CENTESSA PHARMACEUTICALS

Corporate Overview

APRIL 22, 2024

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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, ORX750 and, LB101; strategy; regulatory matters, including the timing and likelihood of success of obtaining approvals to initiate or continue clinical trials or market any products; the Company's ability to successfully conduct its clinical development of ORX750 below the maximum exposure limit set by the U.S. Food and Drug Administration ("FDA") or, in the event the Company plans to exceed the maximum exposure limit, the Company's ability to successfully have the maximum exposure limit removed; 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; 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 geo-political risks such as the Russia-Ukraine war and the conflicts in the Middle East 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 FDA 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.

OUR MISSION

Discovering and developing medicines that are transformational for patients

- Multiple potential blockbuster assets
- Ongoing momentum in 2024 with clinical milestones anticipated across our most advanced programs
- Strong balance sheet

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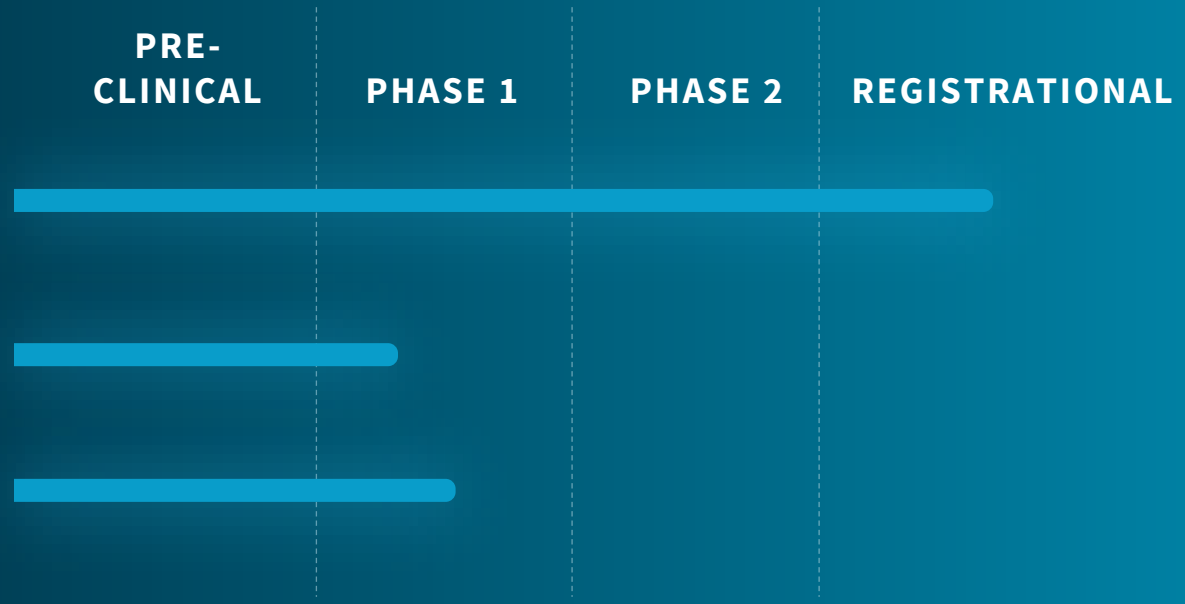
Centessa reported $256.5 million in cash, cash equivalents and short-term investments as of December 31, 2023.

Our Most Advanced Potential First-in-Class/Best-in-Class Medicines for Patients

ASSET	DISEASE	MECHANISM
SerpinPC	**Hemophilia B**	Activated Protein C Inhibitor
ORX750	**Narcolepsy**	Orexin Receptor-2 (OX2R) Agonist
LB101	**Solid Tumors**	PD-L1xCD47 LockBody®



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Centessa has multiple early-stage programs including LB206 and additional orexin agonists and discovery-stage programs not reflected on this slide.

2024 Driving Momentum

ANTICIPATED MILESTONES

HEMOPHILIA PROGRAM

SerpinPC

Registrational study interim analysis expected in **2024**

OREXIN AGONIST PROGRAM

ORX750

Clinical PoC data in healthy volunteers expected in **2H of 2024**

LOCKBODY TECHNOLOGY PLATFORM

LB101

Phase 1/2 study **ongoing**

Hemophilia Program

Orexin Agonist Program

LockBody Technology Platform

Hemophilia B: Large Growing Market with Unmet Need

~$2.6B+
Hemophilia B Market[1]

- A safe, subcutaneous and effective treatment has the potential to transform care for hemophilia B
- No subcutaneous treatment option currently available for hemophilia B in the US[2]
- Limited options for hemophilia B with inhibitors[2]

1. Evaluate Pharma Analyst Consensus for 2023. 2. In Canada, a subcutaneous option is available for hemophilia B with inhibitors.

***SerpinPC** has the potential to be a **first-in-class subcutaneous** therapy with a **differentiated** safety profile for people with hemophilia B*[1]

- Novel mechanism of action
- Showed significant reduction in bleeding[1]
- Shown to have a favorable safety and well tolerated profile to date; No thrombosis observed to date[1]

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. ABR is annualized bleed rate. 1. Ongoing Phase 2a Study 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. Part 5: Blood (2023) 142 (Supplement 1): 2619. https://doi.org/10.1182/blood-2023-179969. Part 3-4: Blood (2022) 140 (Supplement 1): 460–461. https://doi.org/10.1182/blood-2022-159631. Additional information on the trial can be accessed at www.clinicaltrials.gov (NCT04073498).

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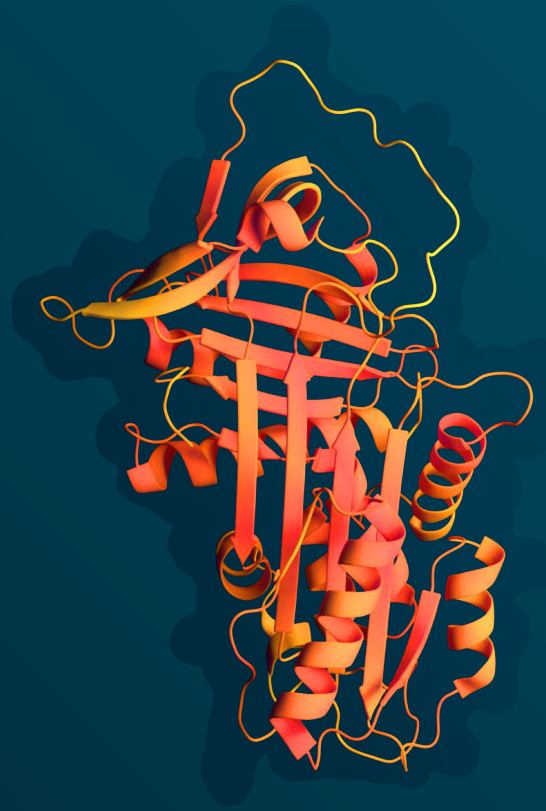
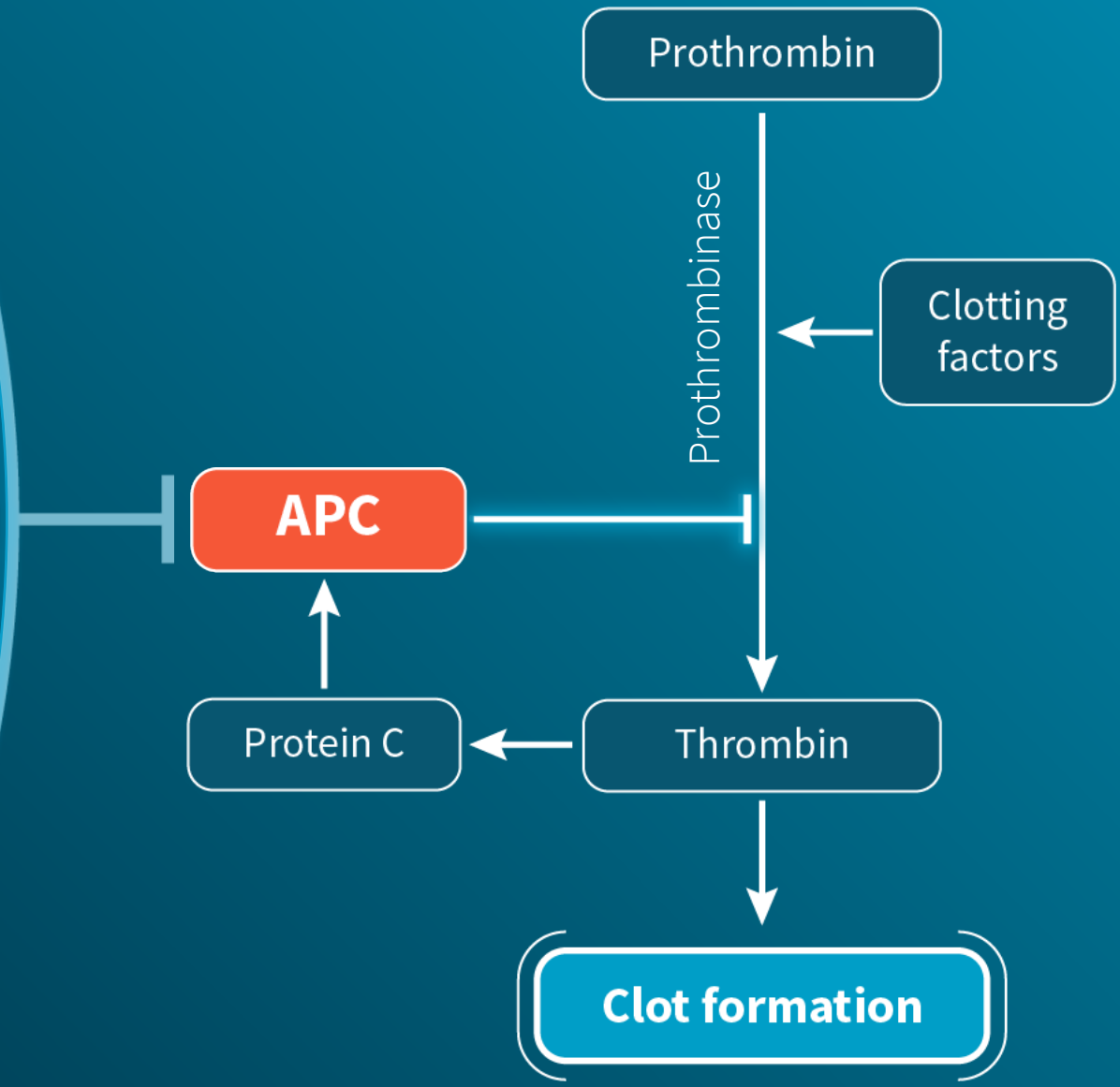
SerpinPC: Novel Approach Designed to Prevent and Reduce Bleeding



