"It's all about the hinge"



Novel pharmacology focused on human IgG-derived hinges susceptible to natural intra-tumoral hinge cleavage

Designed as **single agent systemic treatment** to selectively drive potent effector function activity, such as **CD47 or CD3**, in a solid tumor while avoiding systemic toxicity

Robust non-clinical activity demonstrating potential **wide therapeutic index**

LB101 (PD-L1xCD47) in Phase 1/2a study

LB206 (PD-L1xCD3) development candidate

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LB101 and LB206 are investigational agents that have not been approved by the FDA or any other regulatory authority. Company initiated Phase 1/2a clinical trial of LB101 and dosed first subject in March 2023. LB206 was announced a PD-L1xCD3 development candidate in Aug. 2023. TME is tumor micro-environment.

LB101: A novel, conditionally tetravalent PD-L1xCD47 bispecific monoclonal antibody

Designed to optimally deliver PD-L1 targeted anti-CD47 activity to the TME

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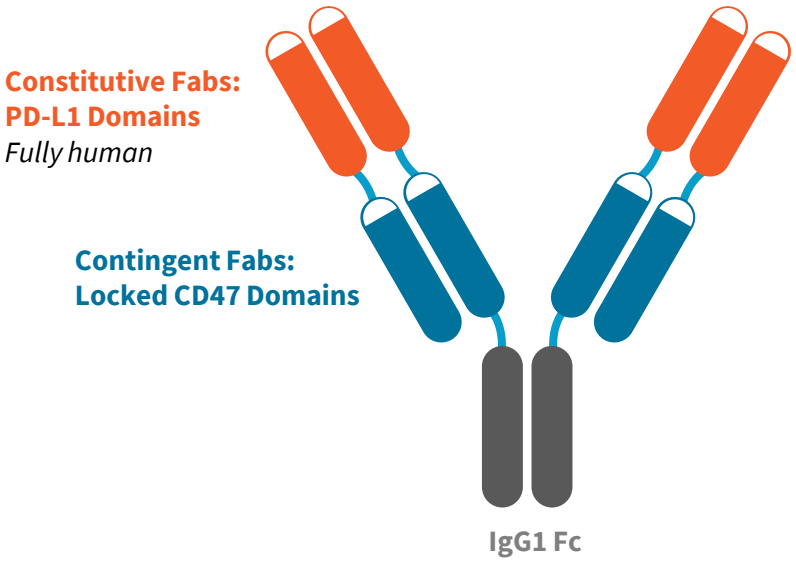

1. Constitutive Fabs drive tumor enrichment

2. Natural cleavage of IgG-derived hinges in tumors

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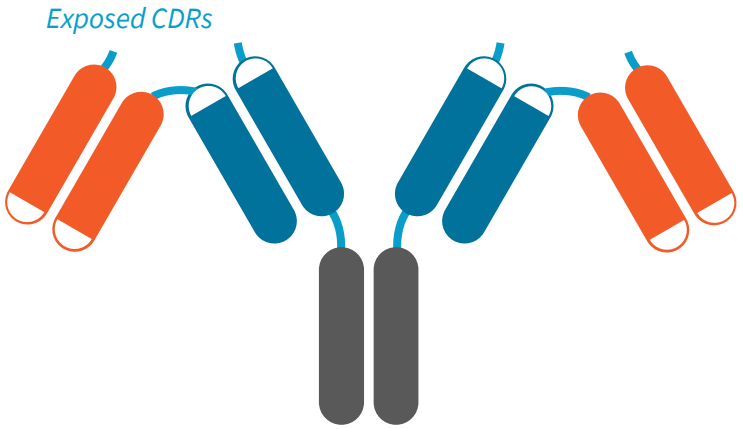


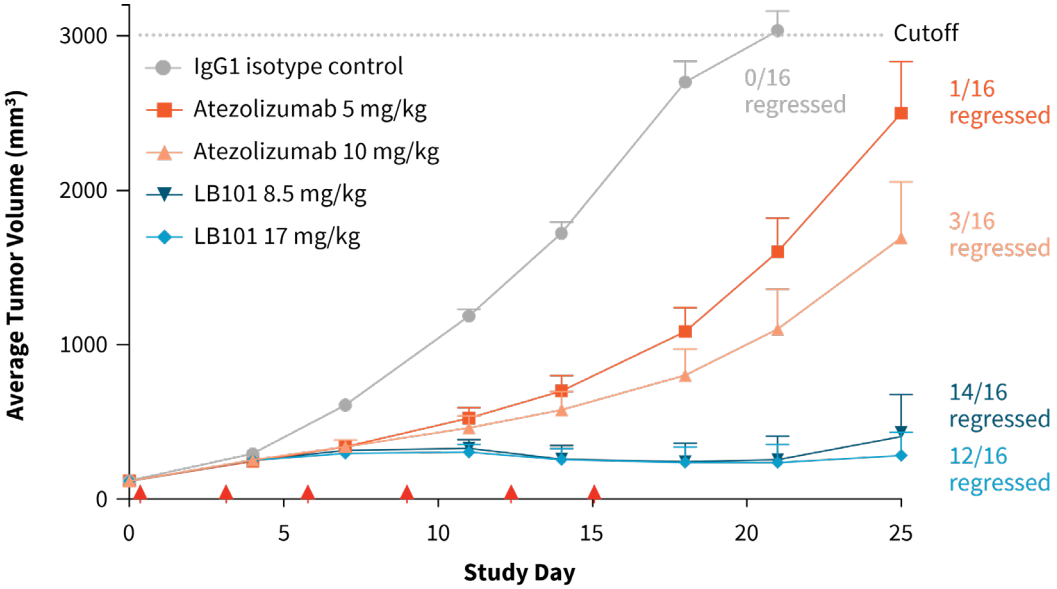
Peripheral Stability: IgG1 hinges naturally resistant to cleavage in serum

