CENTESSA PHARMACEUTICALS

Corporate Overview

September 26, 2024

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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

CENTESSA PHARMACEUTICALS

Centessa reported $294.8 million in cash, cash equivalents and short-term investments as of June 30, 2024. In addition, Centessa received approximately $242.7 million in aggregate net proceeds from a public offering of ADSs in September 2024. Cash runway estimated into mid-2027.

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

ASSET	DISEASE/CONDITION	MECHANISM
SerpinPC	**Hemophilia B**	Activated Protein C Inhibitor
ORX750	**Sleep-Wake Disorders** *NT1, NT2 & IH*	Orexin Receptor 2 (OX2R) Agonist
ORX142	**Excessive Daytime Sleepiness (EDS)** *In neurological, neurodegenerative & psychiatric disorders**	Orexin Receptor 2 (OX2R) Agonist
LB101	**Solid Tumors**	PD-L1xCD47 LockBody®

Centessa has multiple early-stage assets not reflected on this slide. NT1 (narcolepsy type 1); NT2 (narcolepsy type 2); IH (idiopathic hypersomnia)
*Select neurological, neurodegenerative and psychiatric disorders with EDS.

2024 Driving Momentum

ANTICIPATED MILESTONES

OREXIN AGONIST PROGRAM

ORX750

Plan to rapidly advance into Phase 2 studies in patients with NT1, NT2, and IH beginning in **Q4 of 2024**

ORX142

IND-enabling studies ongoing

HEMOPHILIA PROGRAM

SerpinPC

PRESent-2 Part 1 interim analysis planned in **2024**; Part 1 data planned for **late 2024/early 2025**

LOCKBODY TECHNOLOGY PLATFORM

LB101

Phase 1/2 study **ongoing**

Orexin Agonist Program

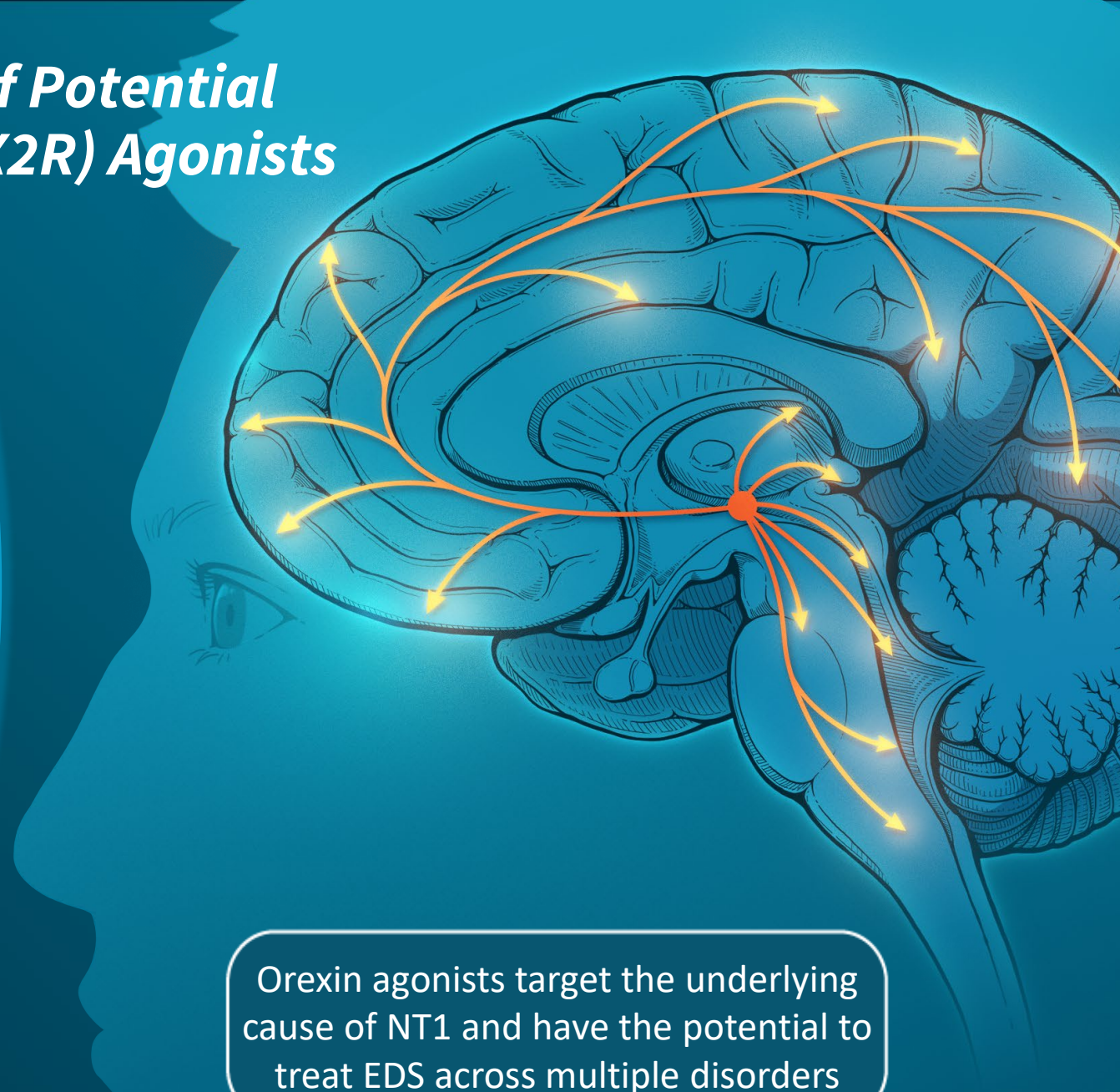
Hemophilia Program

LockBody Technology Platform

Orexin agonists have the potential to transform the standard of care for individuals with sleep-wake disorders and excessive daytime sleepiness (EDS) across select disorders

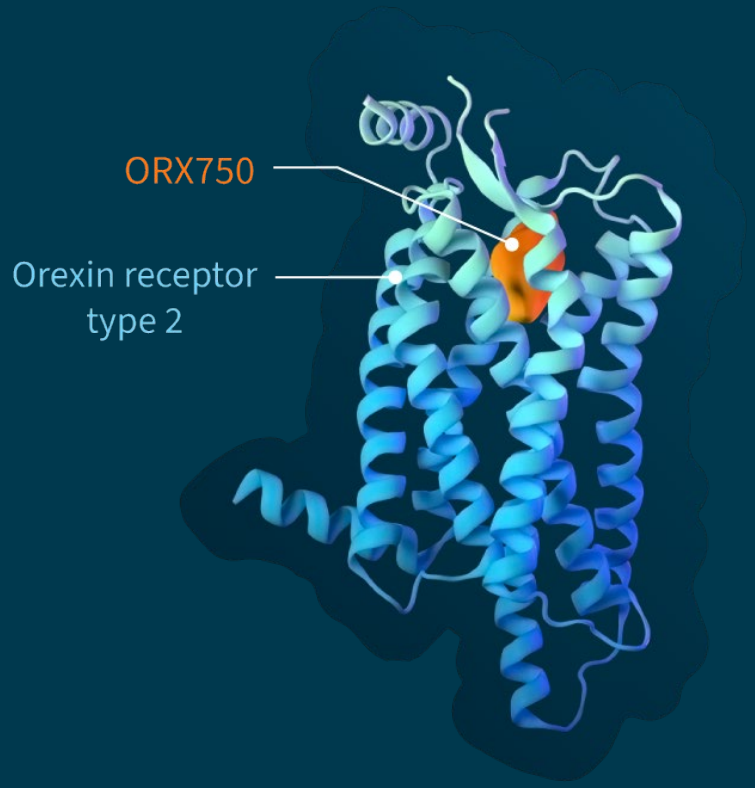
Centessa is Developing a Pipeline of Potential Best-in-Class Orexin Receptor 2 (OX2R) Agonists

- **ORX750** for the treatment of **NT1, NT2 and IH**
- **ORX142** for the treatment of **EDS in select neurological, neurodegenerative and psychiatric disorders**
- Earlier stage OX2R agonists and therapeutics for **additional potential indications**



Orexin agonists target the underlying cause of NT1 and have the potential to treat EDS across multiple disorders

ORX750 a Potential Best-in-Class Oral OX2R Agonist for the Treatment of Sleep-Wake Disorders (NT1, NT2 and IH)



