CENTESSA PHARMACEUTICALS

Corporate Overview

November 2024

DISCLAIMER AND FORWARD LOOKING STATEMENTS

This presentation has been prepared by Centessa Pharmaceuticals plc (the "Company") for informational purposes only and not for any other purpose. This presentation does not contain all the information that is or may be material to investors or potential investors and should not be considered as advice or a recommendation to investors or potential investors in respect of the holding, purchasing or selling of securities or other financial instruments and does not take into account any investor's particular objectives, financial situation or needs. The communication of this presentation may be restricted by law; it is not intended for distribution to, or use by any person in, any jurisdiction where such distribution or use would be contrary to local law or regulation. This presentation is not directed to or intended for distribution, or transfer, either directly or indirectly to, or use by, any person or entity that is a citizen or resident or located in any locality, state, country or other jurisdiction where such distribution, transfer, publication, availability or use would be contrary to law or regulation or which would require any registration or licensing within such jurisdiction.

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 ORX750, ORX142, ORX489, 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

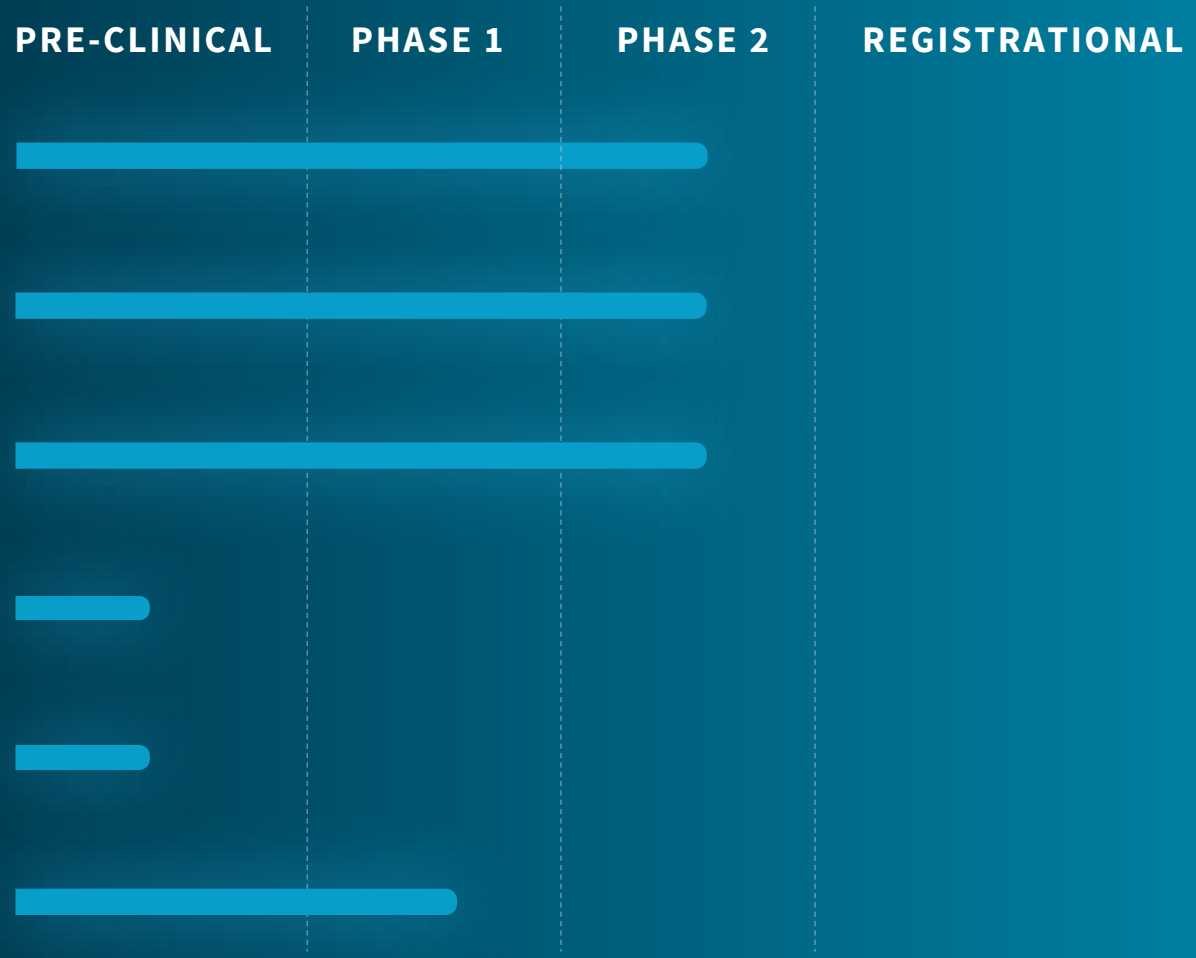
- Potential best-in-class / first-in-class orexin agonist franchise
- Ongoing momentum in 2024 with clinical milestones anticipated across our orexin agonist pipeline in 2025
- Strong balance sheet