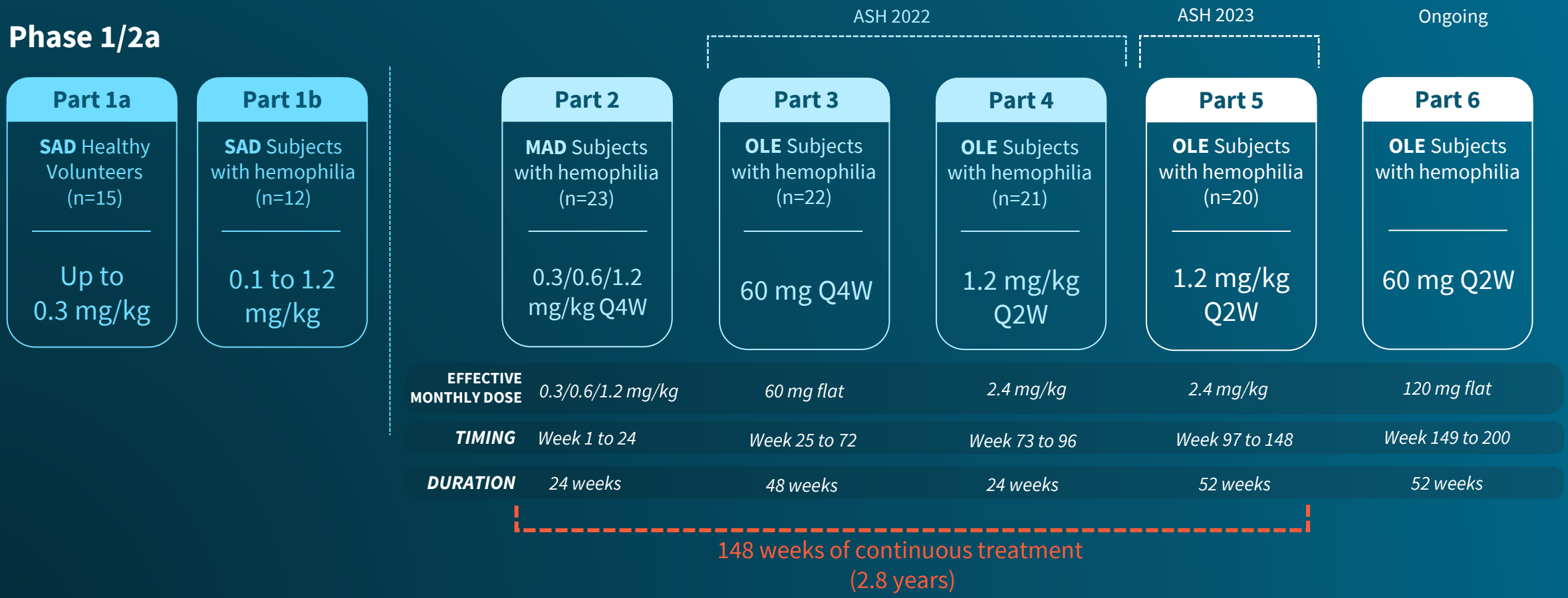
SerpinPC

Designed to reduce levels of circulating activated protein C (APC)



Phase 2a | Ongoing Study of SerpinPC in Hemophilia

AP-0101 (NCT04073498) | An adaptive, first-in-human study to investigate the safety, tolerability, efficacy, and pharmacokinetics of SerpinPC in male persons with severe hemophilia

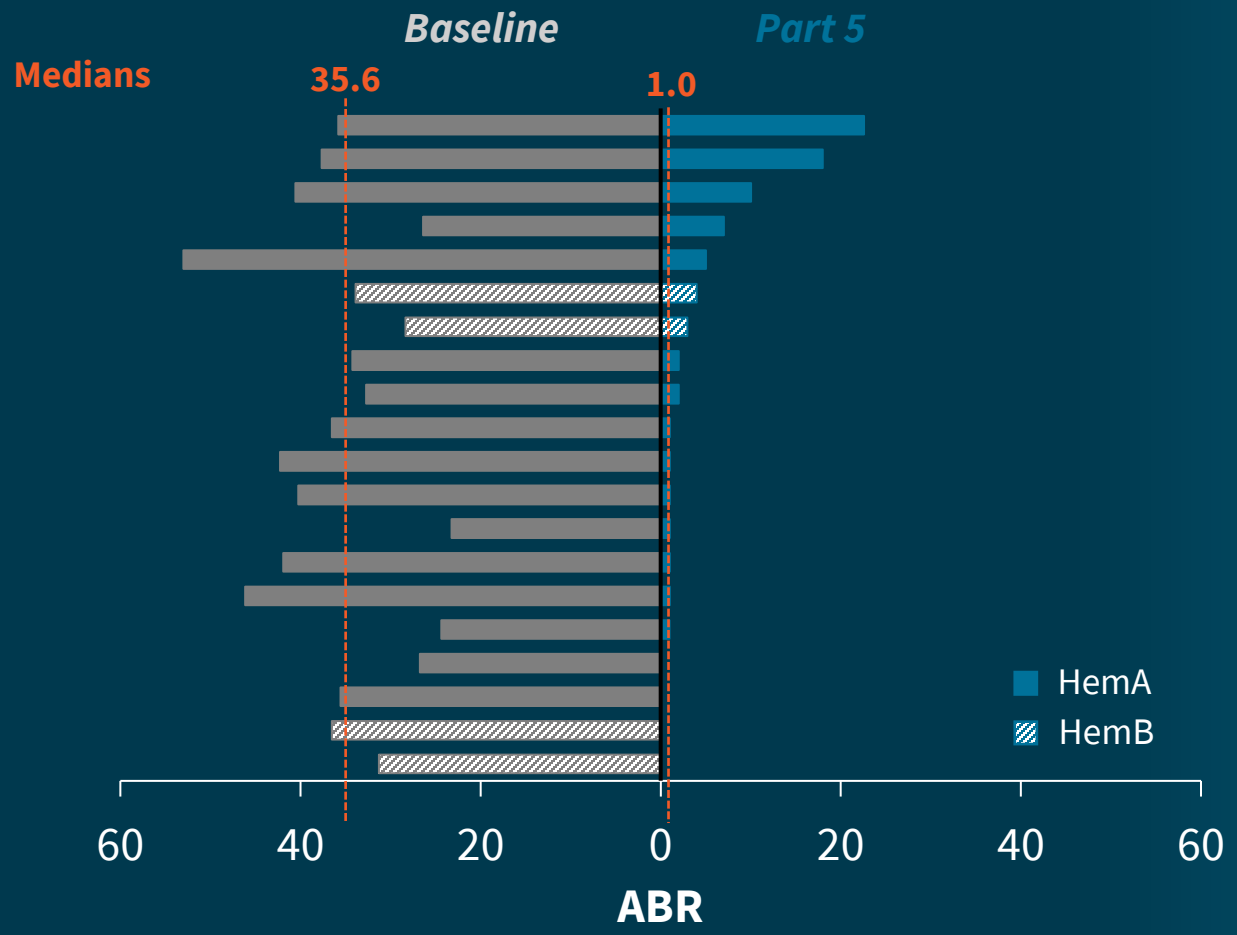


PK=pharmacokinetics; SAD=single ascending dose; MAD=multiple ascending dose; OLE=open-label extension.

Reference: ClinicalTrials.gov. NCT04073498. Accessed January 18, 2024.

Phase 2a Part 5: SerpinPC Achieved a 96% Reduction in Median All-Bleeds ABR[1]

AP-0101 Part 5 all bleed ABR at 1.2 mg/kg Q2W (n=20)[1]



96% Reduction in Bleeding[1]

In Part 5, SerpinPC reduced median all-bleeds ABR to **1.0**, a **96%** reduction from prospective baseline. Subjects in Part 5 participated in Parts 2, 3 and 4 and therefore, received continuous treatment with SerpinPC for approximately 2.8 years.

ABR is annualized bleeding rate. 1. Part 5 of Phase 2a study as presented at ASH in December 2023. Results reflect approximately 2.8 years of continuous treatment with SerpinPC at dose levels that varied between Parts 2, 3 and 4. Four subjects discontinued during Part 5 (one due to femoral fracture, one due to lengthy travel from study site, and two due to emigration). ABRs calculated based on number of weeks on study drug.