ORX750

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

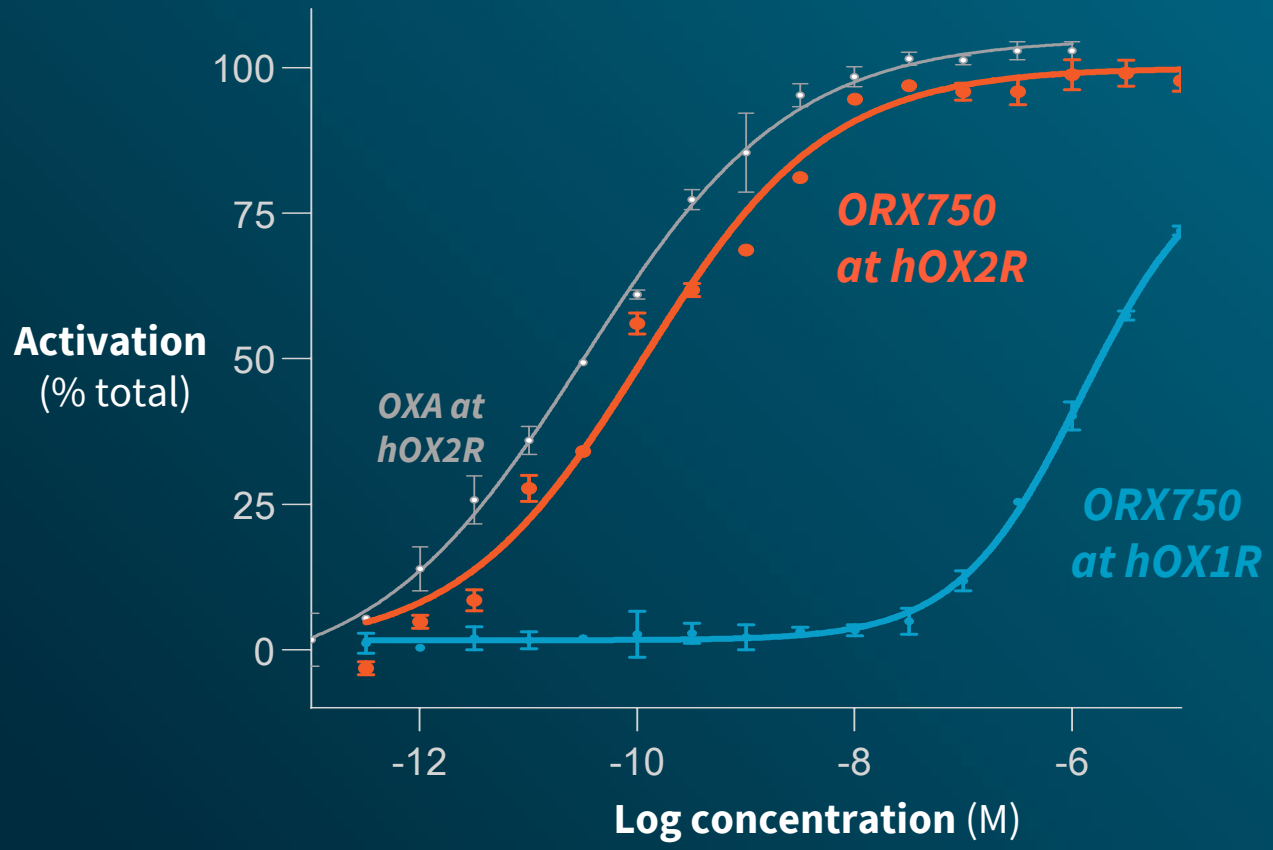
- Highly potent, selective, novel OX2R agonist with linear PK profile to support **once-daily, oral dosing** with rapid absorption[1]
- Shown to restore **normative wakefulness**[2] in acutely sleep deprived healthy volunteers with mean sleep latency of **32 mins (MWT)** at **2.5 mg dose**[1]
- **Favorable safety and tolerability profile;**[1] No observations of frequently reported on-target AEs associated with OX2R agonists, hepatotoxicity, visual disturbances or hallucinations, to date[1]

MWT is Maintenance of Wakefulness Test. Phase 1 Study is ongoing,

1. Interim Phase 1 study data reported September 10, 2024. Data cutoff date of August 26, 2024.
2. Doghramji K, et al., "A normative study of the maintenance of wakefulness test (MWT)." *Electroencephalogr Clin Neurophysiol* 1997; 103:554-62.

PRECLINICAL DATA

ORX750 is a Highly Potent and Selective OX2R Agonist



***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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PHASE 1 STUDY

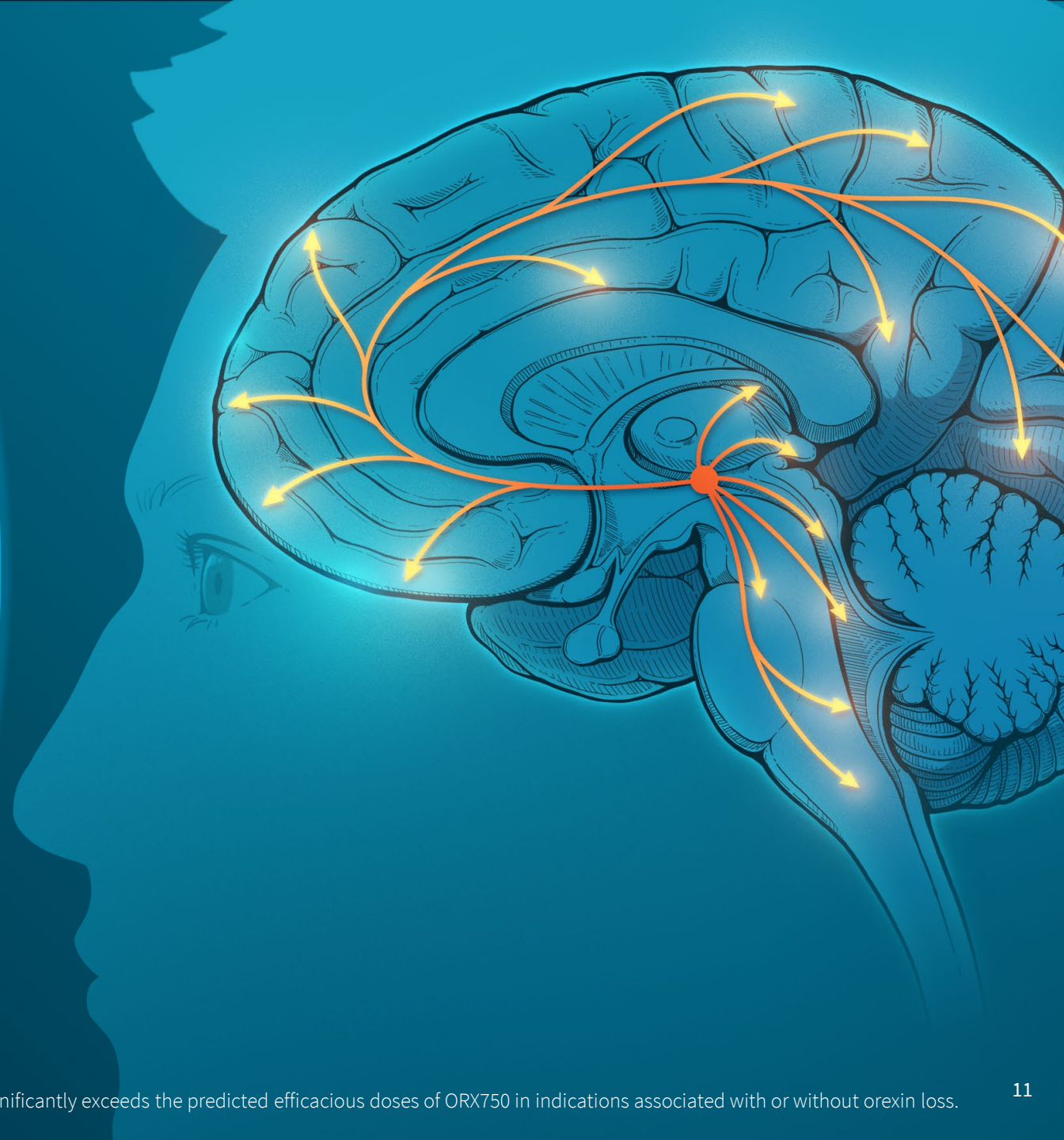
ORX750 First-in-Human Healthy Volunteer (HV) Study

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

- Efficacy assessments are being performed using the **Maintenance of Wakefulness Test (MWT)*** and **Karolinska Sleepiness Scale (KSS)** in acutely sleep-deprived healthy adult subjects

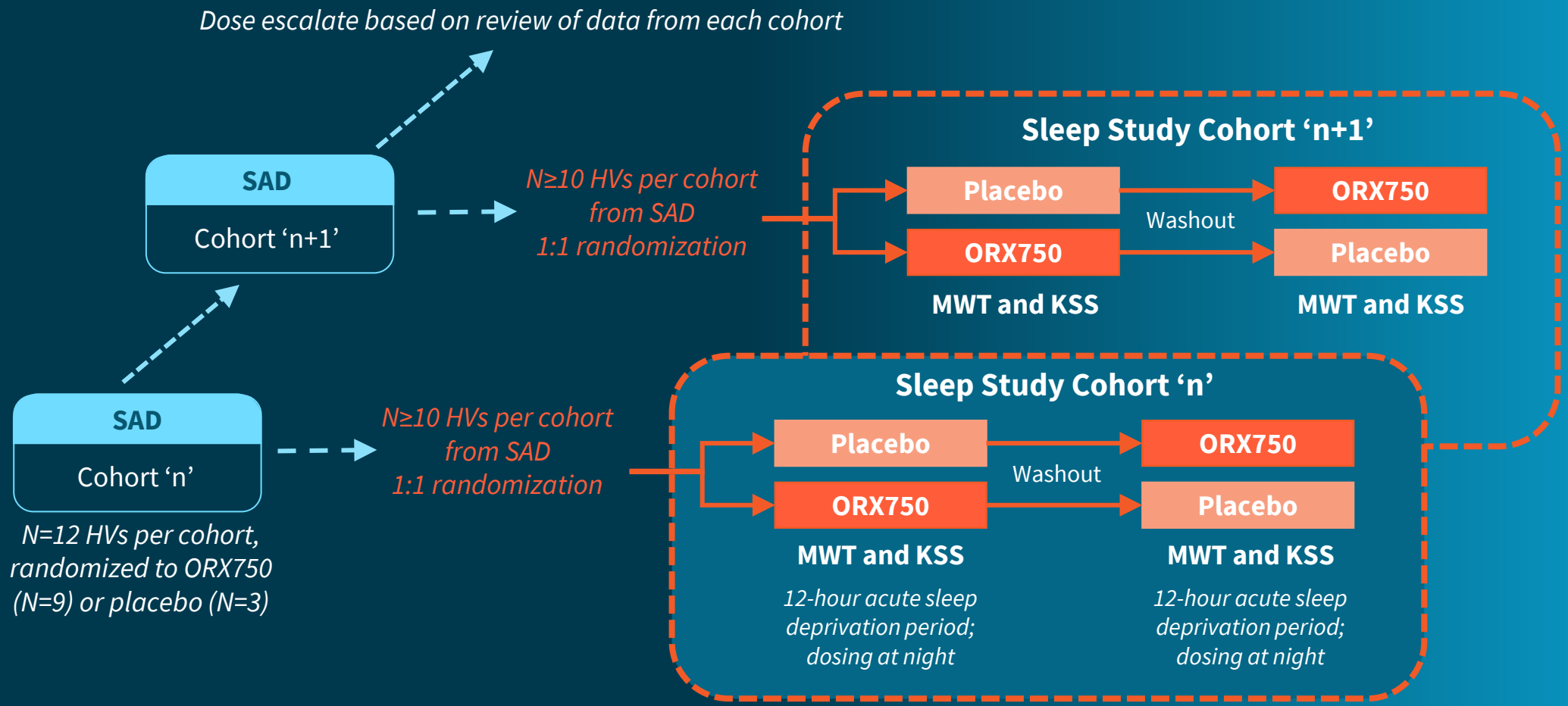


*MWT is an established registrational and objective endpoint in EDS in sleep-wake disorders.
The Phase 1 study has a maximum exposure limit specified by the FDA which the company believes significantly exceeds the predicted efficacious doses of ORX750 in indications associated with or without orexin loss.