CENTESSA PHARMACEUTICALS

Centessa reported **$518.4 million** in cash, cash equivalents and short-term investments as of September 30, 2024. Cash runway estimated into mid-2027.

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

ASSET	DISEASE/CONDITION	MECHANISM
ORX750	Narcolepsy Type 1 (NT1)	OXR2 Agonist
ORX750	Narcolepsy Type 2 (NT2)	OXR2 Agonist
ORX750	Idiopathic Hypersomnia (IH)	OXR2 Agonist
ORX142	Neurological, Neurodegenerative & Psychiatric Disorders	OXR2 Agonist
ORX489	Neurological, Neurodegenerative & Psychiatric Disorders	OXR2 Agonist
LB101	Solid Tumors	PD-L1xCD47 LockBody®



CENTESSA PHARMACEUTICALS

Centessa has multiple early-stage assets not reflected on this slide.

2024 Driving Momentum

ANTICIPATED MILESTONES

OREXIN AGONIST PROGRAM

ORX750

Initiated Phase 2a study in patients with NT1, NT2, and IH; Data expected in **2025**

Presentation of Phase 1 data planned for **Q2 2025**

ORX142

IND-enabling studies ongoing; Clinical data in acutely sleep-deprived healthy volunteers expected in **2025**

ORX489

Entering IND-enabling studies

LOCKBODY TECHNOLOGY PLATFORM

LB101

Phase 1/2a study **ongoing**

Orexin Agonist Program

LockBody Technology Platform

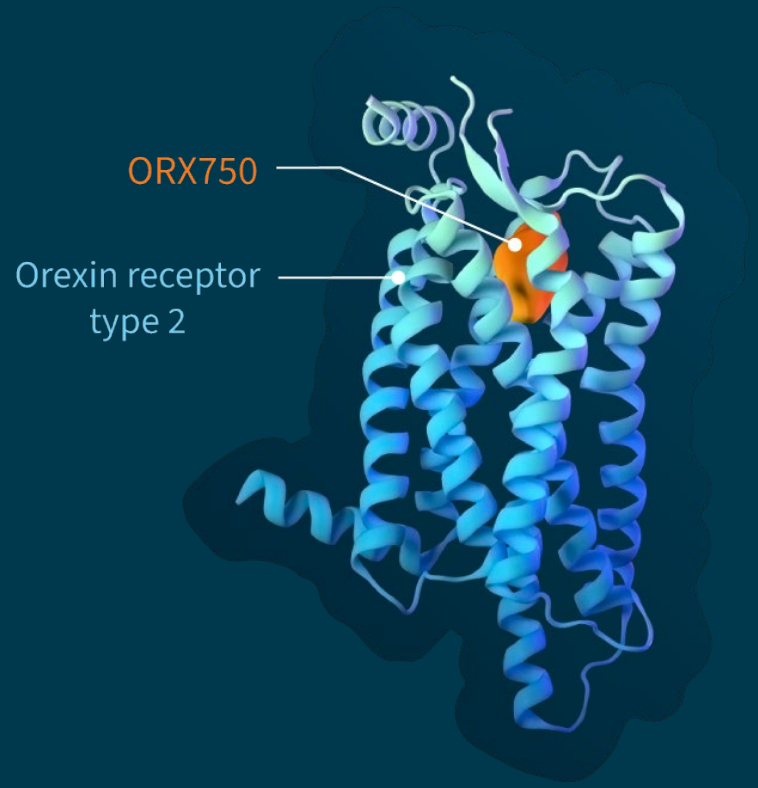
Orexin agonists have the potential to transform the standard of care for individuals with sleep-wake, neurological, neurodegenerative and psychiatric disorders