Tumor Unlocking: IgG1 hinges susceptible to cleavage in diseased tissue by various natural processes

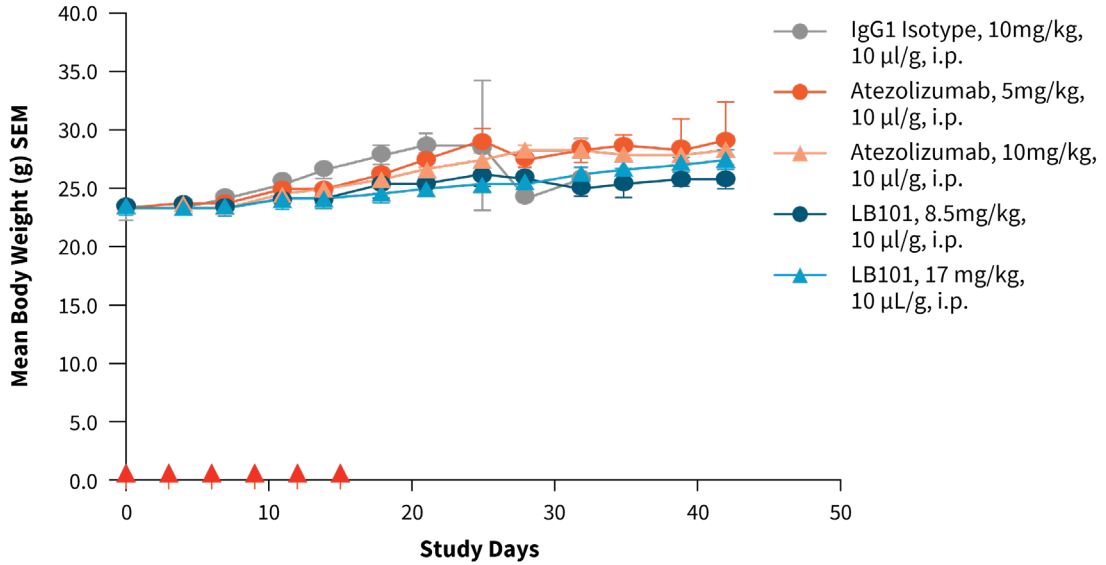
TME is tumor micro-environment

LB101 showed improved efficacy and durability over atezolizumab in a difficult-to-treat mouse model while being well tolerated

In vivo study showed systemically delivered LB101 exhibited significant tumor regression



In vivo study showed LB101 was well tolerated with no weight loss



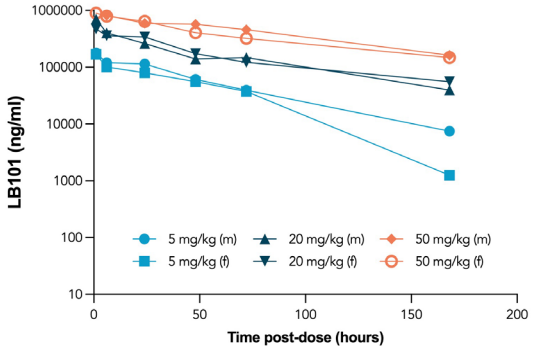
MC38 hPD-L1+ syngeneic model in mouse; Arrows indicate dosing every 3 days (Q3d x 6) at Days 0, 3, 6, 9, 12, and 15. 5 mg/kg of atezolizumab is equivalent to 8.5 mg/kg of LB101.