SerpinPC Shown to Have Favorable Safety and Tolerability Profile to Date

No observations of treatment-related adverse events in Part 5

Treatment Emergent Adverse Events (TEAEs)	**Number of subjects (%)** n=20
All TEAEs (total 41 events)	16 (80%)
Related to SerpinPC	**0**
Leading to discontinuation	1 (5%)
Leading to death	0
AEs of special interest	0
Serious adverse events	2 (10%)*
Thromboembolic events	0
Injection site reactions	0
Anti-drug antibodies	1#
Neutralizing anti-drug antibodies	0#

Source: Phase 2a study data of SerpinPC. Part 5: Blood (2023) 142 (Supplement 1): 2619 .
*Two SAEs occurred and were considered unrelated to study drug: (1) traumatic fracture of femur (led to discontinuation) (2) traumatic epididymitis
Preliminary finding.

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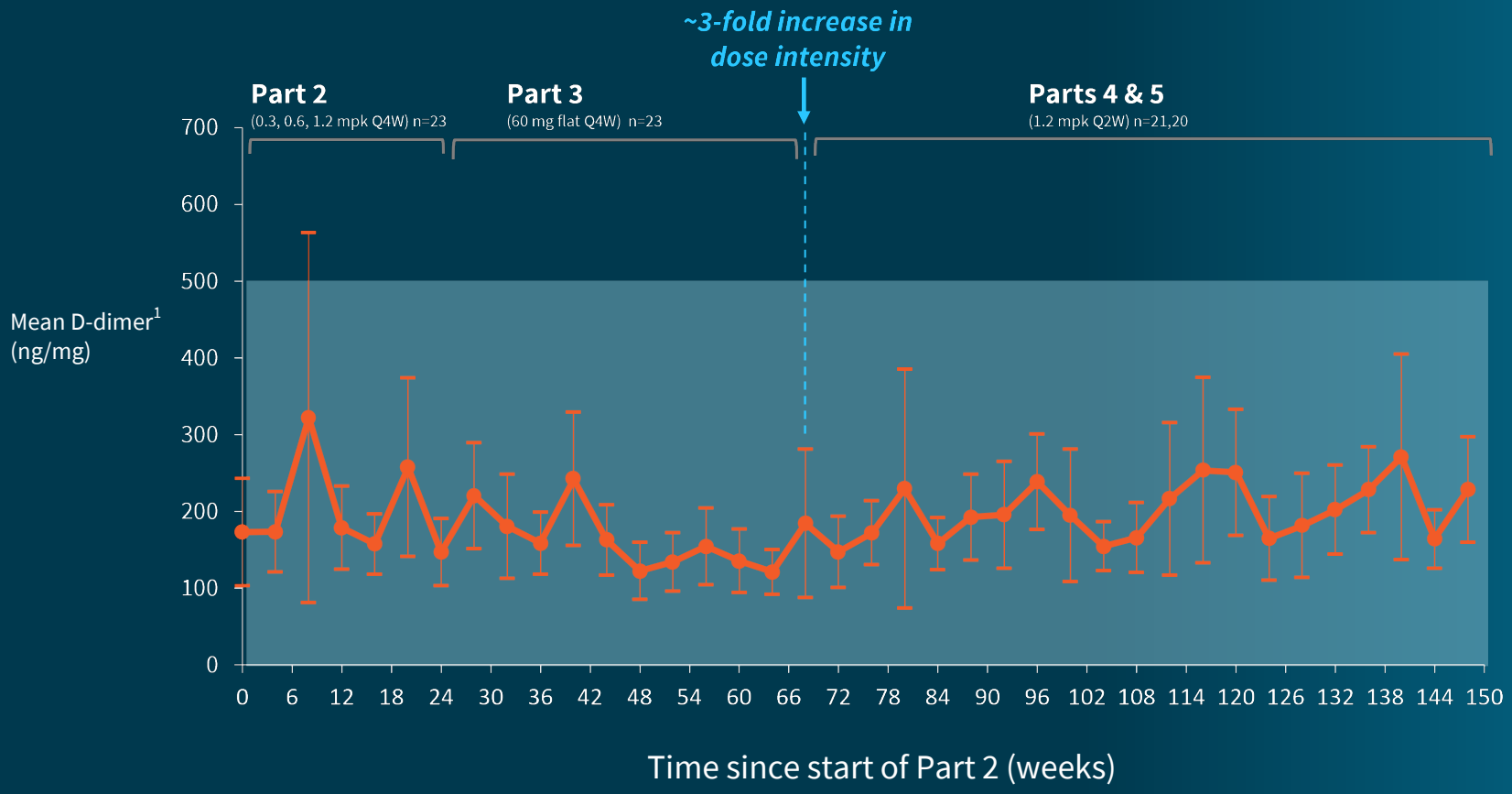
SerpinPC's Potential for Differentiated Safety Profile



- **No observation of thrombosis to date**[2]
  No observations of treatment-related, non-transient elevations in D-dimer across study[2]
- **For Part 5, 96% of D-dimer results were <500 ng/ml** [2]

1. Error bars represent 95% confidence interval. Note: Values from three instances of trauma, cancer and infection determined to represent explained D-dimer elevation and omitted from calculation (Subject 200-012 traumatic hip bleed, week 68 and 72; Subject 300-041 rectosigmoid cancer, Weeks 60-98; Subject 300-032 periodontitis, weeks 128 to 1301. 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 Ongoing Global Registrational Studies for Hemophilia B

PRESent-2

Hemophilia B without inhibitors (n = 120)

Primary Endpoint: ABR at 24 weeks

PRESent-3

Hemophilia B with inhibitors (n ≥ 12)

Primary Endpoint: ABR at 24 weeks

73 SITES
18 COUNTRIES

ABR is annualized bleeding rate. Primary endpoint is the rate of treated bleeds (expressed as ABR) during the first 24 weeks of treatment with SerpinPC (Part 2 of PRESent-2) compared to the observation period. Interim Analysis for Part 1 of PRESent -2 Study expected in 2024. Additional information on the registrational program can be accessed at www.clinicaltrials.gov (NCT05605678, NCT05789524, NCT05789537).

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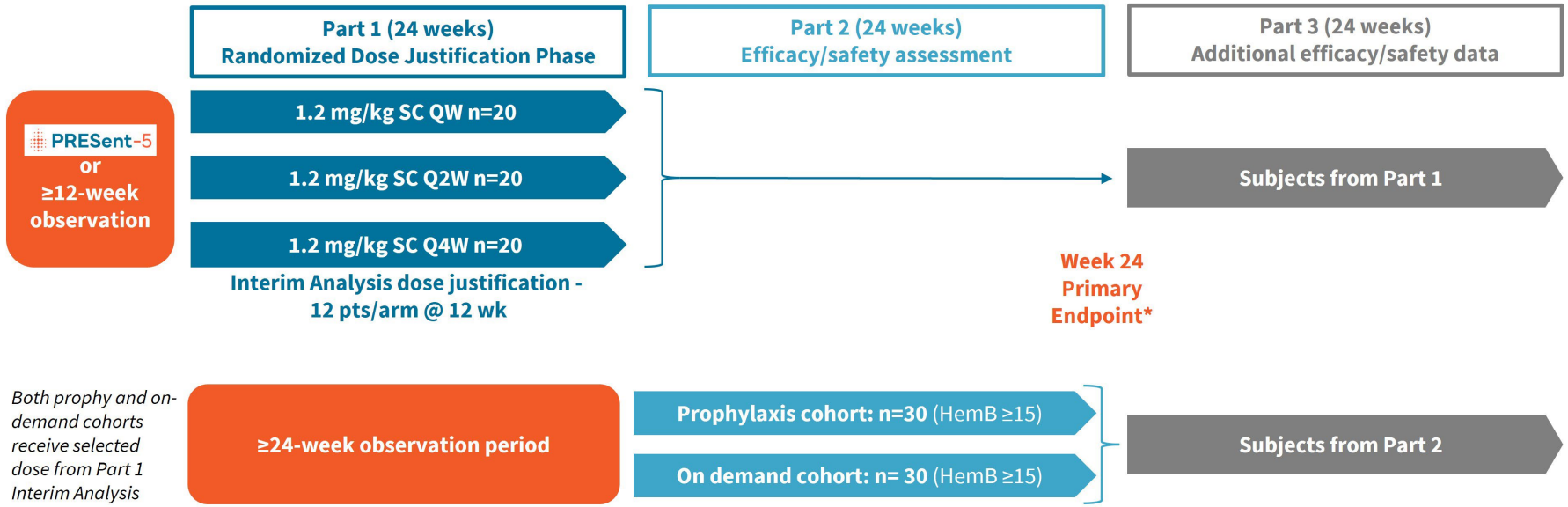
SerpinPC

Ongoing Global Registrational Studies for Hemophilia B

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

PRESent-2

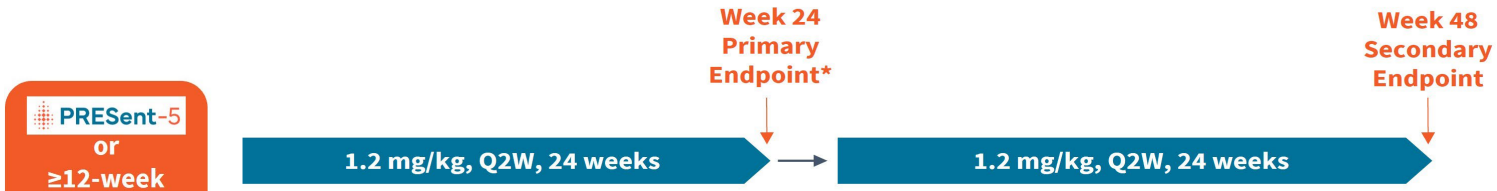
Hemophilia B without inhibitors (n=120) *Study to also include hemophilia A subjects to support safety database*



***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*

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Potential Multi-Billion-Dollar Market Opportunities

Hemophilia B **without** inhibitors

Hemophilia A

SerpinPC

Hemophilia B **with** inhibitors

Rare bleeding disorders

significant expansion opportunities

Evaluate Pharma Analyst Consensus for 2023.