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

- **ORX750** for the treatment of **NT1, NT2 and IH**
- **ORX142** for the treatment of **neurological, neurodegenerative and psychiatric disorders**
- **ORX489** for the treatment of **additional neurological, neurodegenerative and psychiatric disorders**
- Earlier stage OX2R agonists and therapeutics for additional potential indications

	hOX2R EC_{50}	Selectivity vs. hOX1R
ORX750	0.110 nM	9,800x
ORX142	0.069 nM	13,000x
ORX489	0.035 nM	8,800x

ORX750 a Potential Best-in-Class Oral OX2R Agonist for the Treatment of 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 **34 mins (MWT)** at **3.5 mg dose**[1]
- **Favorable safety and tolerability profile;**[1] No observations of hepatotoxicity, visual disturbances or hallucinations, as of Oct. 31, 2024 data cutoff date[1]

MWT (Maintenance of Wakefulness Test); Phase 1 study ongoing

1. Interim Phase 1 study data
2. Doghramji K, et al., "A normative study of the maintenance of wakefulness test (MWT)." *Electroencephalogr Clin Neurophysiol* 1997; 103:554-62

CENTESSA PHARMACEUTICALS

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

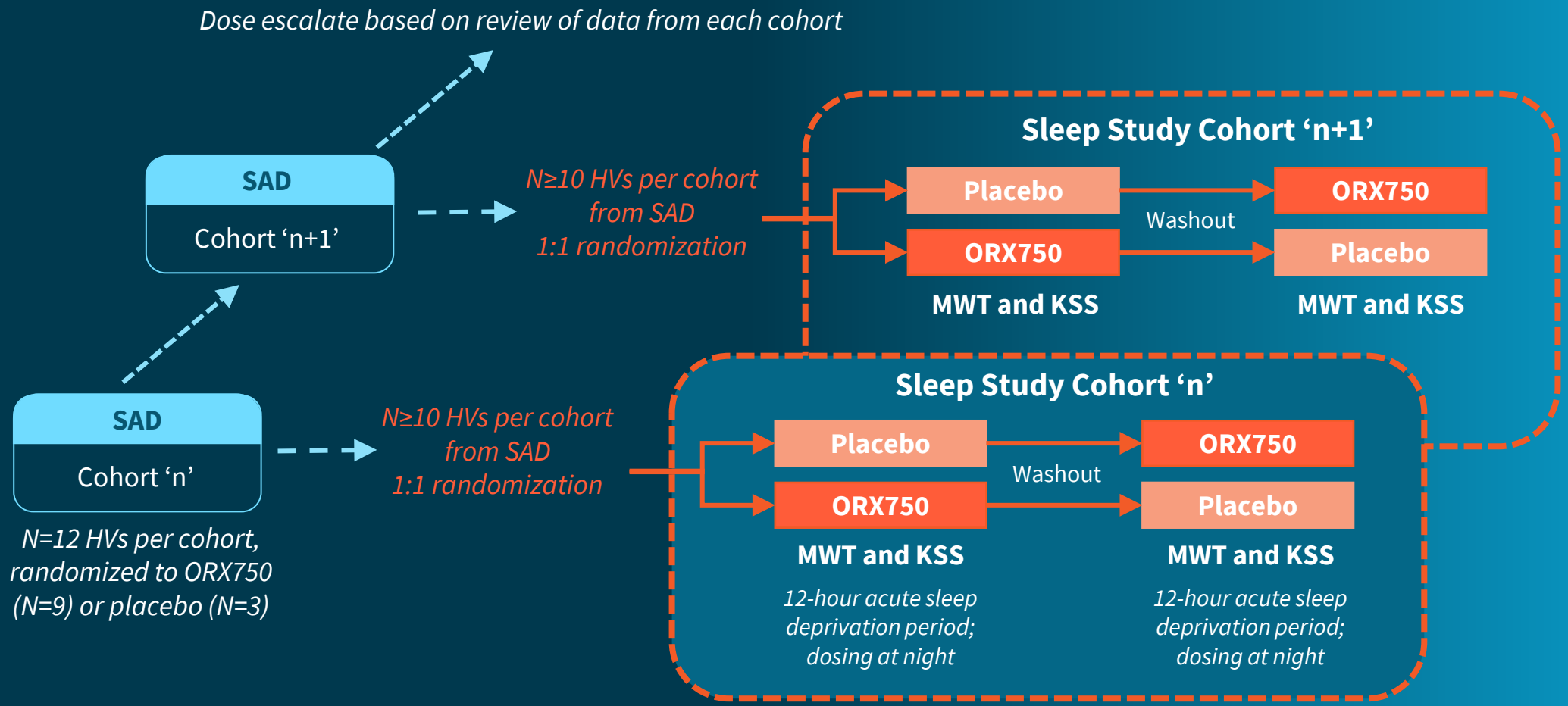
- Efficacy assessments are being performed using the **Maintenance of Wakefulness Test (MWT)*** and **Karolinska Sleepiness Scale (KSS)** in acutely sleep-deprived healthy adult subjects