PHASE 1 STUDY

SAD Combined with Efficacy Assessment in Acutely Sleep-Deprived HV

PoC-sleep study cohorts to assess efficacy 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



INTERIM PHASE 1

ORX750 Significantly Improved Mean Sleep Onset Latency (measured by MWT) at First Two Doses Compared to Placebo

	Post Dose LS Mean (95% CI) Sleep Onset Latency (Minutes)	LS Mean Difference Compared To Placebo In Mean Sleep Onset Latency (95% CI)	
		Estimate (95% CI)	*P-value*
ORX750 1.0 mg *(n=8)*	**17.6** (12.1, 23.2)	**8.1** (0.3, 15.9)	**0.04**
ORX750 2.5 mg *(n=8)*	**32.0** (22.2, 41.8)	**15.2** (4.7, 25.8)	**0.01**

- The 2.5 mg dose was shown to **restore normative wakefulness**[1] in acutely sleep-deprived healthy volunteers with mean sleep onset latency of **32 minutes** (MWT)
- Acutely sleep-deprived healthy volunteers who received a 2.5 mg dose of ORX750 showed a significant **1.6 point improvement** versus placebo in mean KSS score compared to baseline (p-value = 0.03)

Phase 1 study is ongoing. Interim data cutoff date of August 26, 2024. Least squares (LS) mean.
Consistent with the Phase 1 study design, a sleep study cohort (MWT) is optional at each SAD level, and as of the data cut off date, has been conducted only for 1 mg and 2.5 mg doses.
Mean sleep onset latency on the MWT (time to sleep onset over the four sessions performed at ~2, 4, 6, and 8 h after dosing at 11 p.m.; maximum 40 min per session).
1. Doghramji K, et al., A normative study of the maintenance of wakefulness test (MWT). *Electroencephalogr Clin Neurophysiol* 1997; 103:554-62.

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INTERIM PHASE 1

ORX750 Demonstrated a Favorable Safety and Tolerability Profile

	Placebo *(n=9)*	ORX750 1.0 mg *(n=9)*	ORX750 2.0 mg *(n=9)*	ORX750 2.5 mg *(n=9)*
Any TEAE, n (%)	**3 (33)**	**4 (44)**	**3 (33)**	**2 (22)**
Related	**2 (22)**	**1 (11)**	**2 (22)**	**1 (11)**
Nonrelated	**1 (11)**	**4 (44)**	**2 (22)**	**1 (11)**
Mild	**3 (33)**	**3 (33)**	**3 (33)**	**2 (22)**
Moderate	**0**	**1 (11)**	**0**	**0**
Severe	**0**	**0**	**0**	**0**
Leading to discontinuation	**0**	**0**	**0**	**0**
Serious TEAEs, n (%)	**0**	**0**	**0**	**0**
Most frequent drug-related TEAEs				
Dizziness	**1 (11)**	**1 (11)**	**0**	**0**
Nausea	**1 (11)**	**0**	**0**	**0**
Frequently reported AEs associated with other OX2R agonists				
Visual disturbances	**0**	**0**	**0**	**0**
Hepatotoxicity	**0**	**0**	**0**	**0**
Insomnia	**0**	**0**	**0**	**0**
Urinary frequency/urgency	**0**	**0**	**0**	**0**
Blood pressure increased	**0**	**0**	**0**	**0**

- No observations of frequently reported on-target AEs associated with OX2R agonists (i.e., urinary frequency/urgency, insomnia, etc.)
- No cases of hepatotoxicity, visual disturbances or hallucinations were observed
- No clinically meaningful, treatment-emergent changes in hepatic and renal parameters, vital signs or electrocardiogram (ECG) parameters

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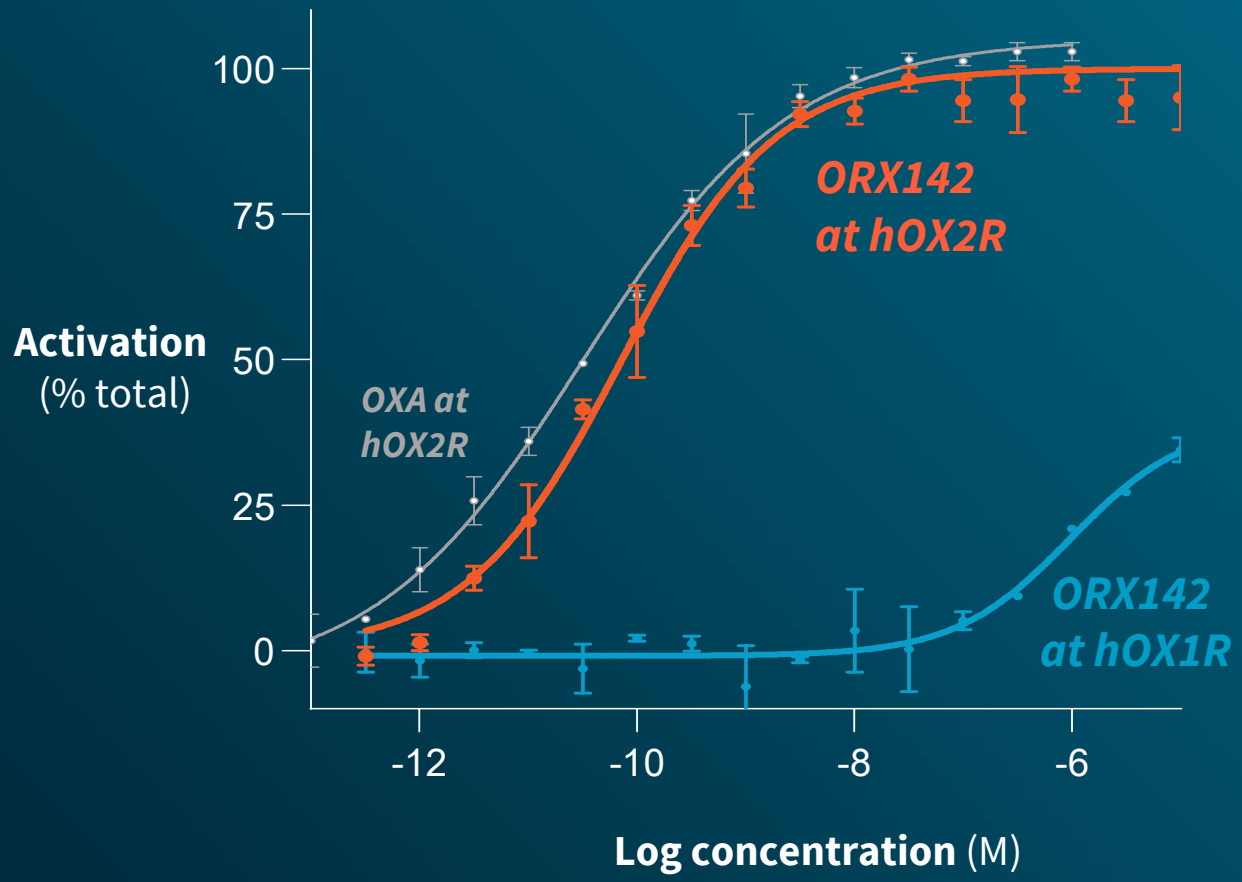
Phase 1 Study is ongoing. Interim data cutoff date of August 26, 2024. Treatment-emergent adverse event (TEAE). Includes safety data from SAD cohorts. Safety data from Sleep Study Cohorts was consistent with SAD. Nonrelated includes unlikely related and not related. Related includes probably and possibly related.

PRECLINICAL DATA

ORX142 Demonstrated High In Vitro Potency and Selectivity



***EC_{50} 0.069 nM** for hOX2R*

***> 13,000-fold selectivity** vs. hOX1R*

- Activation pattern was comparable to 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; ORX142 EC50 at hOX1R = 930 nM.