LB101 shown to have favorable safety and tolerability profile in non-human primates up to 50 mg/kg weekly x 4 weeks

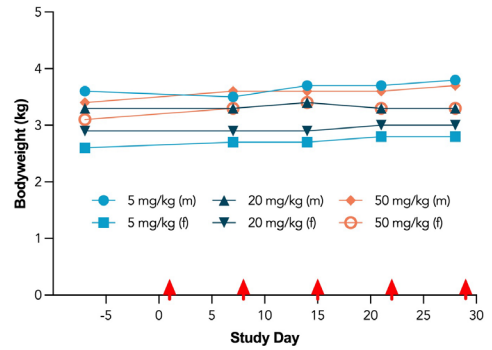
***In-vivo:* LB101 delivered IV at 5, 20, 50mg/kg (q7d x 4) in non-human primates**

- Human IgG1-like PK
- No adverse observations
  - No anemia or thrombocytopenia
  - No changes in pathology, clinical chemistry or coagulation parameters

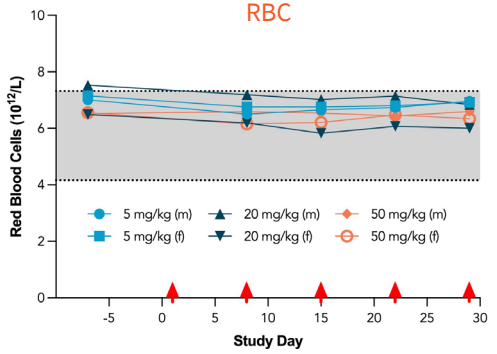
Pharmacokinetics



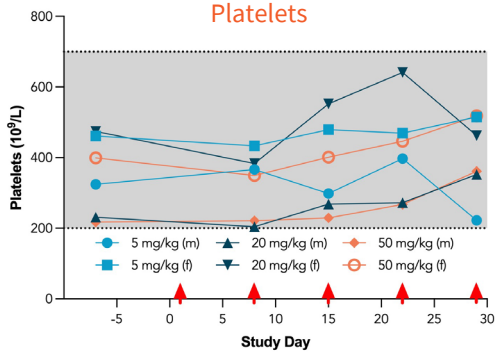
Bodyweight



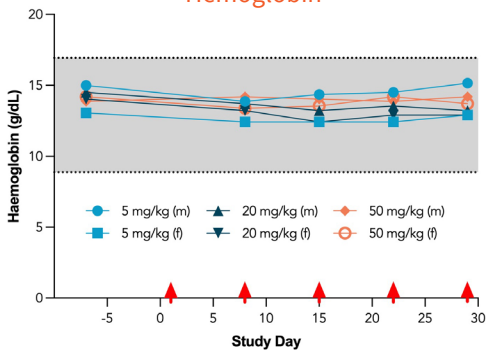
RBC



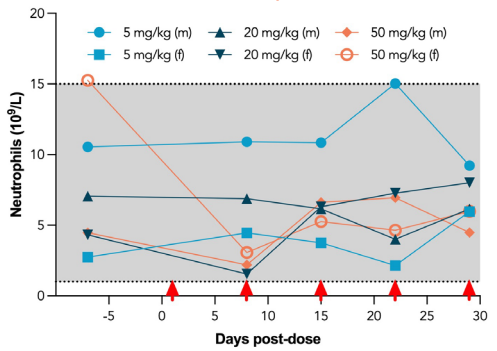
Platelets



Hemoglobin



Neutrophils



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LB101 LockBody in Phase 1/2a Clinical Trial

Dosing subjects in ongoing Phase 1/2a first-in-human clinical trial of LB101

Phase 1/2a Clinical Trial

- Open-label, multicenter, dose escalation with expansion cohorts
- Part 1: LB101 **monotherapy** in subjects with selected, advanced solid tumors; determine recommended dose(s) for expansion (Part 2)
- Part 2: Design depends on Part 1 results; will further evaluate the safety, efficacy, tolerability, pharmacokinetics, and immune response of LB101
- Study to provide insights on LockBody technology platform in clinical setting

LB206: A novel, conditionally bivalent PD-L1xCD3 bispecific monoclonal antibody

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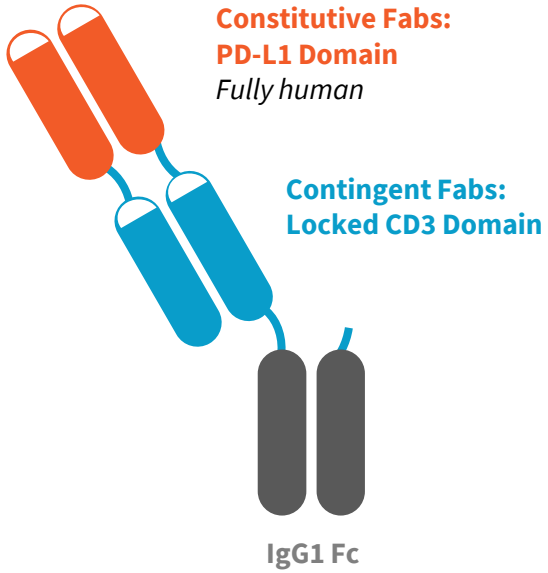