*MWT is an established registrational and objective endpoint in EDS in sleep-wake disorders.

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 Demonstrated Dose-Dependent and Significant Improvements in Mean Sleep Latency

	ORX750 LS Mean (95% CI) Sleep Latency (Minutes)	**Placebo** LS Mean (95% CI) Sleep Latency (Minutes)	**LS Mean Difference** Compared to Placebo (95% CI)	**p-Value**
1.0 mg (n=8)	**18** (12, 23)	**10** (4, 15)	**8** (0, 16)	**p=0.04**
2.5 mg (n=8)	**32** (22, 42)	**17** (7, 27)	**15** (5, 26)	**p=0.01**
3.5 mg (n=10)	**34** (27, 40)	**13** (7, 20)	**20** (15, 25)	**p<0.0001**

The 2.5 and 3.5 mg doses were shown to **restore normative wakefulness**[1] in acutely sleep-deprived healthy volunteers

As of October 31, 2024 data cutoff date. Phase 1 study ongoing. Least squares (LS) mean.
Per the Phase 1 study design, a sleep study cohort (MWT) is optional at each SAD level, and has been conducted for 1 mg, 2.5 mg and 3.5 mg doses.
Mean sleep onset latency in 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.

CENTESSA PHARMACEUTICALS

INTERIM PHASE 1

ORX750 Demonstrated a Favorable Safety and Tolerability Profile in Both Single and Multiple Dose Studies

	SAD Cohorts						MAD Cohorts		
	Placebo *(n=15)*	**ORX750 1.0 mg** *(n=9)*	**ORX750 2.0 mg** *(n=9)*	**ORX750 2.5 mg** *(n=9)*	**ORX750 3.5 mg** *(n=9)*	**ORX750 5.0 mg** *(n=9)*	**Placebo** *(n=4)*	**ORX750 2.0 mg** *(n=8)*	**ORX750 3.0 mg** *(n=8)*
Any TEAE, n (%)	**4 (27)**	**3 (33)**	**3 (33)**	**1 (11)**	**0**	**3 (33)**	**2 (50)**	**4 (50)**	**3 (38)**
Related	**4 (27)**	**0**	**2 (22)**	**1 (11)**	**0**	**2 (22)**	**1 (25)**	**4 (50)**	**2 (25)**
Nonrelated	**1 (7)**	**3 (33)**	**2 (22)**	**0**	**0**	**2 (22)**	**2 (50)**	**2 (25)**	**1 (12)**
Mild	**4 (27)**	**3 (33)**	**3 (33)**	**1(11)**	**0**	**3 (33)**	**2 (50)**	**4 (50)**	**3 (38)**
Moderate	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
Severe	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
TEAEs leading to discontinuation, n (%)	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
Serious TEAEs, n (%)	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
Frequently reported AEs associated with other OX2R agonists									
Insomnia	**0**	**0**	**0**	**0**	**0**	**0**	**1 (25)**	**2 (25)**	**0**
Urinary frequency/urgency	**1 (7)**	**0**	**0**	**0**	**0**	**1 (11)**	**0**	**1 (12)**	**1 (12)**
Visual disturbances	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
Hepatotoxicity	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
Blood pressure increased	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**

- No cases of hepatotoxicity, visual disturbances or hallucinations were observed
- No clinically significant treatment-emergent changes in hepatic and renal parameters, vital signs or electrocardiogram (ECG) parameters

CENTESSA PHARMACEUTICALS

As of October 31, 2024 data cutoff date. Phase 1 Study is ongoing. 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.