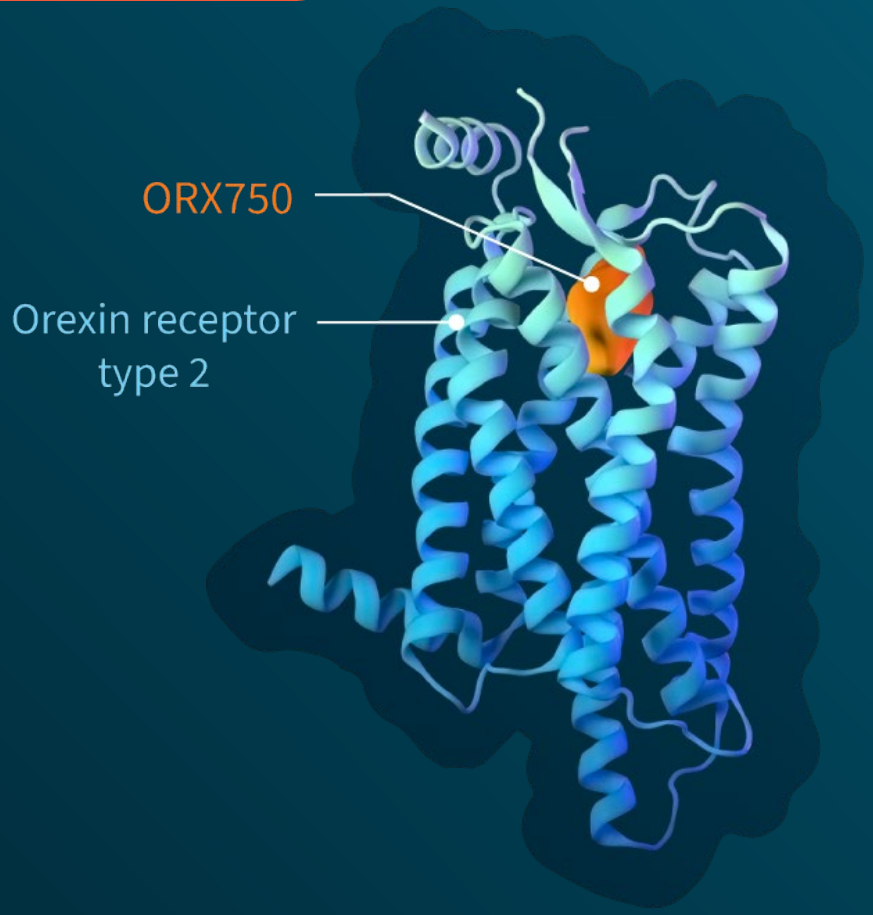
Hemophilia Program

Orexin Agonist Program

LockBody Technology Platform

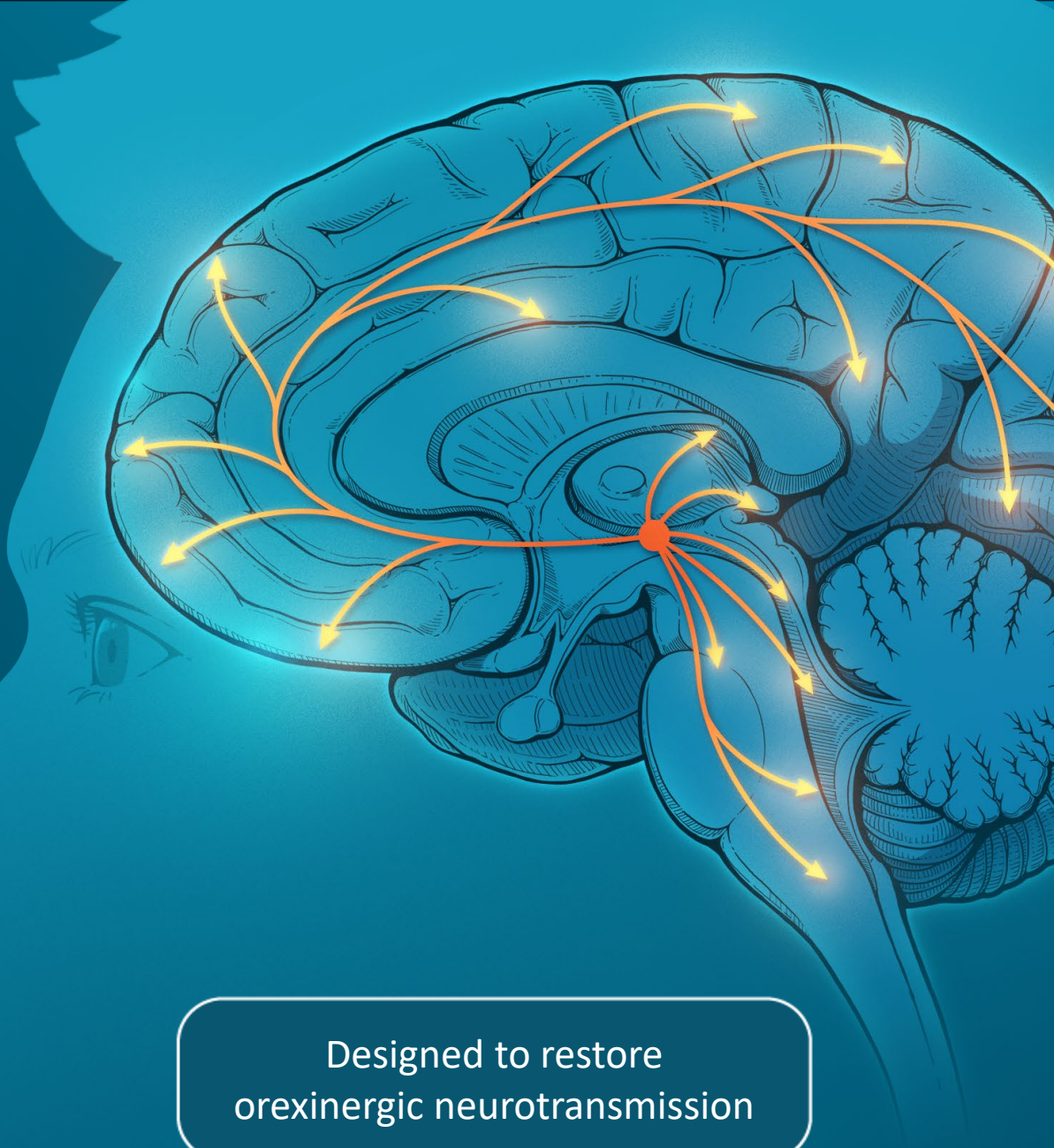
Orexin agonists have the potential to transform standard of care for individuals with sleep-wake disorders

MOA



ORX750

Highly potent, selective orexin receptor type 2 (OX2R) agonist



Designed to restore orexinergic neurotransmission

ORX750 a Potential Best-in-Class Oral OX2R Agonist for the Treatment of Narcolepsy and Other Sleep-Wake Disorders

Highly potent, selective, novel OX2R agonist that closely **mimics function of endogenous peptide**[1]

Achieved **maximal wake times** and **cataplexy suppression** in highly predictive, translational narcolepsy type 1 mouse models[1]

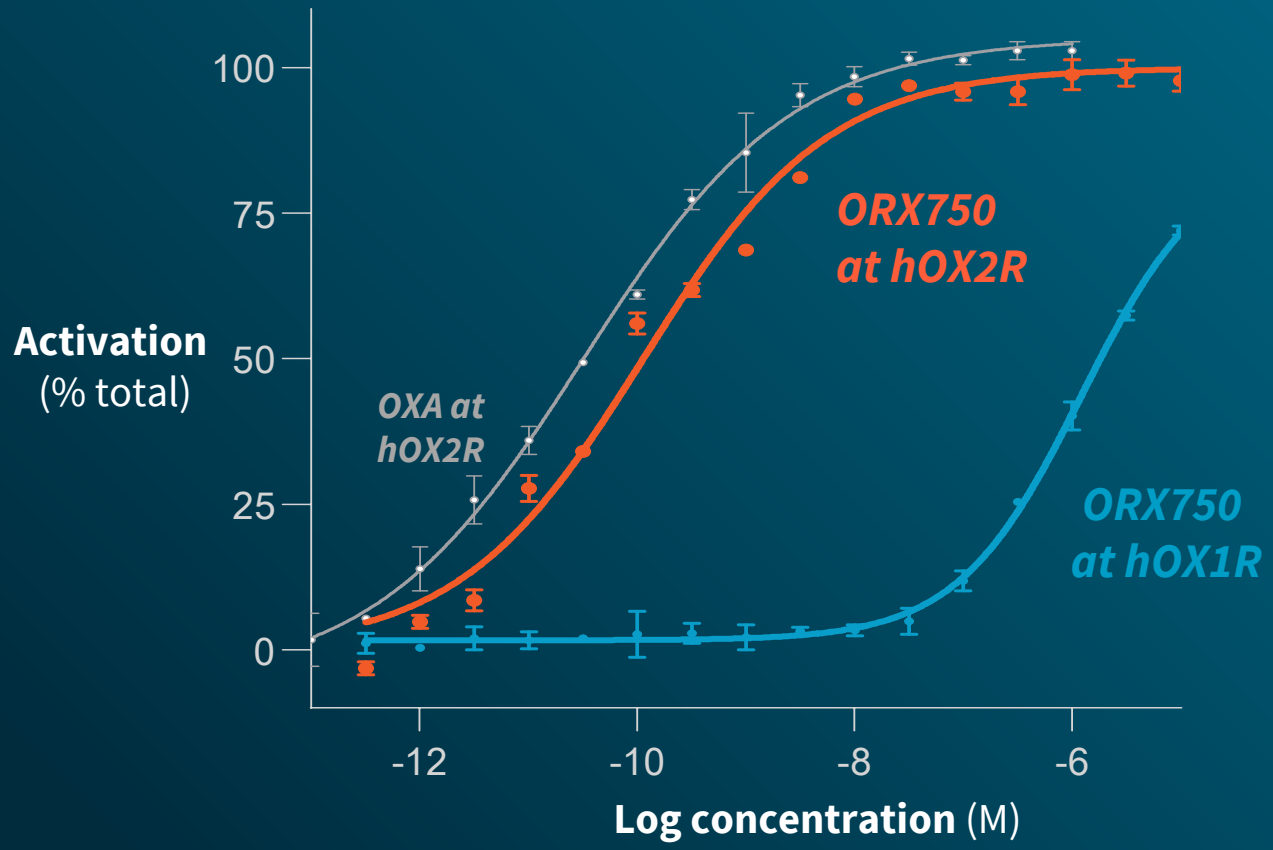
Preclinical data support potential **expansion** into **broader sleep-wake disorders**, including narcolepsy type 2 and idiopathic hypersomnia[1]

Investigational New Drug (IND) application open.