1. Constitutive Fabs drive tumor enrichment

2. Natural cleavage of IgG-derived hinges in tumors

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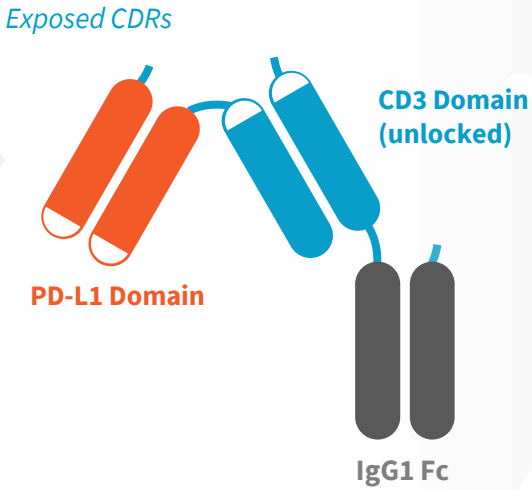

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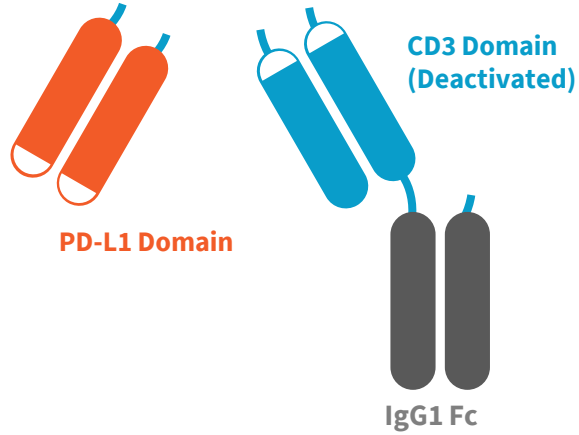


Peripheral Stability: IgG1 hinges naturally resistant to cleavage in serum

Tumor Unlocking: IgG1 hinges susceptible to cleavage in diseased tissue by various natural processes

Deactivation: Second cleaving event terminates CD3 activity

CENTESSA PHARMACEUTICALS

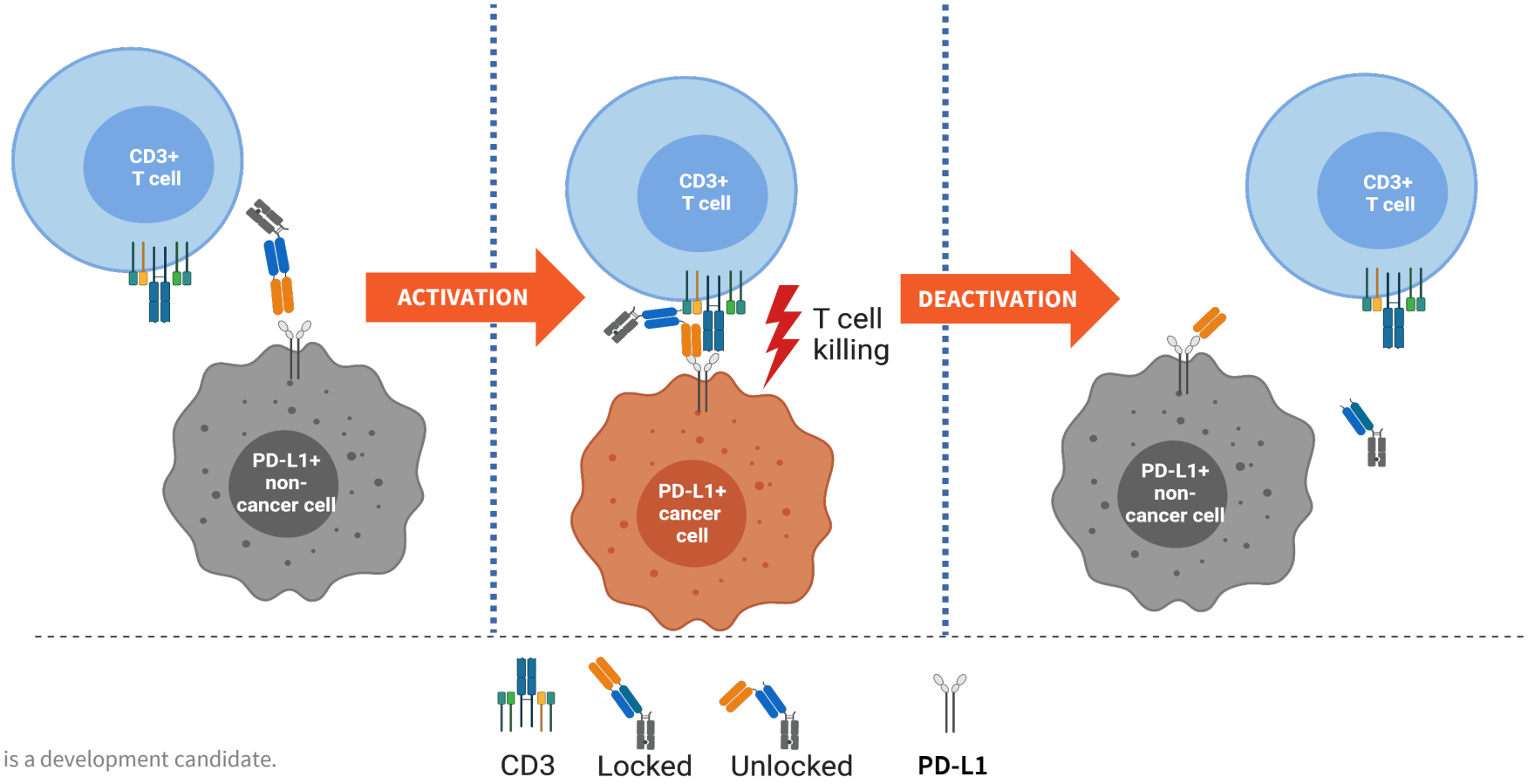
LB206 is a development candidate.