PHASE 2a STUDY

Phase 2a Study of ORX750 in Patients with NT1, NT2, IH

- Evaluate safety, tolerability, and pharmaco-kinetics in NT1, NT2, and IH patients
- Efficacy assessments will evaluate excessive daytime sleepiness using the **Maintenance of Wakefulness Test (MWT)*** and **Epworth Sleepiness Scale (ESS)***, **weekly cataplexy rate*** (NT1 patients only), and overall symptom improvement**
- Exploratory efficacy assessments will measure sleep, cognition, attention, memory, and general health

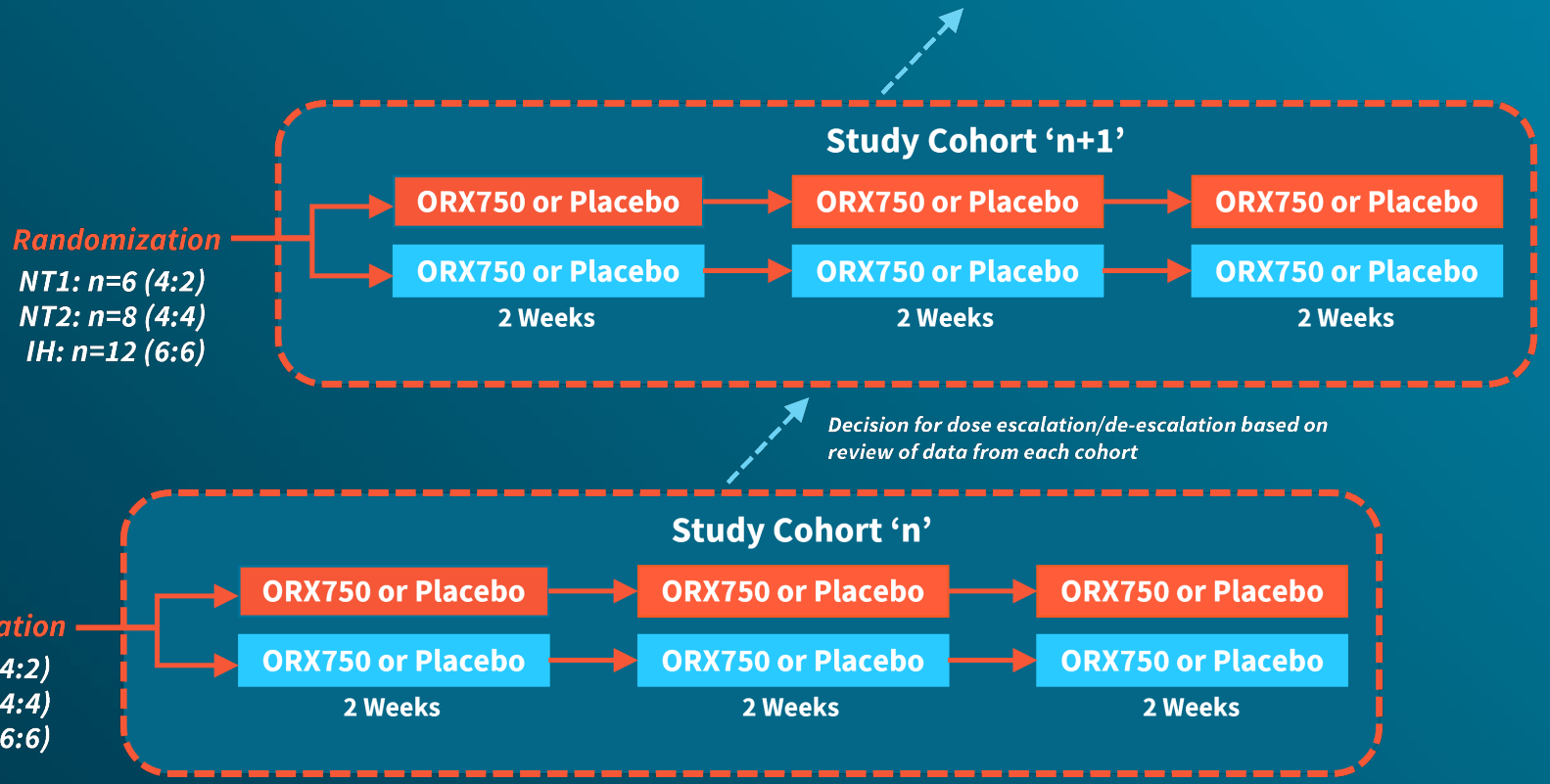
*MWT and ESS are established registrational endpoints for EDS in sleep-wake disorders and weekly cataplexy rate is an established registration endpoint for cataplexy in NT1
** Measured by Narcolepsy Severity Scale (NSS) and Idiopathic Hypersomnia Severity Scale (IHSS)