1. ORX750 preclinical data presentation at World Sleep Congress, Oct. 25, 2023. https://investors.centessa.com/static-files/7377defd-f7b4-49fe-8806-e86c31e8e5de.

PRECLINICAL DATA

ORX750 Showed High In Vitro Potency at OX2R and Selectivity vs. OX1R



***EC_{50} 0.11 nM** for hOX2R*

***9,800-fold selectivity** vs. hOX1R*

- Activation pattern was indistinguishable from OXA with lack of biased agonism[1]
- No significant differences in OX2R potency were observed across species[2]
- No significant pharmacological activity observed in GPCR selectivity and in vitro safety panels[3]

Fluorescent imaging plate reader (FLIPR) assay with Chinese hamster ovary (CHO) cells stably expressing recombinant human OX1R or OX2R; OXA EC50 at hOX2R = 0.035 nM; ORX750 EC50 at hOX1R = 1100 nM.

1 Pathhunter β-arrestin recruitment assay with CHO cells co-expressing ProLink™ (PK)-tagged OX2R and Enzyme Acceptor (EA)-tagged β-arrestin.

2 HumSafetyan, mouse, rat, dog, monkey recombinant receptors *in vitro.*

3 Safety 47 and GPCRMax168 from >60 receptor families.

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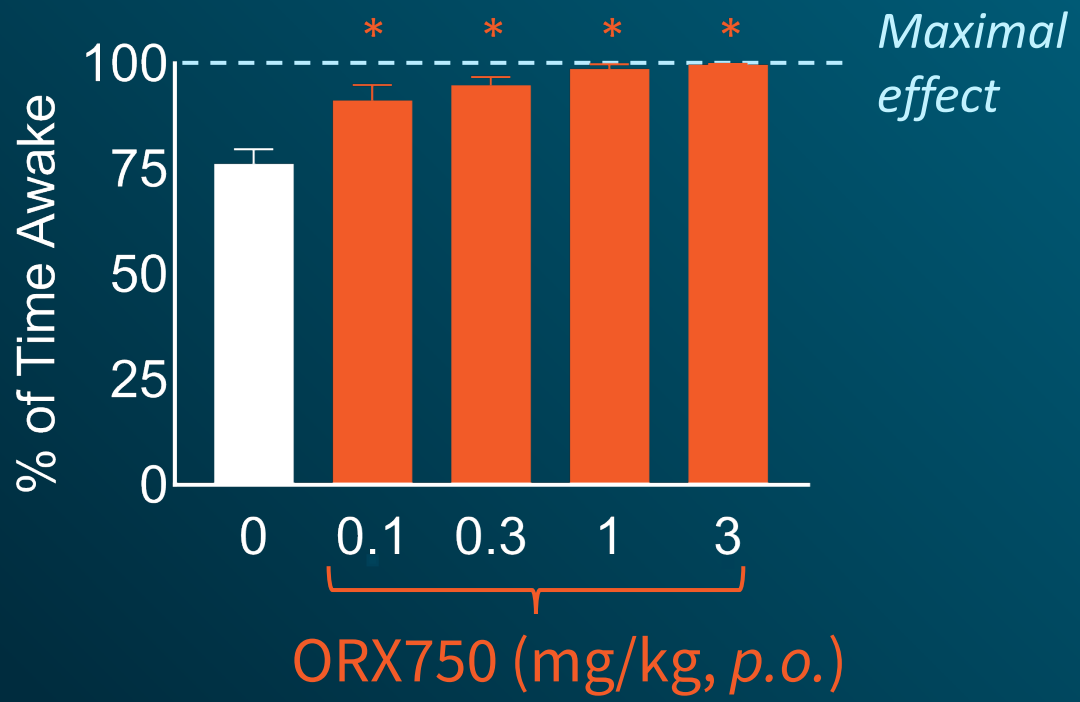
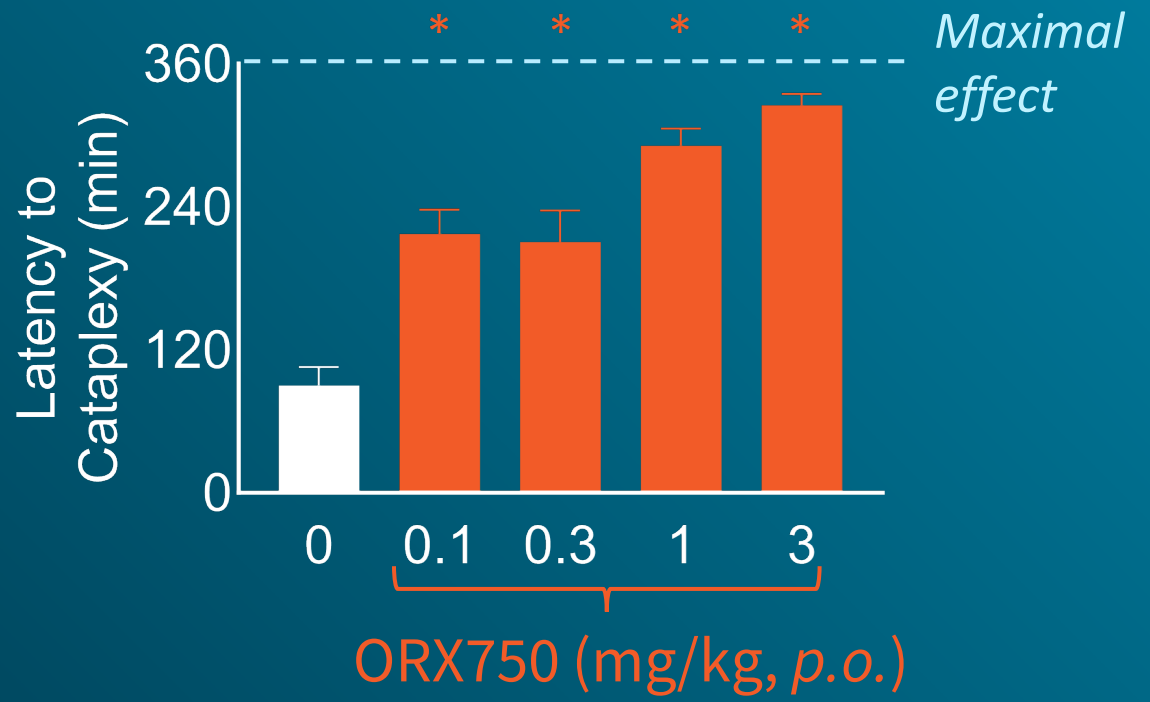
PRECLINICAL DATA

ORX750 Increased Wakefulness and Suppressed Cataplexy in NT1 Mice

Wakefulness



Latency to Cataplexy



NT1 is Narcolepsy Type 1.
% of Time Awake refers to time spent awake in the first 3 hours after oral dosing.
ORX750 preclinical data presentation at World Sleep Congress, Oct. 25, 2023. NT1 model shown is orexin/tTA;tetO diphtheria toxin fragment A (DTA) mice. Age at first dose 23-27 wks (7 wks after removal of doxycycline chow); 16 males used; EEG, EMG recorded using intraperitonially implanted telemeters with video and manually scored in 10-sec epochs; dosing at start of dark period (active phase). *For all doses $p < 0.05$ vs. 0 mg/kg, Holm-Sidak multiple comparisons test following repeated-measures analysis of variance in counterbalanced design.