1 Calculated from FLIPR Ca2+ mobilization and Pathhunter β-arrestin recruitment assays

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

3 SAFETYscan47, gpcrMAX, Drug Abuse Potential Panel, Comprehensive In vitro Proarrhythmia Assay (CiPA) representing > 400 assays

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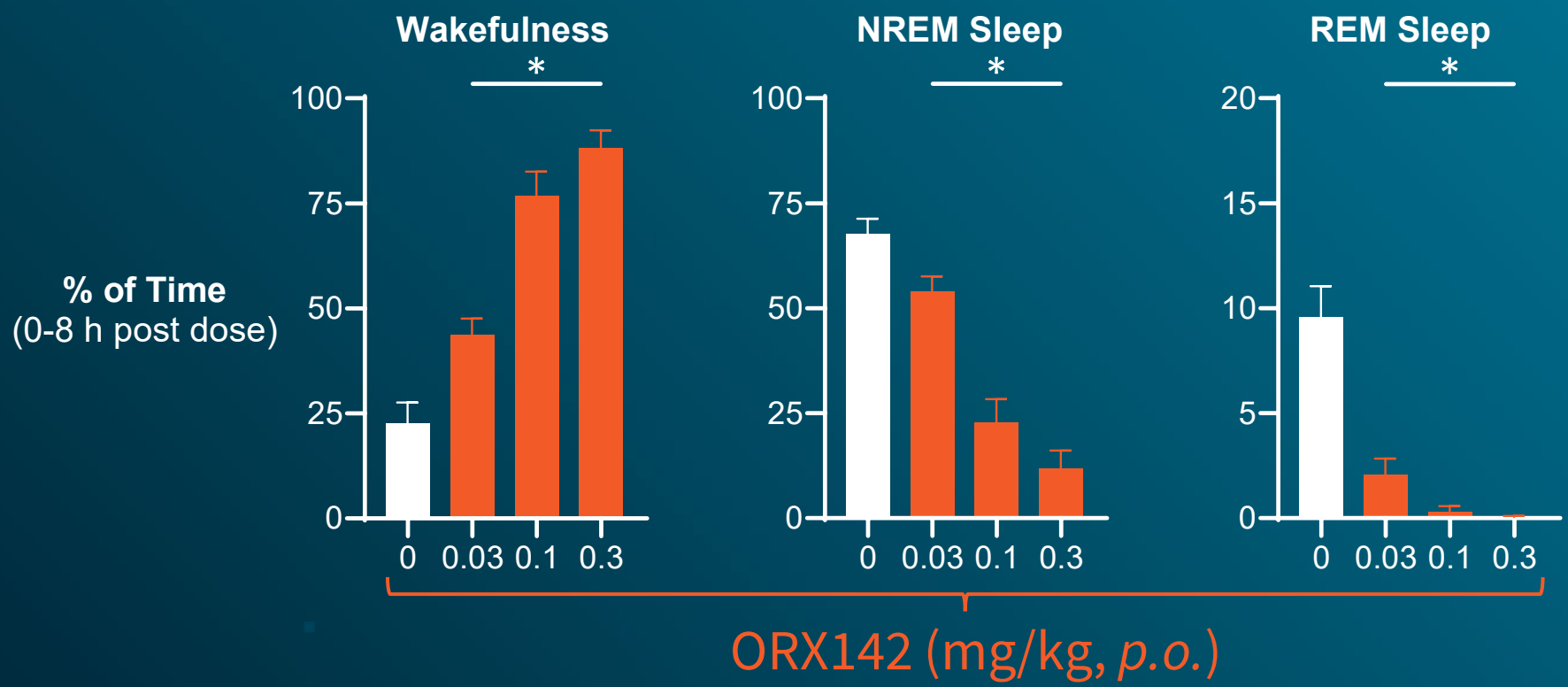
PRECLINICAL DATA

ORX142 Increased Wakefulness and Decreased NREM and REM Sleep in non-human primates (NHPs)



In marmosets wake time increased at **≥ 0.03 mg/kg** (lowest dose tested)

ORX142 preclinical data presentation at the European Sleep Research Congress, September 26, 2024. 4 males and 3 females used; EEG, EMG recorded using intraperitonially implanted telemeters and manually scored in 10-sec epochs; dosing 30 min prior to start of dark period (rest phase). NREM sleep includes all substages of NREM sleep for simplicity. *For all doses $p < 0.05$ vs. 0 mg/kg, Holm-Sidak multiple comparisons test following repeated-measures analysis of variance in counterbalanced design.

Building a Multi-Asset Orexin Agonist Franchise

ORX750

Sleep-Wake Disorders

NT1, NT2 & IH

$5B+

potential market opportunity

ORX142

Excessive Daytime Sleepiness (EDS)

select neurological, neurodegenerative and psychiatric disorders

$10B+

potential market opportunity

Centessa's orexin pipeline also includes earlier stage orexin agonists and therapeutics

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Source: Evaluate Pharma 2030 projected sales for narcolepsy – sales are not risk adjusted; projections for EDS in other disorders based on internal market research

Plan to rapidly advance ORX750 into Phase 2 studies in patients with NT1, NT2 and IH beginning in Q4 of 2024

ORX142 in IND-enabling studies

Orexin Agonist Program

Hemophilia 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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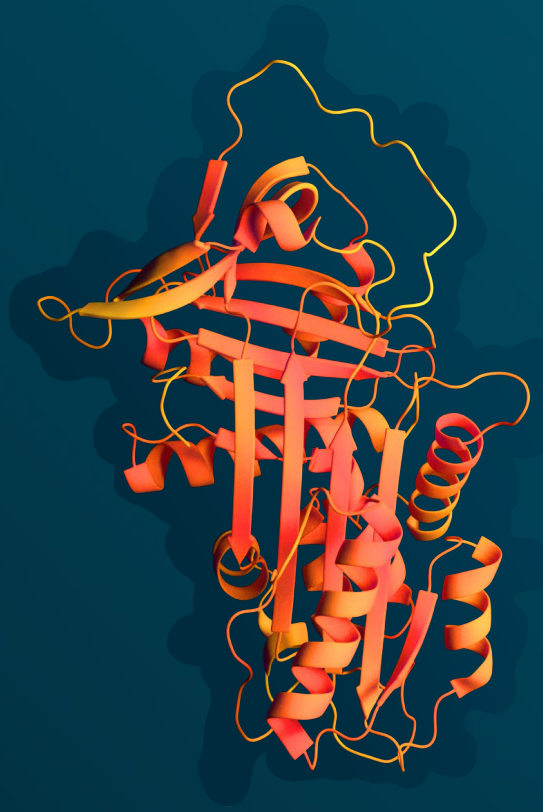
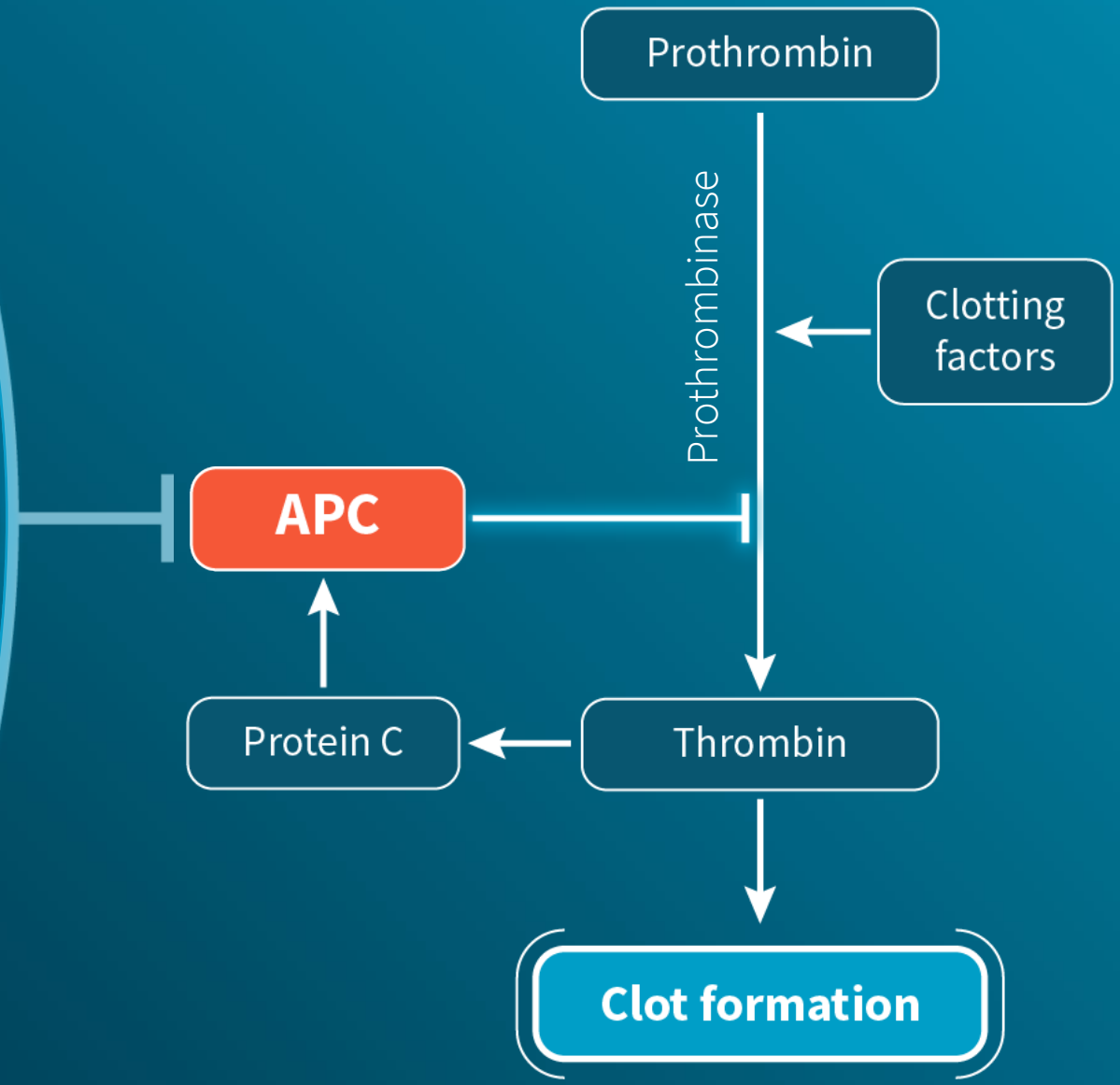
SerpinPC: Novel Approach Designed to Prevent and Reduce Bleeding