LB206: Designed to concentrate and drive potent CD3 activity in solid tumors with a wide therapeutic index

Peripheral Stability
IgG1 hinges naturally resistant to cleavage in serum

Tumor Unlocking
IgG1 hinges susceptible to cleavage in diseased tissue by various natural processes

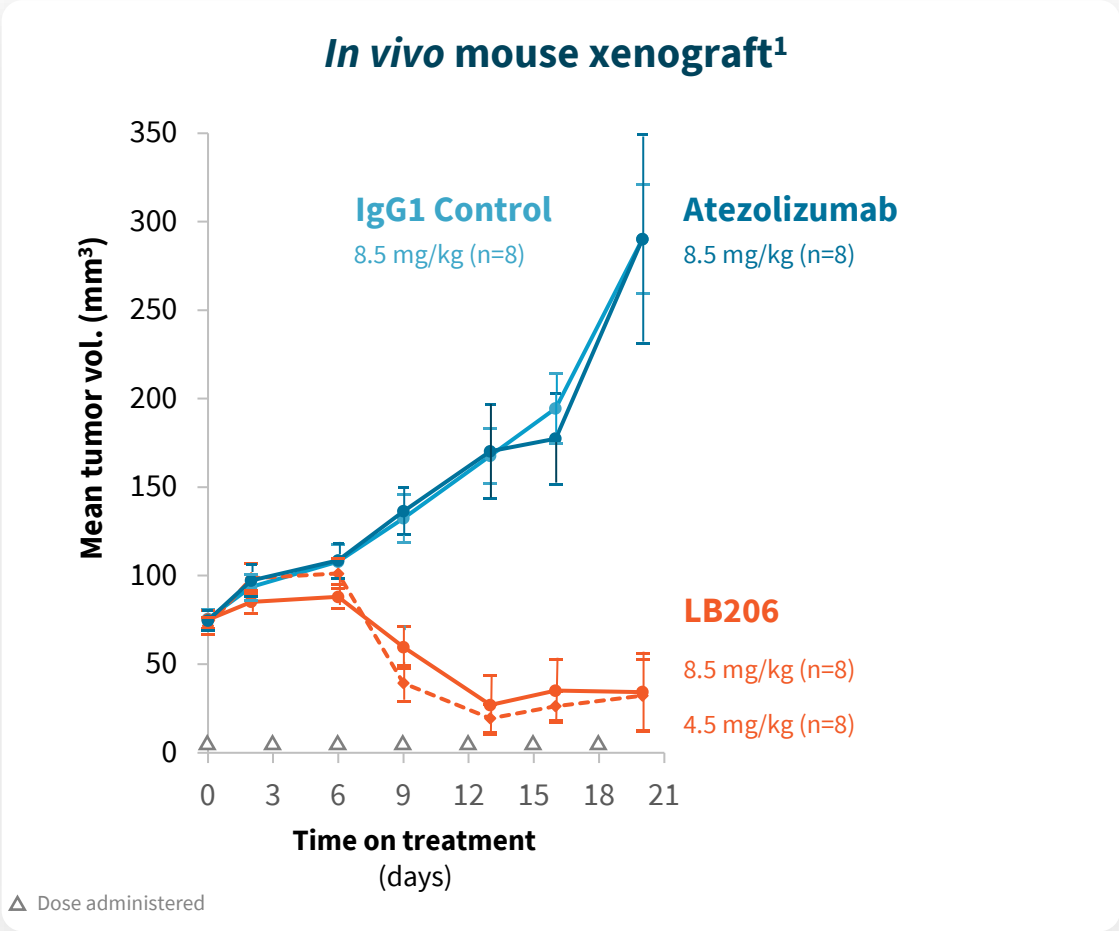
Deactivation
Second cleaving event terminates CD3 activity



LB206 is a development candidate.