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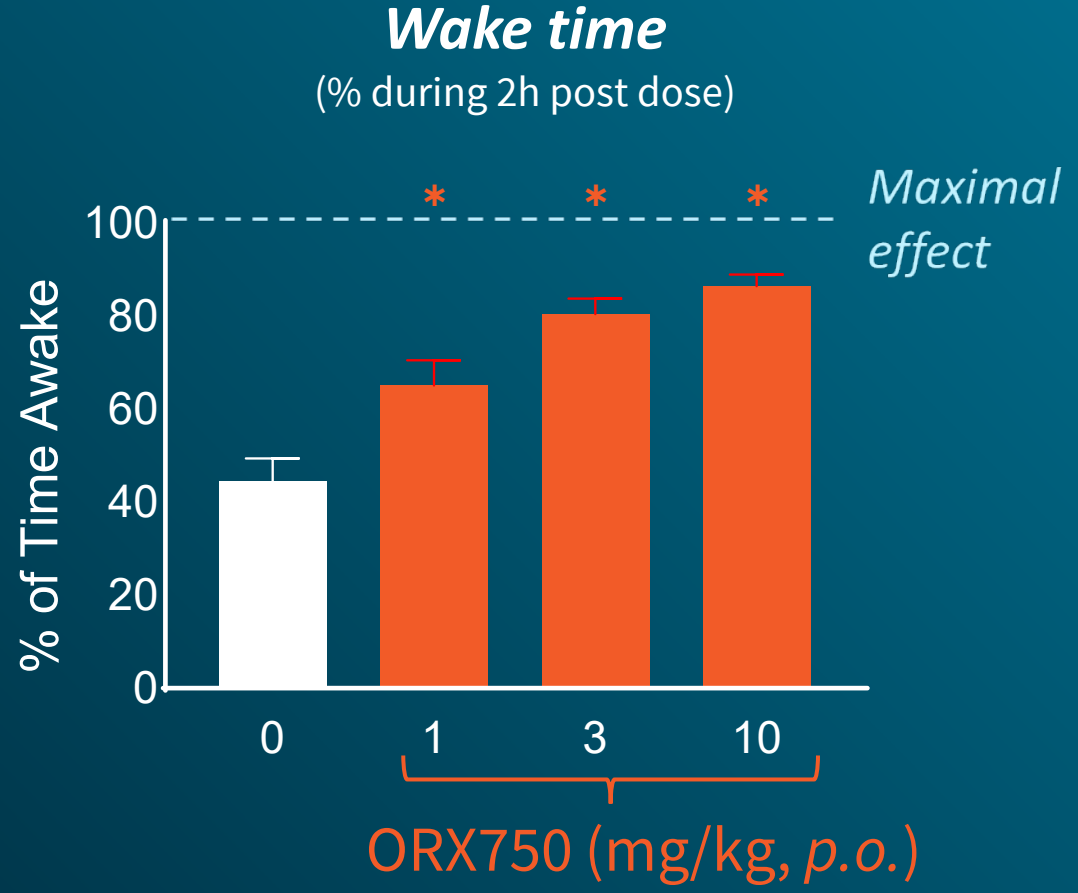
PRECLINICAL DATA

ORX750 Increased Wakefulness in Wild Type (WT) Mice



- In WT mice *(ie: orexin system is intact and functional)*, wake time increased at **≥ 1 mg/kg** (lowest dose tested)

Data collected using PiezoSleep, in which wakefulness readouts based on movement & breath rate highly correlate with EEG/EMG measures (Black, et al., ESRS2022 presentation). Age at first dose was 16-20 wks in male C57BL/6J mice; mice dosed at 5 h after lights on * $p < 0.05$ vs. 0 mg/kg, Holm-Sidak multiple comparisons test following RM-ANOVA in counterbalanced design.

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IND OPEN

ORX750 First-in-Human Healthy Volunteer (HV) PoC Study

Phase 1 clinical study of ORX750:

- Evaluate the safety, tolerability and pharmacokinetics (PK) of single-ascending and multiple-ascending doses in healthy adult subjects

  In parallel

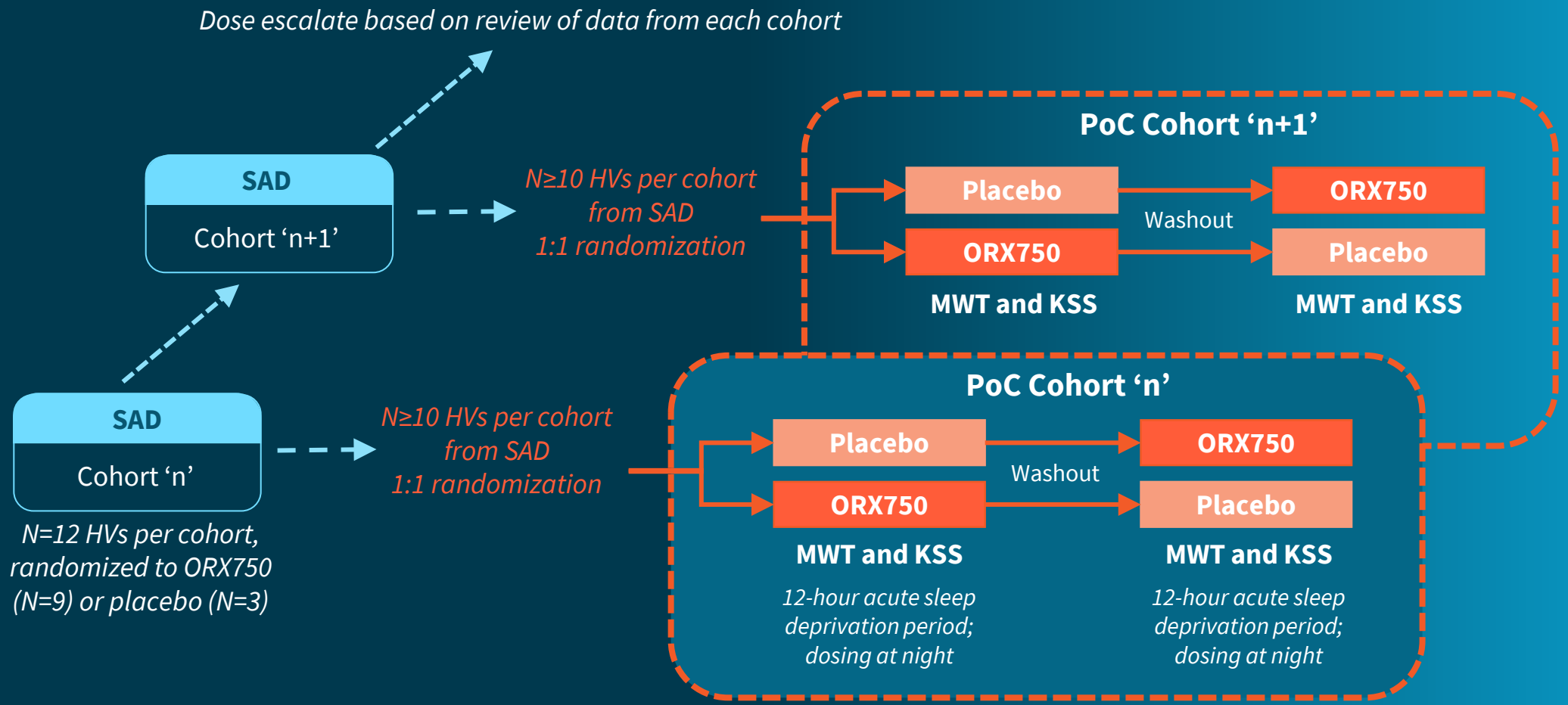
- A cross-over PoC portion of the study to assess pharmacodynamics (PD) using the **Maintenance of Wakefulness Test (MWT)** and **Karolinska Sleepiness Scale (KSS)** in acutely sleep-deprived healthy adult subjects

The Phase 1 study has a maximum exposure limit specified by the FDA which the company believes significantly exceeds the predicted efficacious doses of ORX750 in indications associated with or without orexin loss.

HV PoC DESIGN

SAD Combined with HV Acutely Sleep-Deprivation PoC Study

PoC cohorts to assess pharmacodynamic (PD) effects of ORX750 by measuring sleep latency with the **Maintenance of Wakefulness Test (MWT)** and subjective sleepiness with the **Karolinska Sleepiness Scale (KSS)** in acutely sleep-deprived healthy subjects



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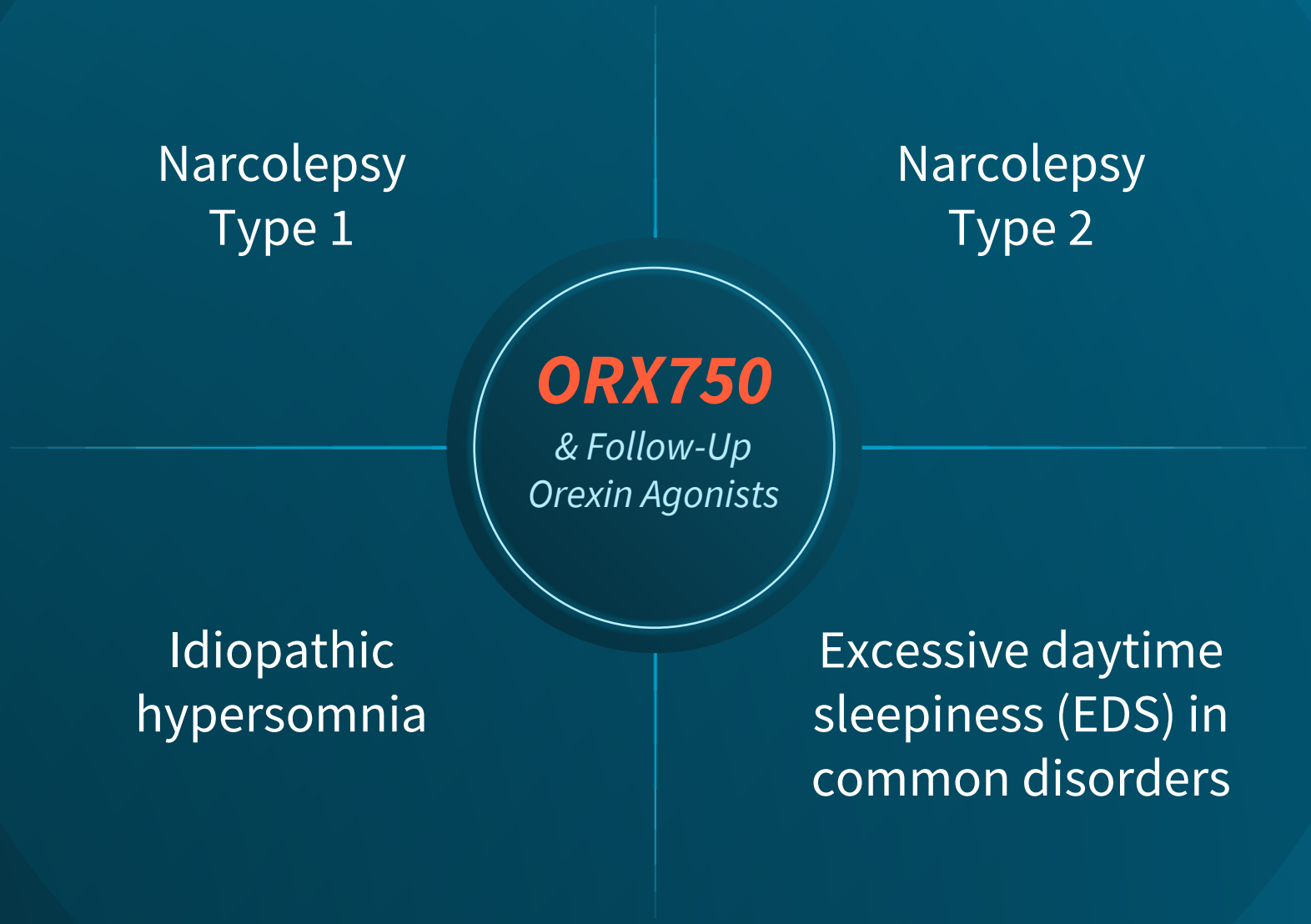
ORX750 Clinical PoC data in sleep-deprived healthy volunteers expected in 2H of 2024