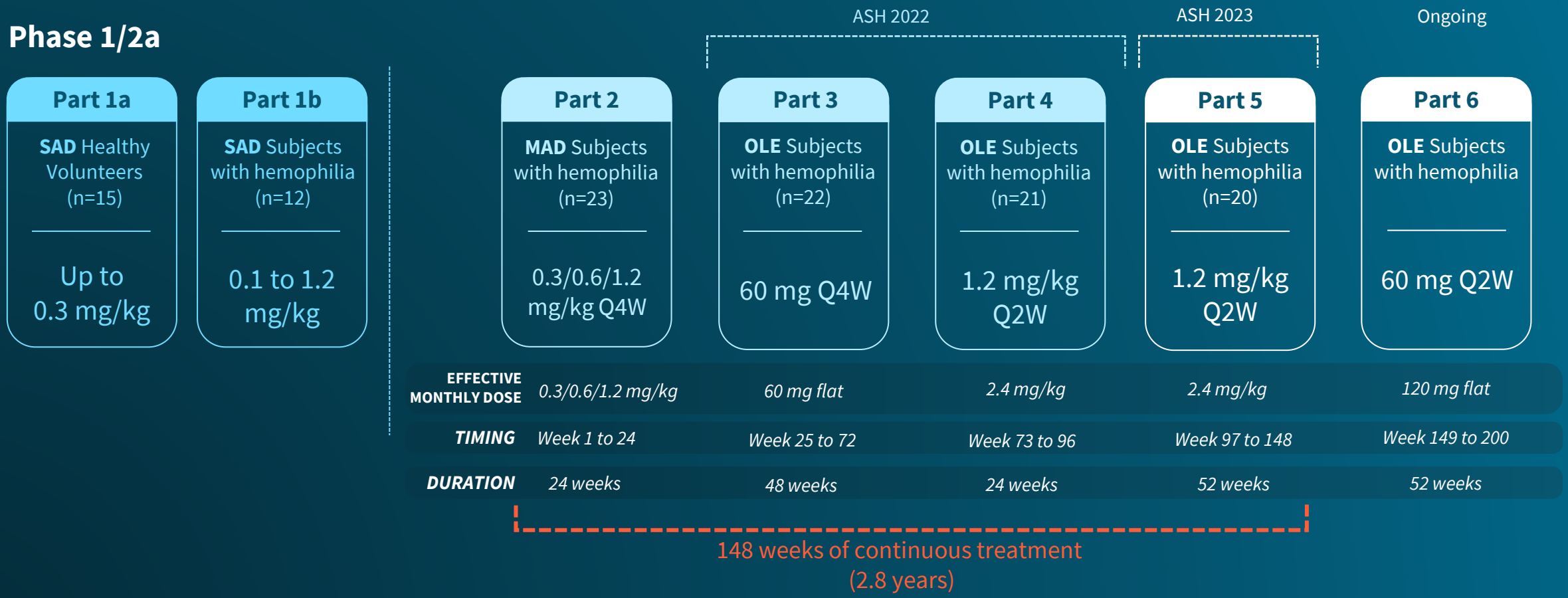
SerpinPC

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



Phase 2a | Ongoing Study of SerpinPC in Hemophilia

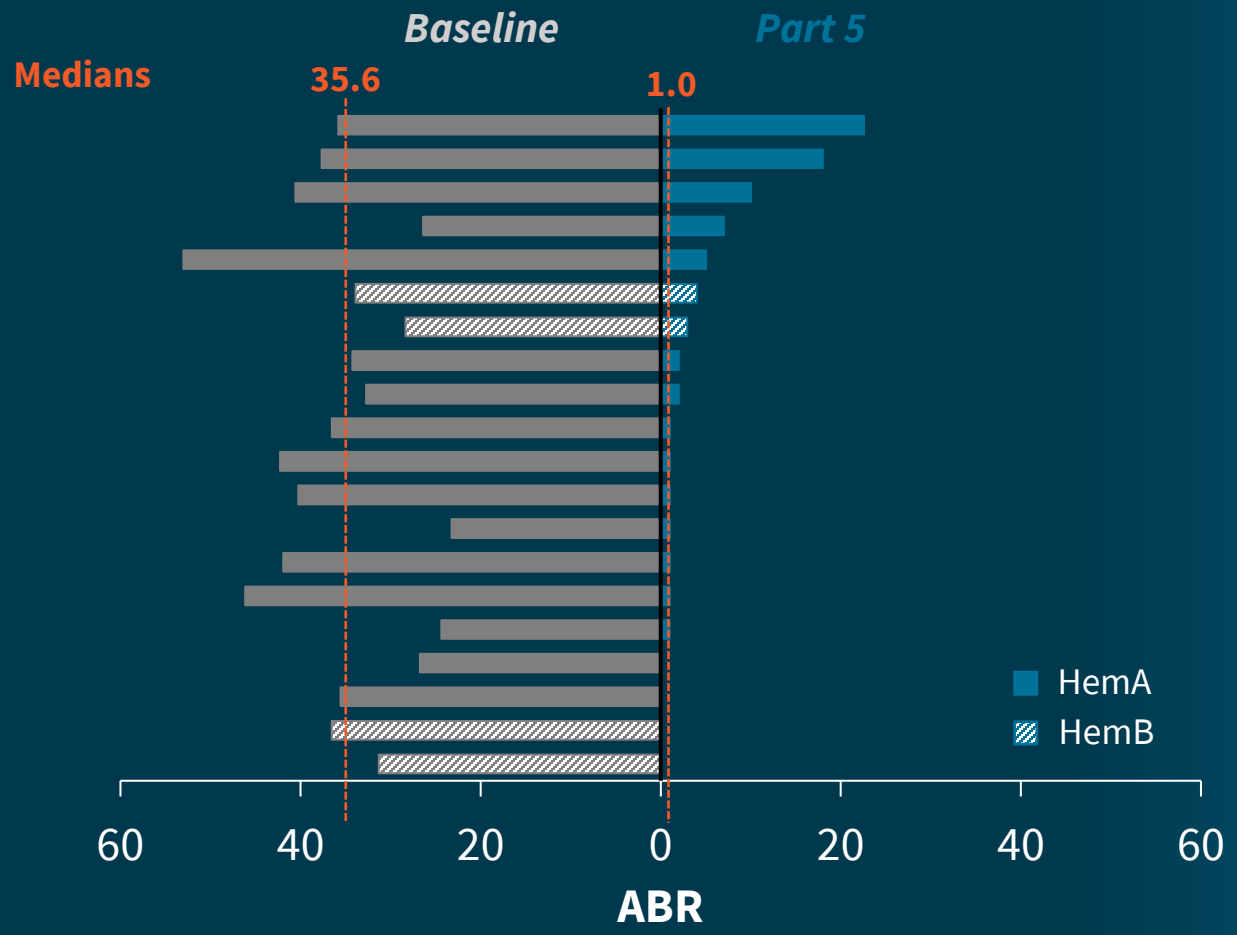
AP-0101 (NCT04073498) | An adaptive, first-in-human study to investigate the safety, tolerability, efficacy, and pharmacokinetics of SerpinPC in male persons with severe hemophilia



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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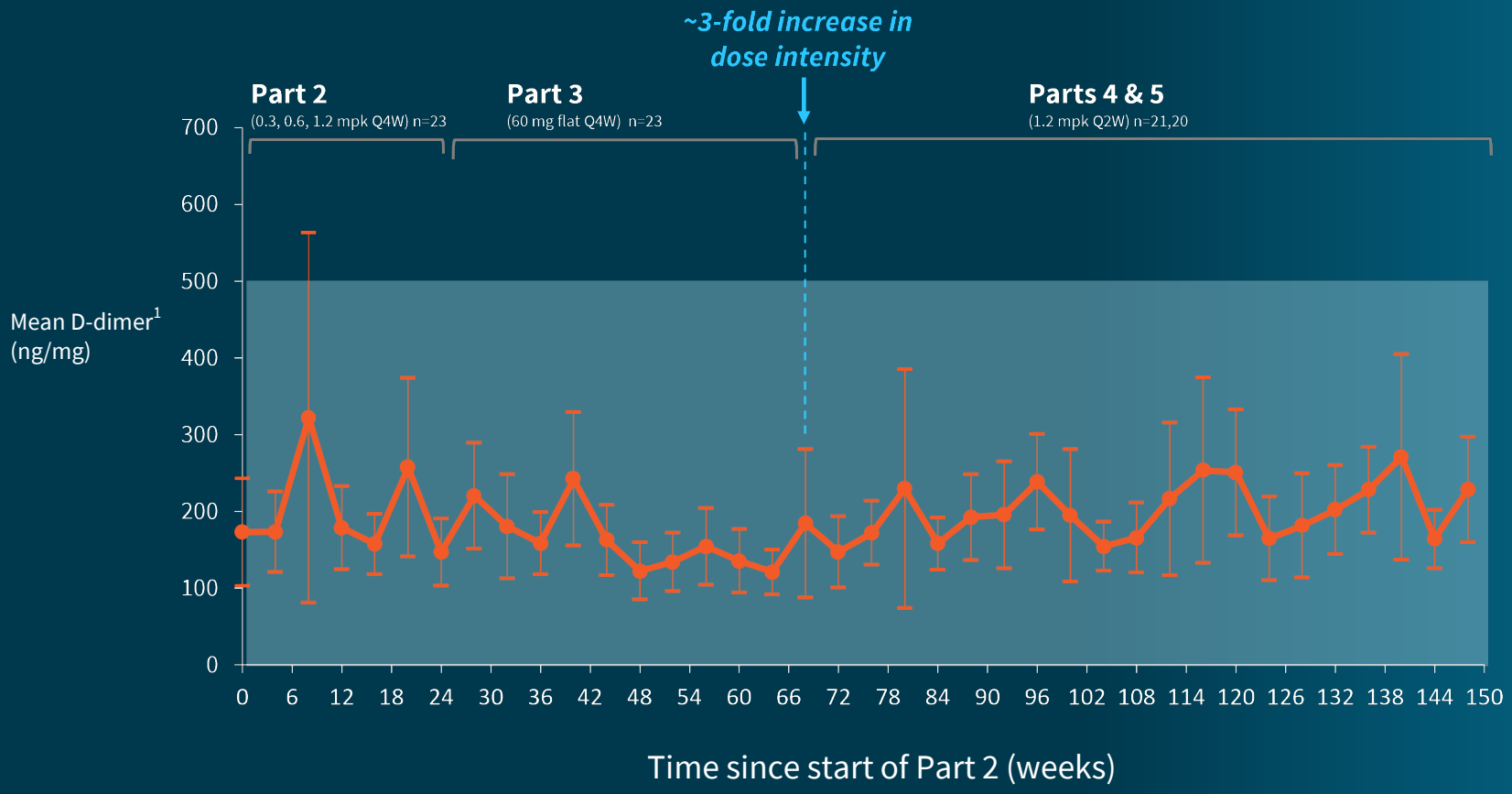
SerpinPC's Potential for Differentiated Safety Profile



- **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.