PHASE 2a STUDY

Randomized, Double-blind, Placebo-Controlled Basket Study of ORX750 in Patients with NT1, NT2, and IH

- Innovative design with potential to enable **well-powered** and efficient data generation
- All patients to receive ORX750 for **at least 4 weeks**
- Optimal number of patients to allow **efficient recruitment**
- Potential for **optimized dose selection**

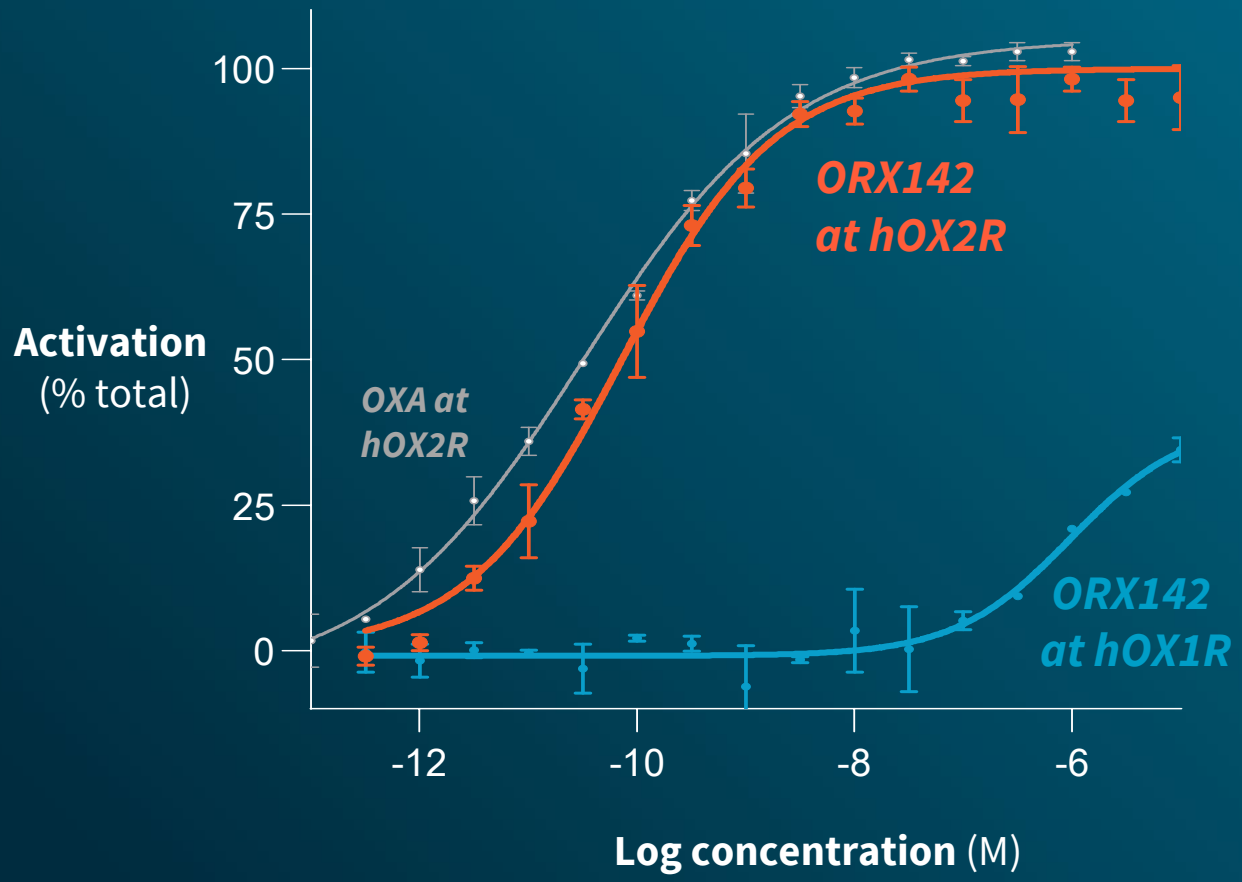
Data expected in all three indications in 2025