Potential Multi-Billion-Dollar Market Opportunities



Evaluate Pharma Analyst Consensus for 2023 and UpToDate.

Hemophilia Program

Orexin Agonist Program

LockBody Technology Platform

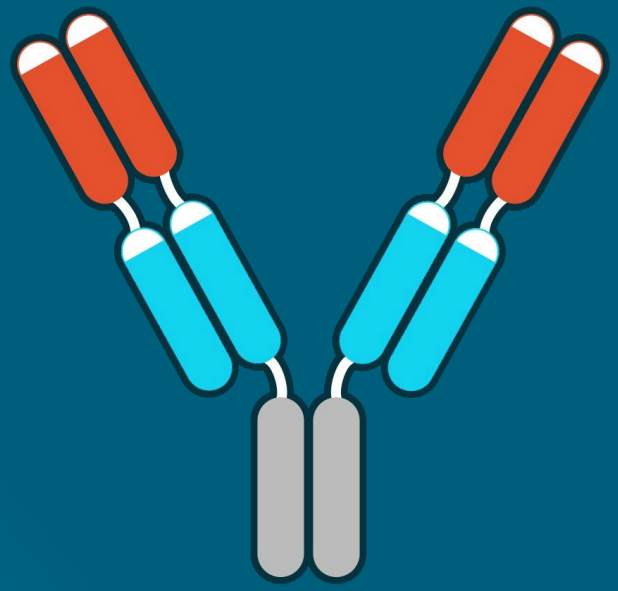
***LockBody* Technology Platform aims to *redefine* immuno-oncology treatment**

- **Novel pharmacology** combining tumor enrichment with activation of effector function
- Designed as **single agent** systemic treatment
- Potential **wide therapeutic index**[1]

LB101 is an investigational agent that has not been approved by the FDA or any other regulatory authority. Information on the Phase 1/2a trial of LB101 can be accessed at www.clinicaltrials.gov (NCT05821777). 1. LB101 *in-vivo* preclinical data: MC38 hPD-L1+ syngeneic model in mouse, and in non-human primates where LB101 was delivered IV at 5, 20, 50mg/kg (q7d x 4).