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SerpinPC Ongoing Global Registrational Program 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

>50 SITES
>15 COUNTRIES

ABR is annualized bleeding rate. The primary endpoint for PRESent-2 is measured in Part 2 and is the rate of treated bleeds (expressed as ABR) for hemophilia B subjects who previously received on-demand therapy compared to their prospective baseline ABR. Additional information on the PRESent studies can be accessed at www.clinicaltrials.gov (NCT05605678, NCT05789524, NCT05789537).

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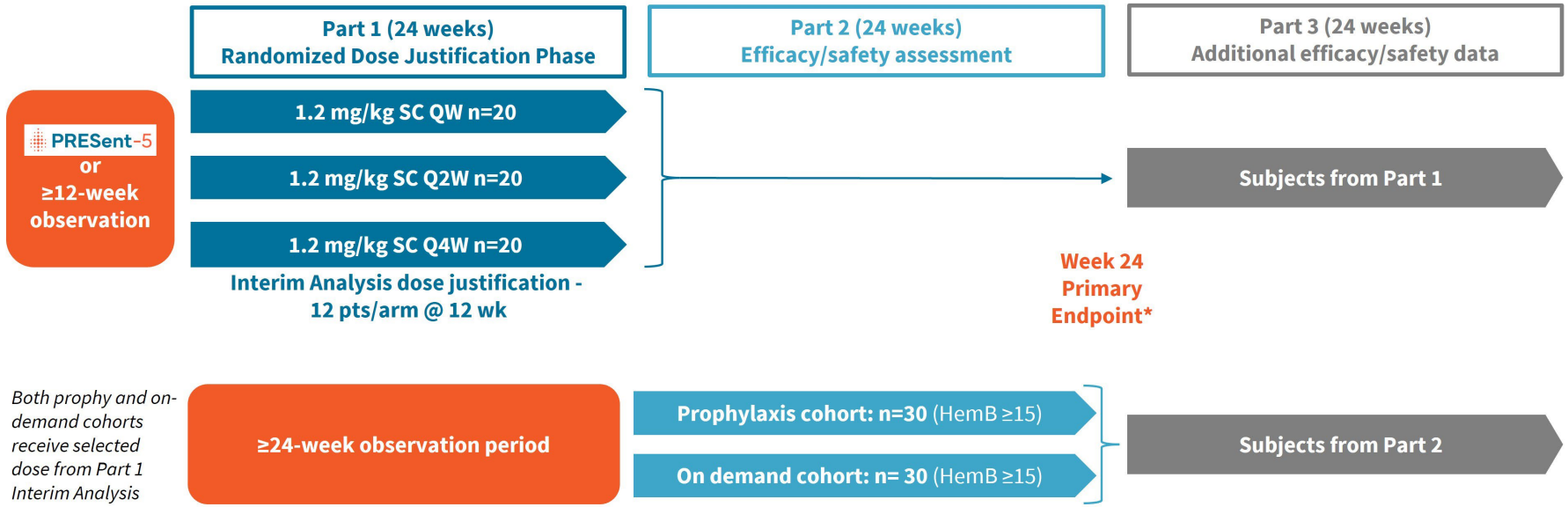
SerpinPC

Ongoing Global Registrational Program 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

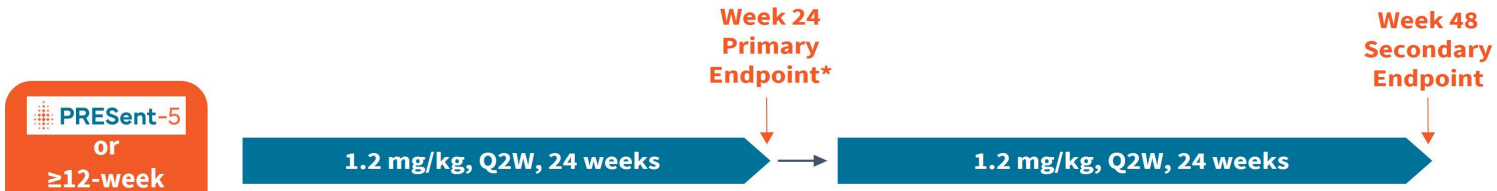
Hemophilia B without inhibitors (n=120) *Study to also include hemophilia A subjects to support safety database*



***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*

CENTESSA PHARMACEUTICALS

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.

Orexin Agonist Program

Hemophilia Program

LockBody Technology Platform

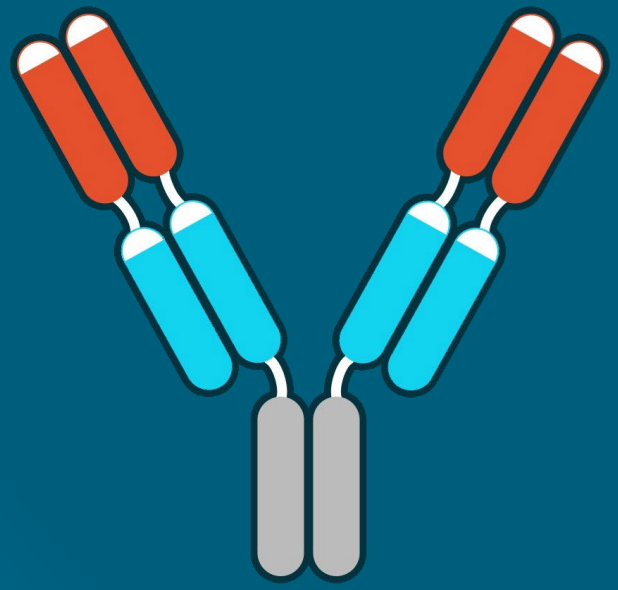
***LockBody* Technology Platform aims to *redefine* immuno-oncology treatment**

- **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).