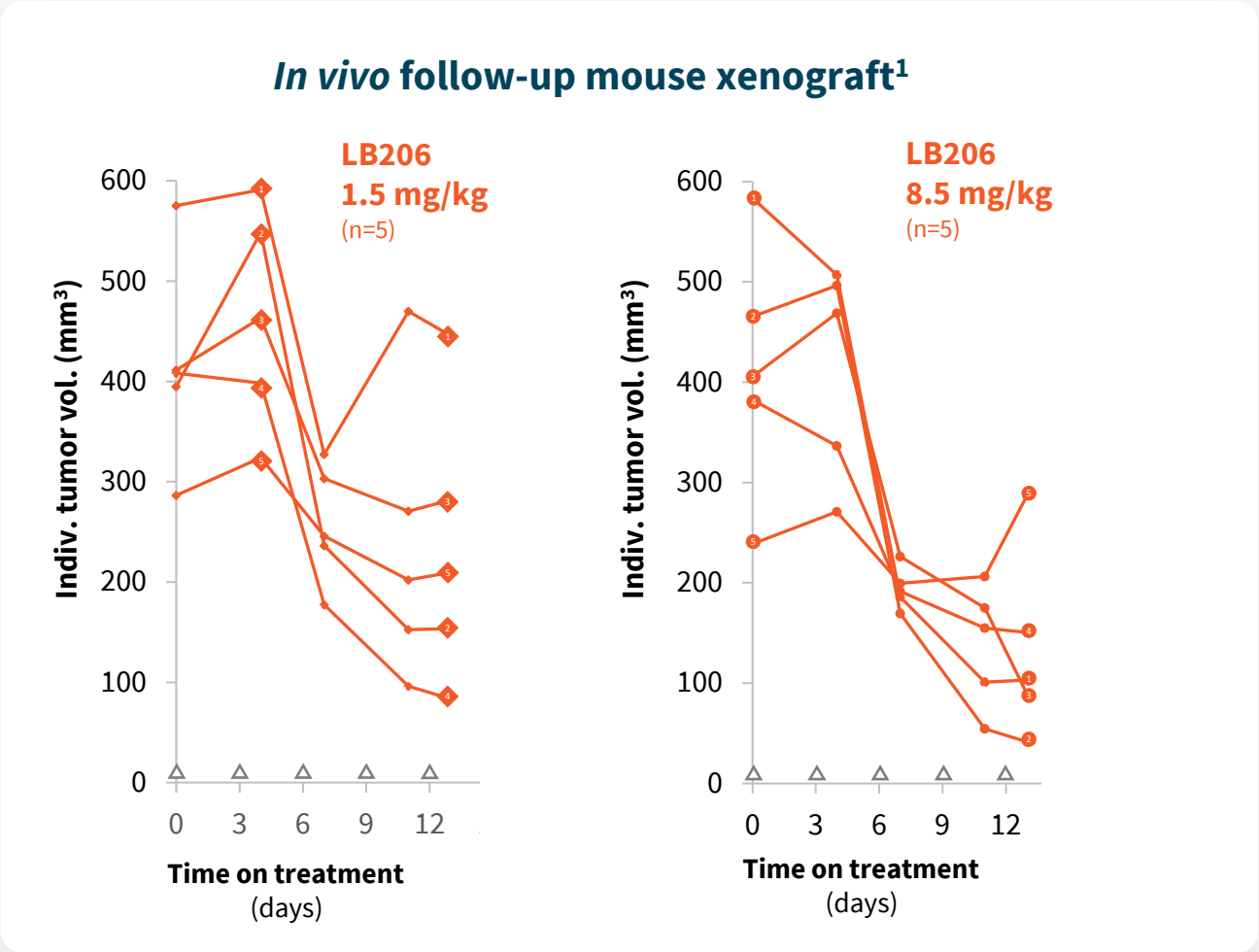
LB206: In vivo data demonstrated significant tumor regressions with LB206 in a difficult-to-treat mouse model

Potent CD3-driven anti-tumor activity observed in MDA-MB-231 mouse xenograft model



1. Mean body weight values for Day 0 and Day 20 within +/- 6% range for each of the four groups.
LB206 is a PD-L1xCD3 development candidate.

LB206: In vivo data from follow-up experiment demonstrated regression of large tumors in a difficult-to-treat mouse model



1. MDA-MB231 mouse xenograft model. For 10 mg/kg IgG1 effector null control, mean tumor volume increased from 426 mm^3 on Day 0 to 784 mm^3 on Day 13 (n=4, 1 control mouse with morbidity sacrificed after Day 4 and excluded from calculation of mean).
LB206 is a PD-L1xCD3 development candidate.