After each 2-week period, treatment assignment (ORX750 or Placebo) may change

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

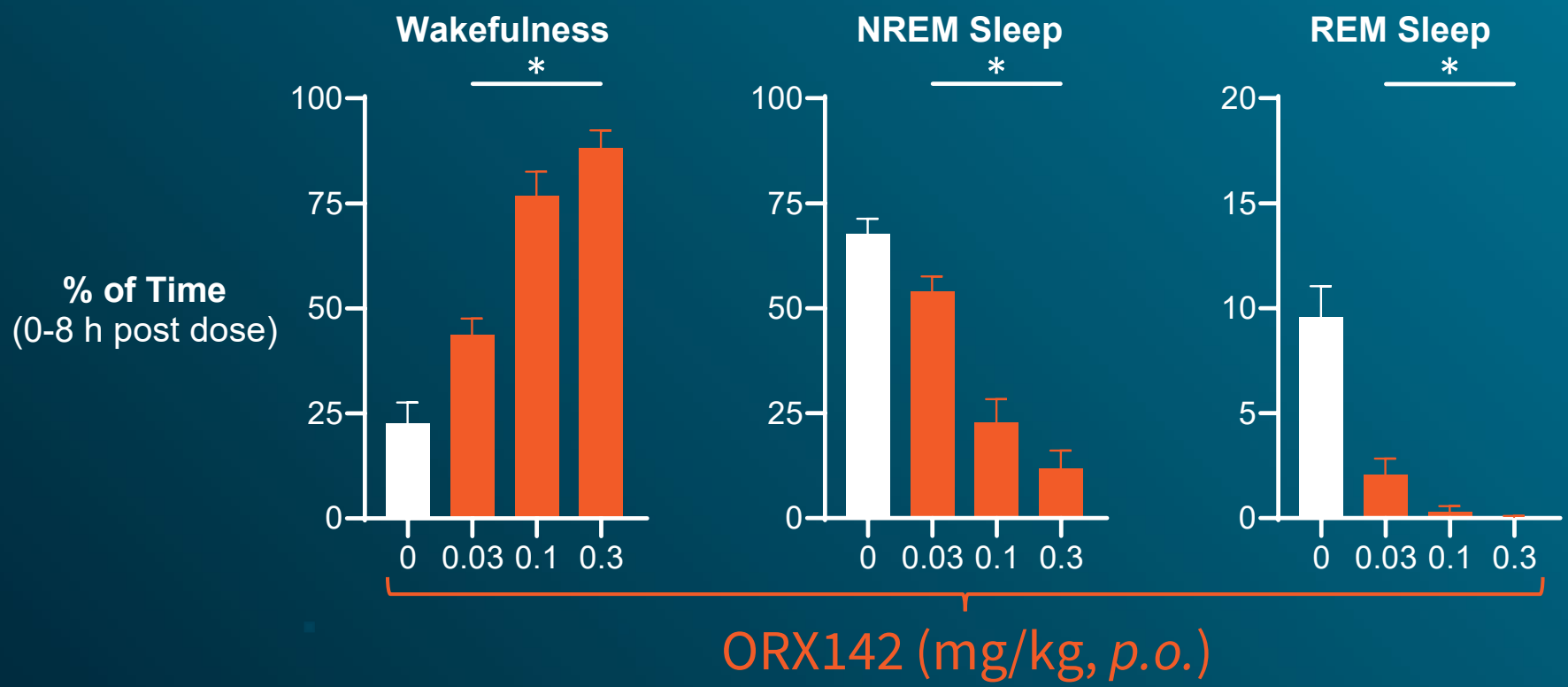
2 Human, mouse, rat, dog, monkey recombinant receptors *in vitro.*