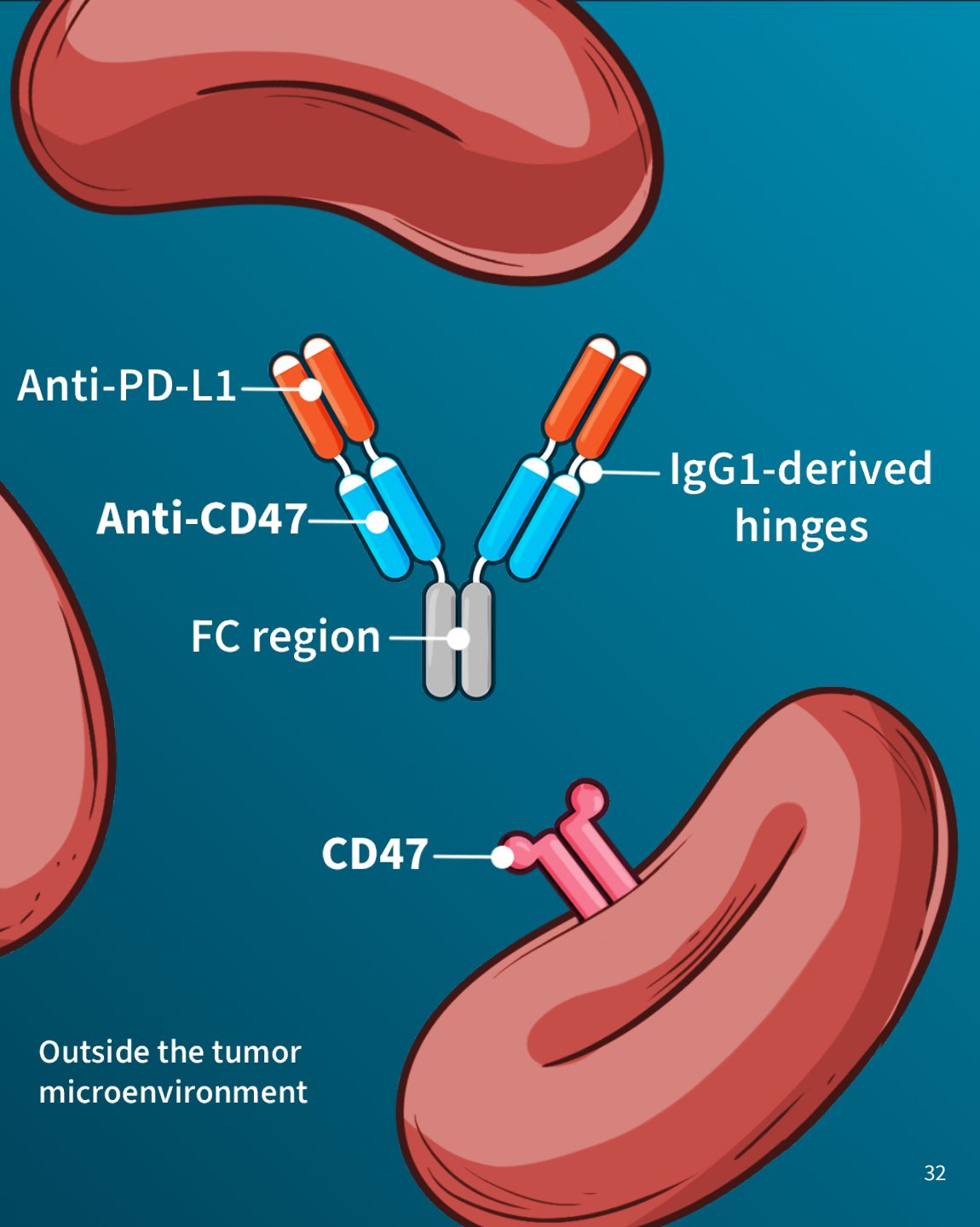
MOA

Locked Configuration



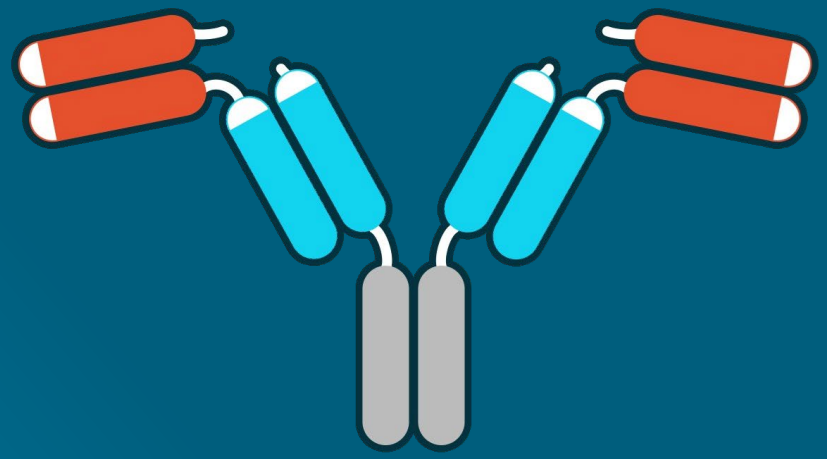
LockBody LB101

Conditionally tetravalent PD-L1xCD47 bispecific monoclonal antibody



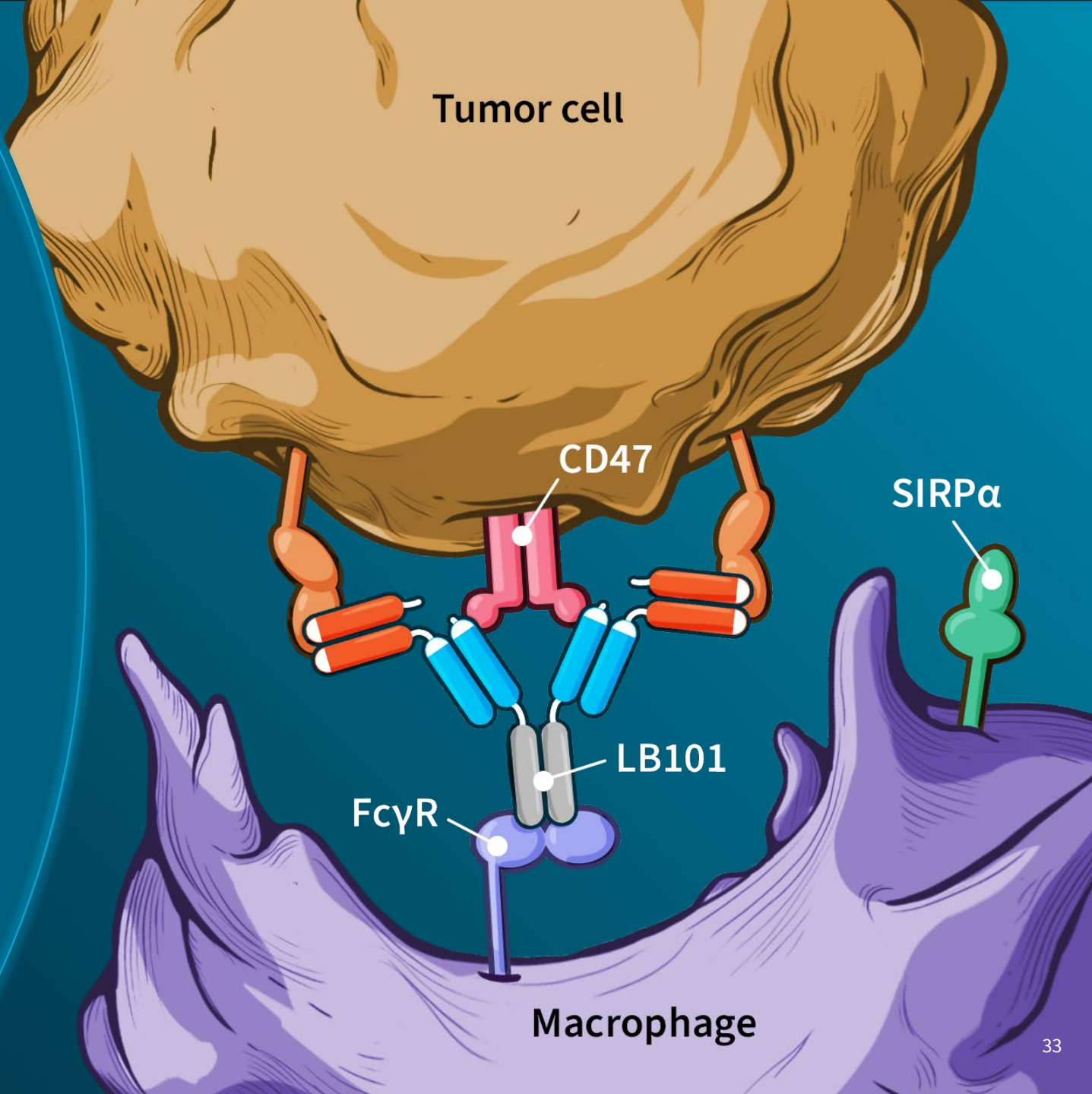
MOA

Unlocked Configuration



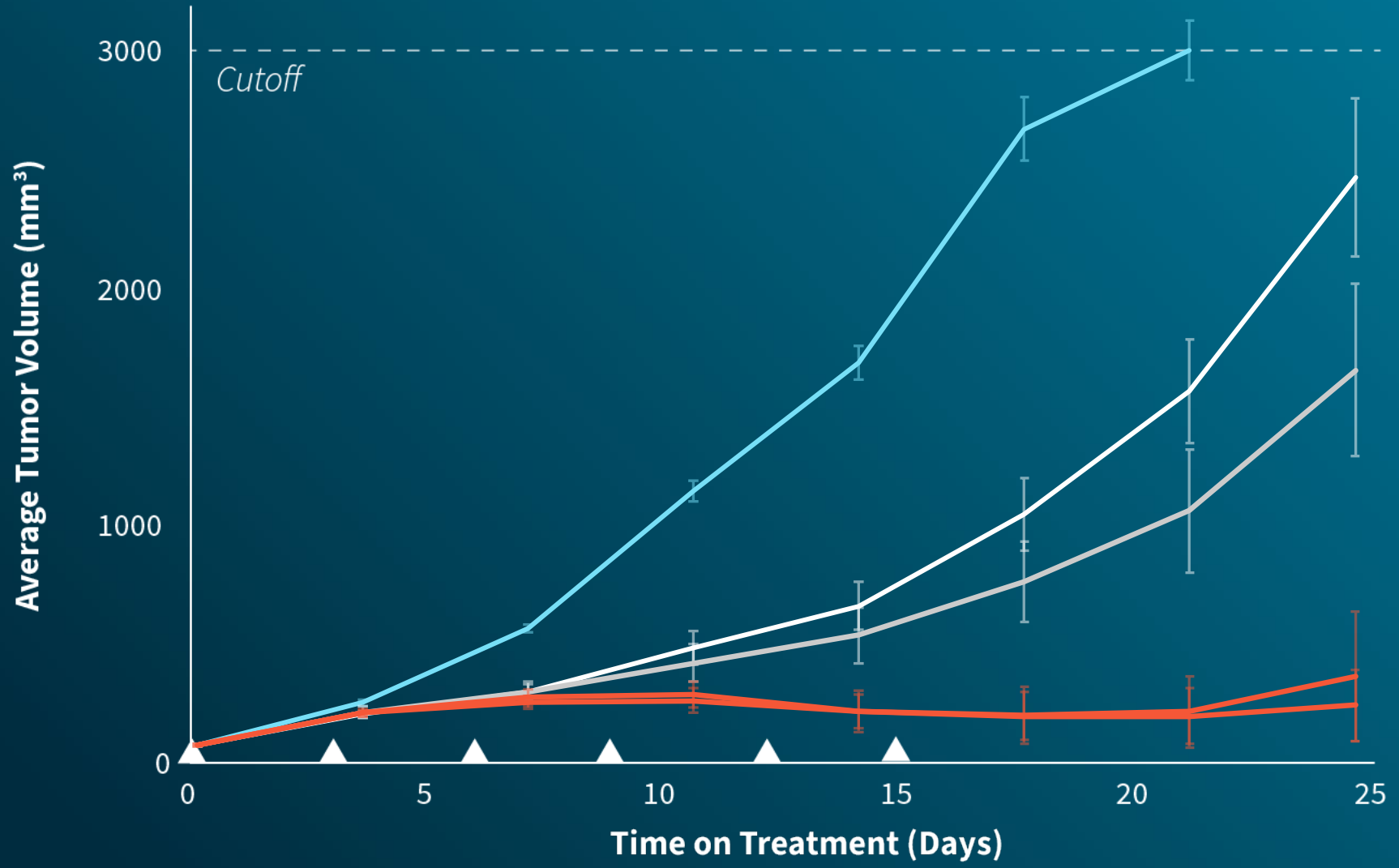
LockBody LB101

Conditionally tetravalent PD-L1xCD47 bispecific monoclonal antibody



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

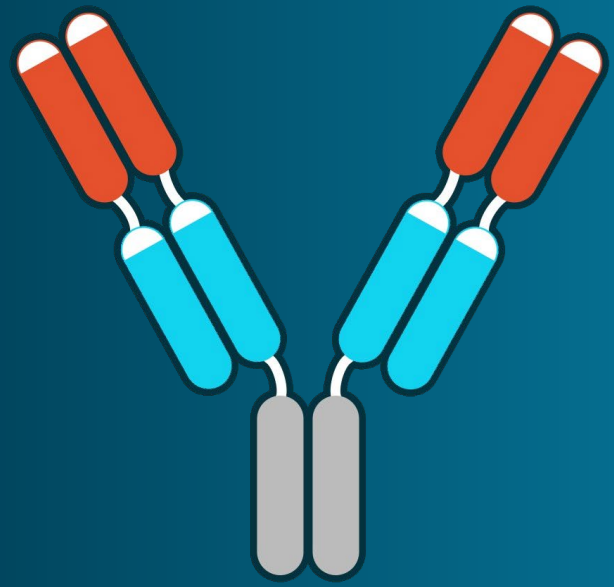
No anemia/ thrombocytopenia

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.