CENTESSA PHARMACEUTICALS

ORX750 in Narcolepsy

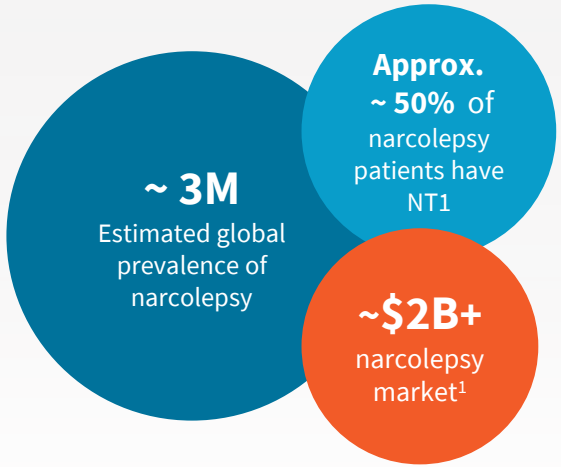
ORX750: Orally administered, selective orexin receptor-2 (OX2R) agonist

In preclinical development for treatment of NT1; IND-enabling activities underway

Narcolepsy Type 1 (NT1)

A rare neurological condition that affects the brain's ability to regulate the normal sleep-wake cycle

Caused by a profound loss of orexin neurons in the brain



High unmet need

Current treatments do not restore normal function; symptoms persist despite polypharmacy

75% patients experience EDS[1]

50% patients still have 1-2 cataplexy episodes per day[2]

ORX750 designed to **reactivate orexin** signaling in the brain

Highly validated human target with clinical proof of concept in NT1

Exploring follow-up orexin agonists for potential expansion opportunities into sleep disorders and broader neurological indications

EDS is excessive daytime sleepiness. In March 2023, ORX750 was announced as the Company's product candidate for the treatment of NT1 with potential expansion into other sleep disorders. 1. Evaluate Pharma 2021. 2. Maski K, et al. J Clin Sleep Med 2017;13;419–25.

Structure-based drug design has enabled the discovery of ORX750 as potential orexin signaling ‘replacement therapy’ for NT1, with potential indication expansion beyond NT1

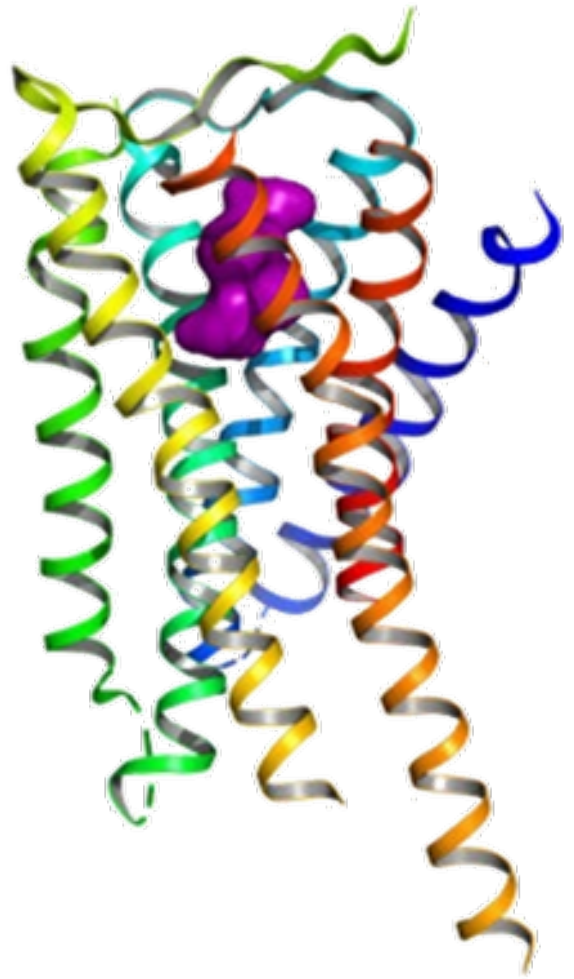
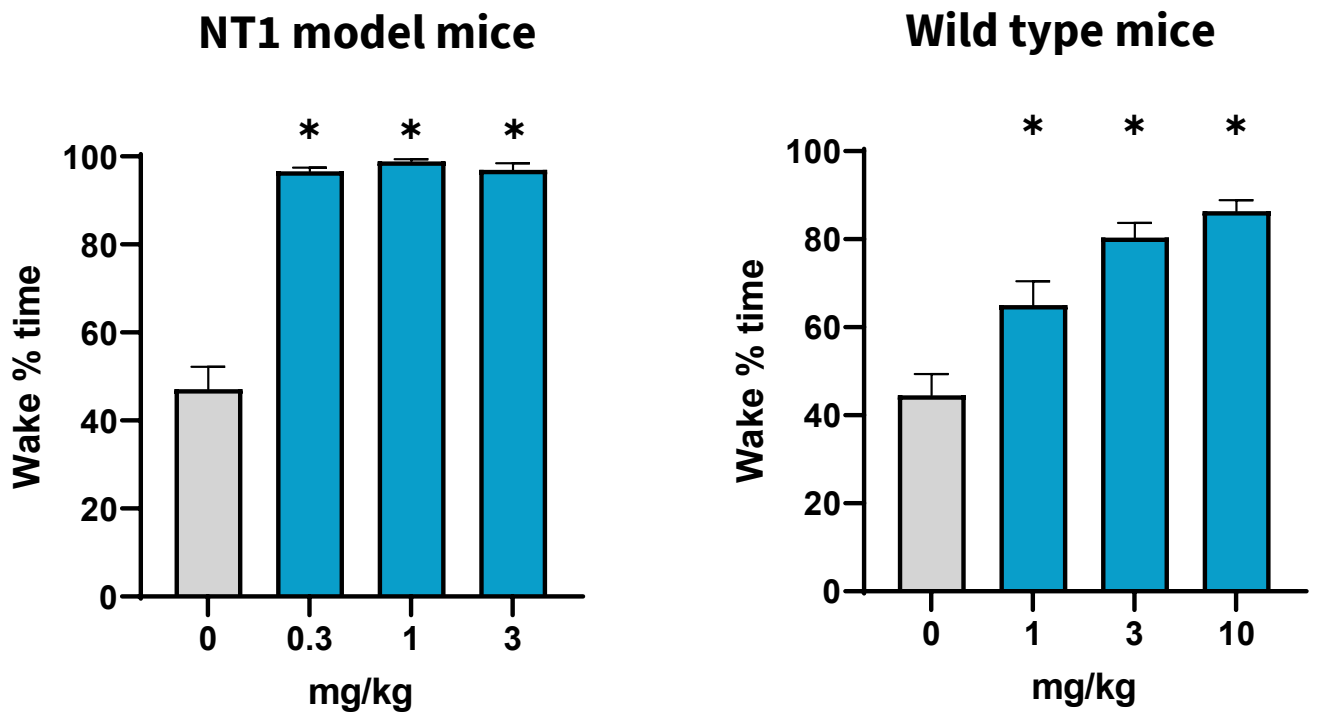