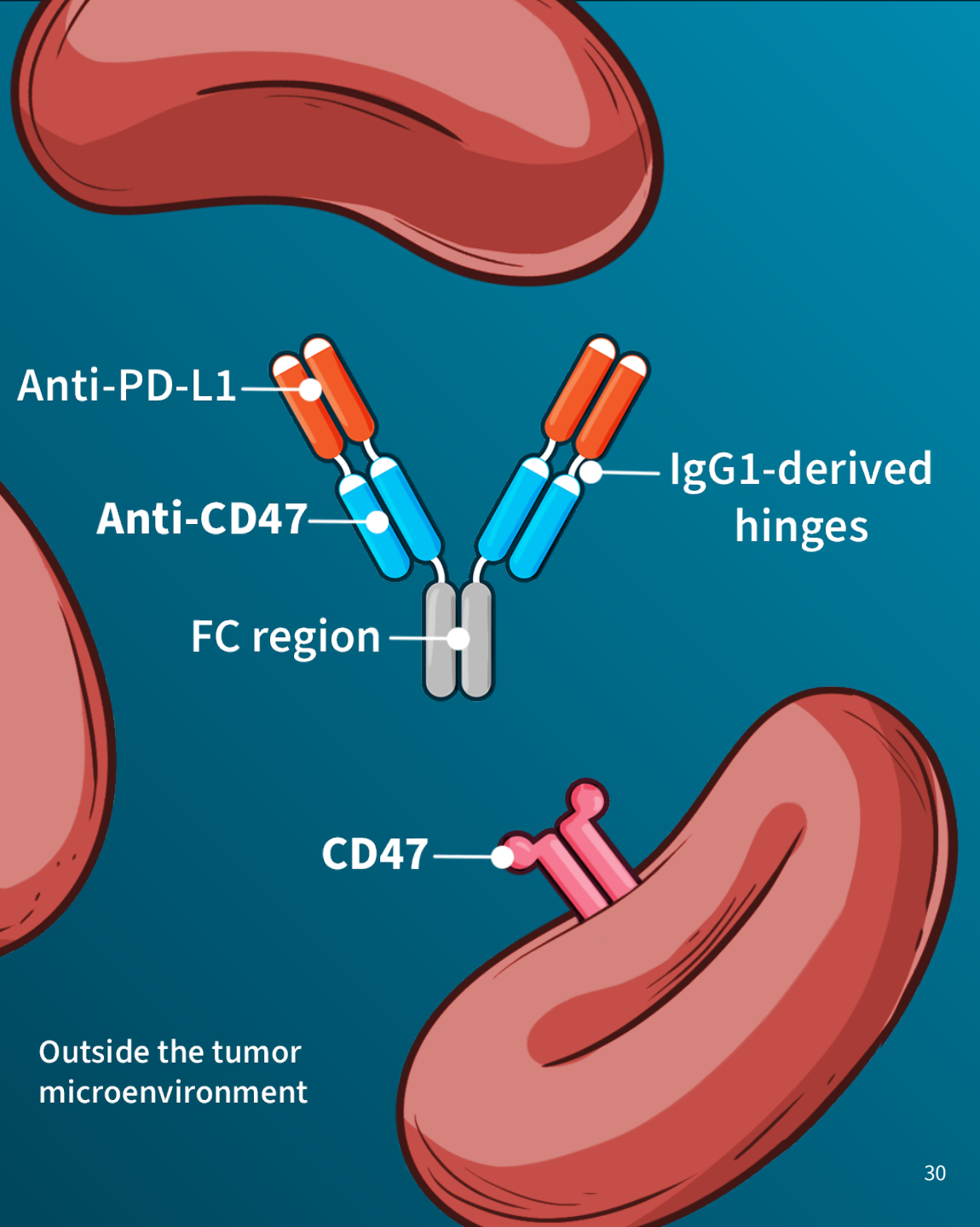
MOA

Locked Configuration



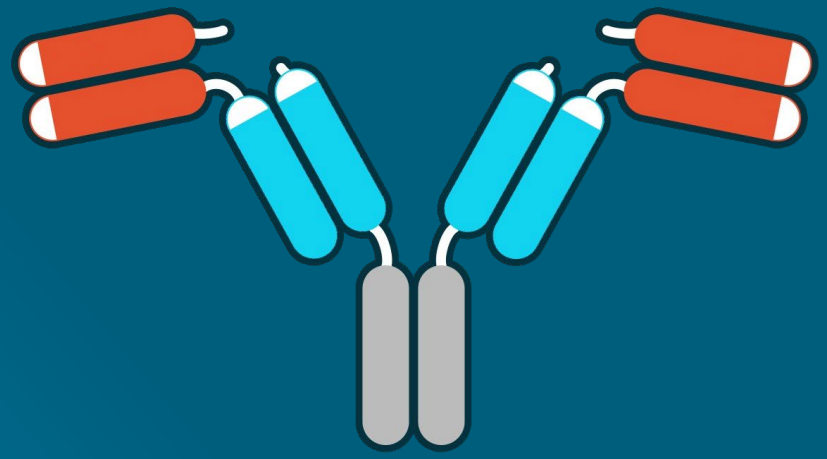
LockBody LB101

Conditionally tetravalent PD-L1xCD47 bispecific monoclonal antibody



MOA

Unlocked Configuration



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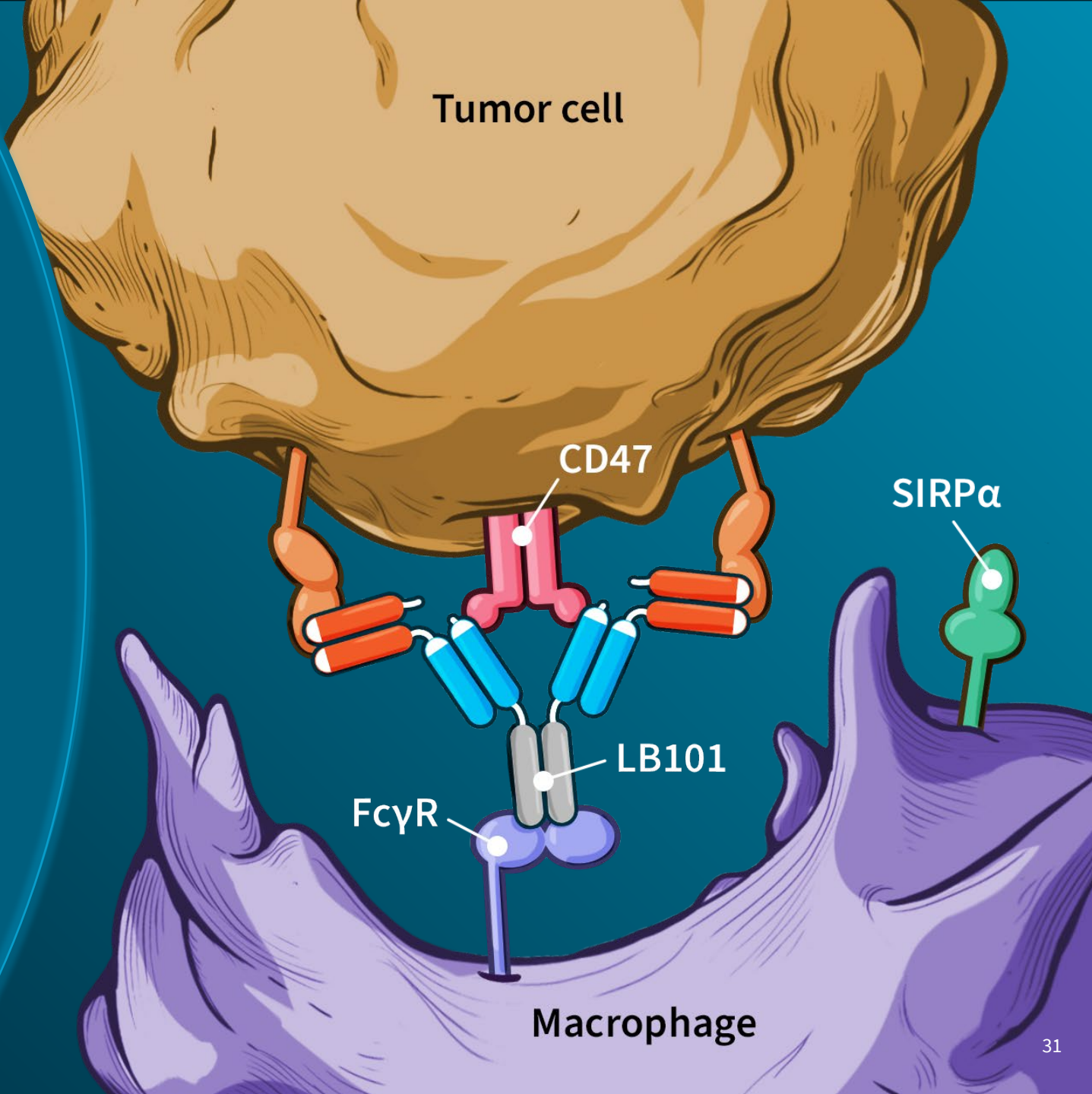
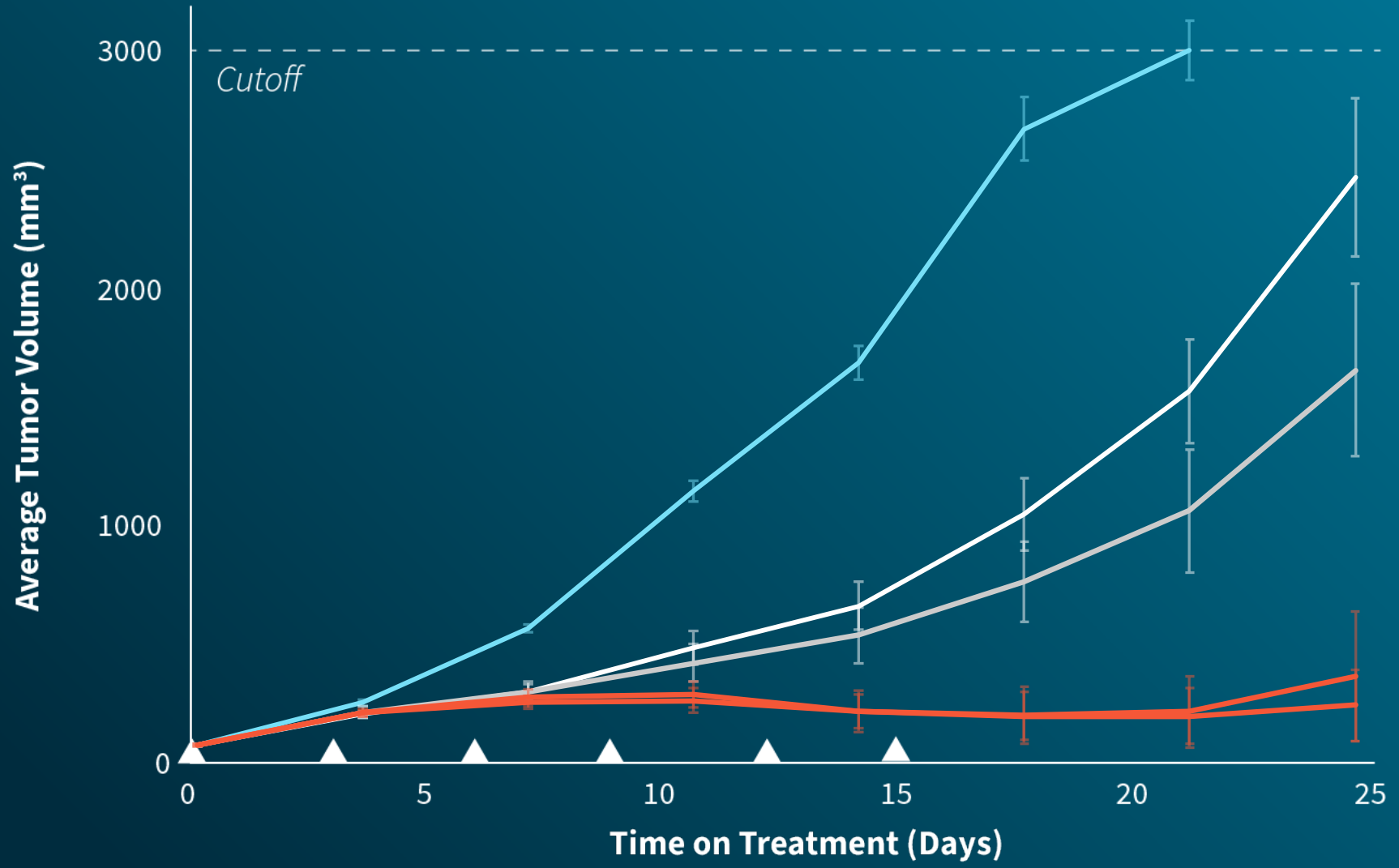


PRECLINICAL DATA

Significant Tumor Regression Observed In-Vivo with LB101



IgG1 isotype control
0/16 regressed

Atezolizumab 5 mg/kg
1/16 regressed

Atezolizumab 10 mg/kg
3/16 regressed

LB101 8.5 mg/kg
14/16 regressed

LB101 17 mg/kg
12/16 regressed

CENTESSA PHARMACEUTICALS

Source: *In vivo*- 5 mg/kg of atezolizumab is equivalent to 8.5 mg/kg of LB101. Data presented at ASCO in June 2022. https://investors.centessa.com/static-files/2f9bffb4-97a6-4320-8885-70f12aa4d036. MC38 hPD-L1+ syngeneic model in mouse. Triangles indicate dosing schedule.

PRECLINICAL DATA

Observed to be Well Tolerated in Non-Human Primates (NHPs) with LB101 Doses up to 50mg/kg

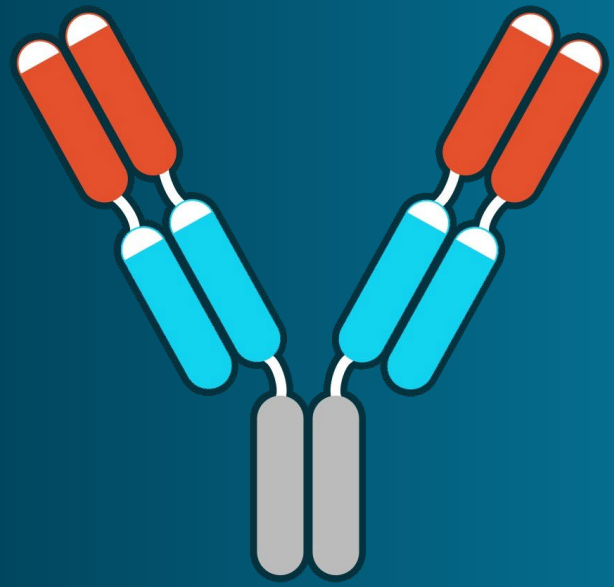
No anemia/ thrombocytopenia

No weight loss

No change in red blood cell or hemoglobin

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

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



CENTESSA PHARMACEUTICALS

2024 Driving Momentum

ANTICIPATED MILESTONES

HEMOPHILIA PROGRAM

SerpinPC

Registrational study interim analysis expected in **2024**

OREXIN AGONIST PROGRAM

ORX750

Clinical PoC data in healthy volunteers expected in **2H of 2024**

LOCKBODY TECHNOLOGY PLATFORM

LB101

Phase 1/2 study **ongoing**

OUR MISSION

Discovering and developing medicines that are transformational for patients

- Multiple potential blockbuster assets
- Ongoing momentum in 2024 with clinical milestones anticipated across our most advanced programs
- Strong balance sheet

CENTESSA PHARMACEUTICALS

Centessa reported $256.5 million in cash, cash equivalents and short-term investments as of December 31, 2023.

CENTESSA

PHARMACEUTICALS