LB101 is in an ongoing Phase 1/2a first-in-human clinical trial



CENTESSA PHARMACEUTICALS

2024 Driving Momentum

ANTICIPATED MILESTONES

OREXIN AGONIST PROGRAM

ORX750

Plan to rapidly advance into Phase 2 studies in patients with NT1, NT2, and IH beginning in **Q4 of 2024**

ORX142

IND-enabling studies ongoing

HEMOPHILIA PROGRAM

SerpinPC

PRESent-2 Part 1 interim analysis planned in **2024**; Part 1 data planned for **late 2024/early 2025**

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 $294.8 million in cash, cash equivalents and short-term investments as of June 30, 2024. In addition, Centessa received approximately $242.7 million in aggregate net proceeds from a public offering of ADSs in September 2024. Cash runway estimated into mid-2027.

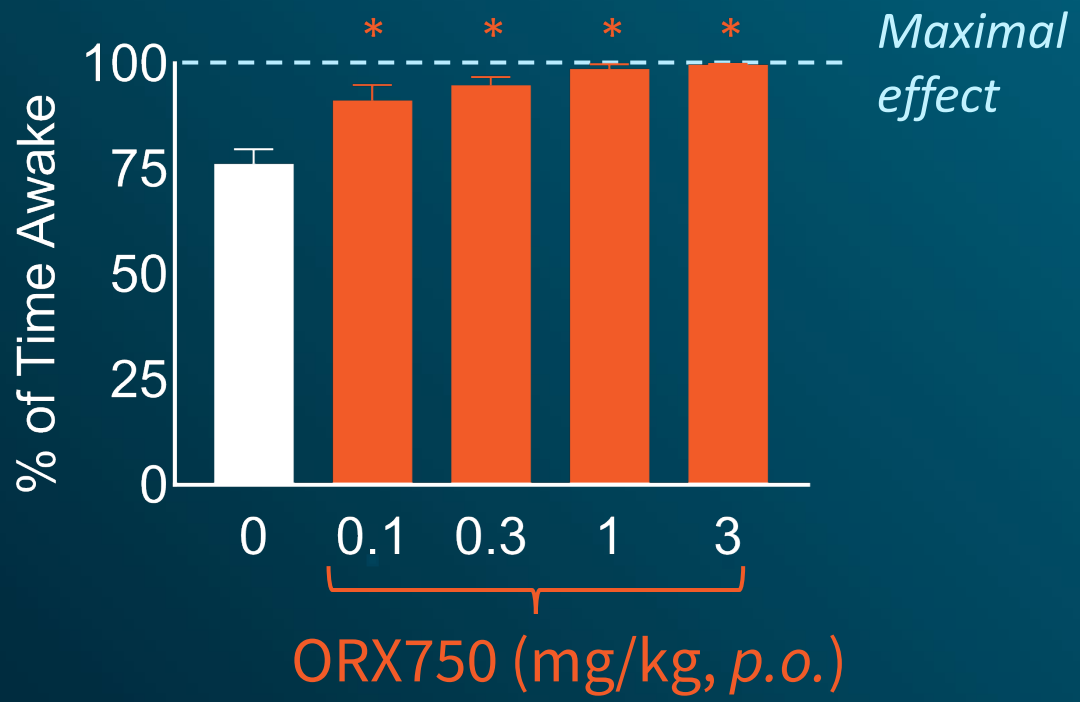
CENTESSA

PHARMACEUTICALS

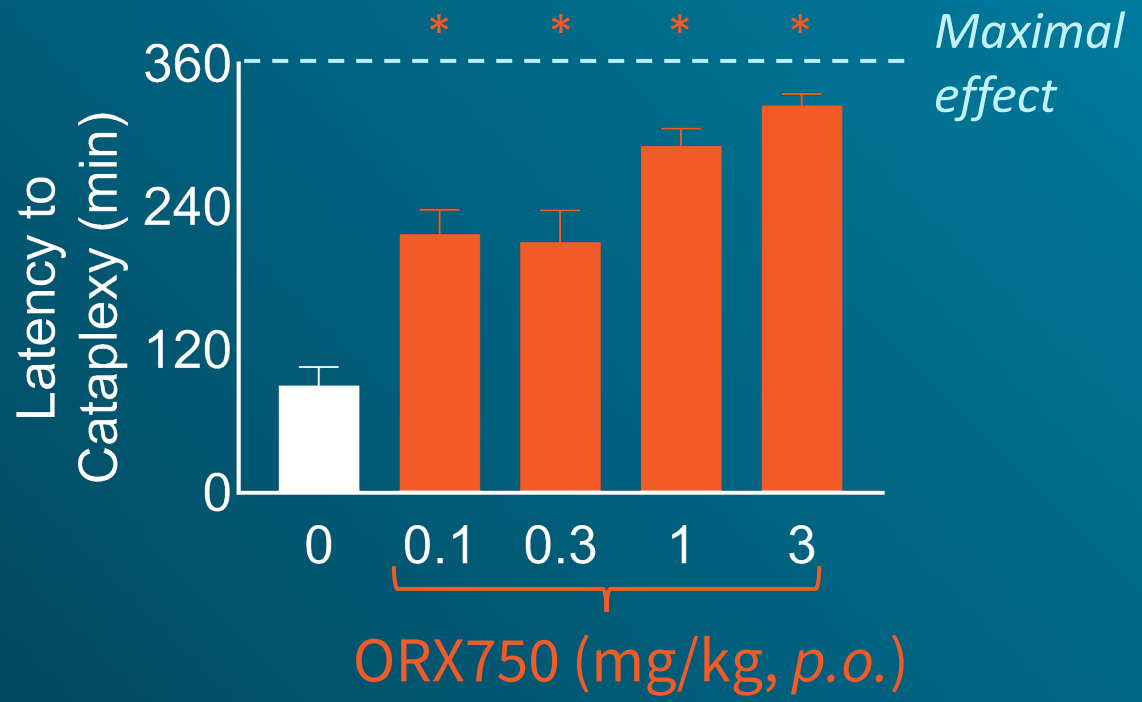
PRECLINICAL DATA

ORX750 Increased Wakefulness and Suppressed Cataplexy in NT1 Mice

Wakefulness



Latency to Cataplexy

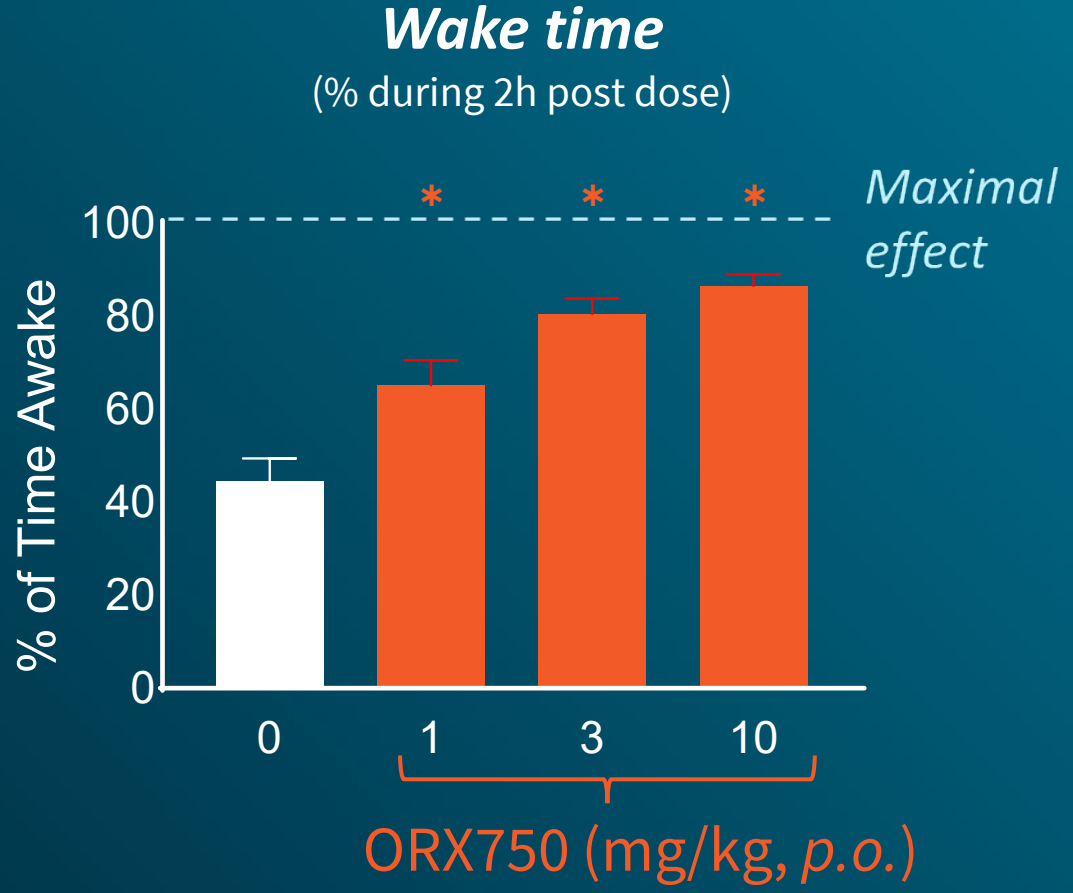


NT1 is Narcolepsy Type 1.
% of Time Awake refers to time spent awake in the first 3 hours after oral dosing.
ORX750 preclinical data presentation at World Sleep Congress, Oct. 25, 2023. NT1 model shown is orexin/tTA;tetO diphtheria toxin fragment A (DTA) mice. Age at first dose 23-27 wks (7 wks after 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.

CENTESSA PHARMACEUTICALS

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.

CENTESSA PHARMACEUTICALS