Illustration of OX2R structure
bound to prototype small molecule orexin agonist
(shown in purple)

ORX750 increased wakefulness in NT1 model and wild type mice



ORX750 was dosed orally during the rest phase in the PiezoSleep assay; percent time spent awake in the first 2 h after dosing is quantified.

NT1 model shown here is orexin/ataxin-3 (Atax) mice, which recapitulates the degeneration of orexin neurons associated with NT1.

*P < 0.05 vs. 0 mg/kg

- ORX750 increased time awake in an NT1 mouse model, showing maximal wake promotion (ceiling effect) at doses shown
- Wake % time in wild type mice showed a dose-related response which supports potential indication expansion beyond NT1
- Additional ORX750 preclinical data to be presented at **World Sleep** in Oct. 2023

ORX750 preclinical data to be presented at World Sleep Congress

October 20-25 WORLD SLEEP 2023 Rio de Janeiro BRAZIL

***In vitro* data[1] showed:**

- ORX750 is highly potent:
  - Human OX2R (EC50 = 0.11 nM)
  - 9,800-fold selectivity over OX1R

***In vivo* data[1] showed:**

- ORX750 increased latencies to sleep and cataplexy in a dose-related manner, starting at 1.6 h and 1.4 h over vehicle levels, respectively, at the lowest dose tested (0.3 mg/kg) in NT1 model mice

- ORX750 increased time awake and the consolidation of wakefulness in a dose-related manner when administered to WT and NT1 mice

Selected published data on OX2R candidate profiles

Molecule	hOX2R EC50 (nM) (as reported)	Selectivity vs. hOX1R (as reported)
Native ligand orexin-A (OXA)[1]	0.035	
ORX750[1]	**0.11**	**9,800X**
TAK-861[2]	2.5	3,000X
TAK-994[2]	19	740X
E2086[3]	2.3	2,000X

[1] Black et al., World Sleep 2023 Abstract
[2] Kimura, et al., World Sleep 2023 Abstract
[3] Hatanaka, et al., ACNP 2022 Poster
Note: Data is NOT from a head to head study. Slide contains public data as reported by each company, separately.

1. Black et al., World Sleep 2023 Abstract

Centessa is fueling multiple pathways to value creation

- Multiple potential blockbuster assets
- Cash runway into 2026 enables multiple clinical readouts
- World-class R&D team

Note: The Company reported $303.6 million in cash, cash equivalents and short-term investments as of June 30, 2023. In addition, the Company received approximately $15.0 million in gross proceeds through ATM sales in August 2023.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PHARMACEUTICALS