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

CENTESSA PHARMACEUTICALS

PRECLINICAL DATA

ORX142 Increased Wakefulness and Decreased NREM and REM Sleep in Non-Human Primates (NHPs)



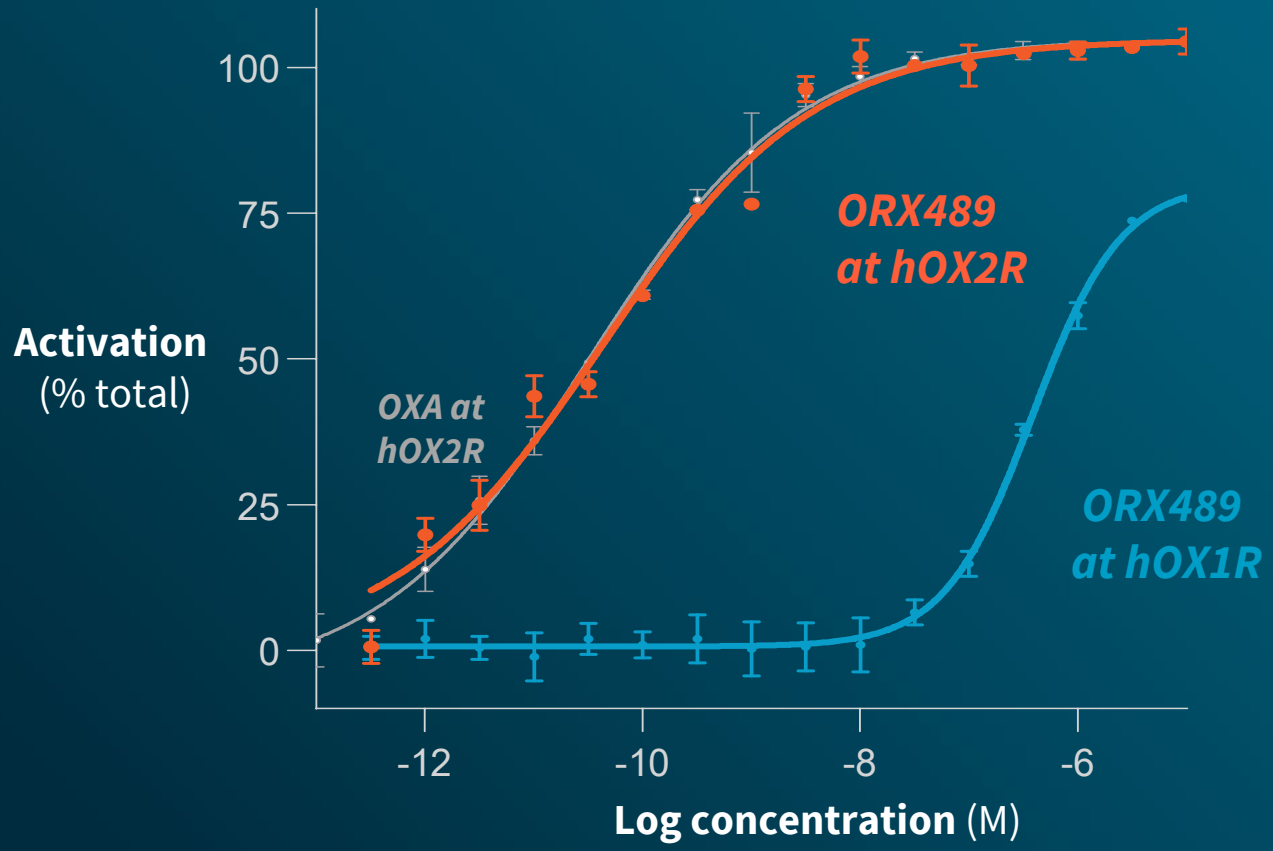
- In marmosets wake time increased at **≥0.03 mg/kg** (lowest dose tested)

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.

CENTESSA PHARMACEUTICALS

PRECLINICAL DATA

ORX489 Designed as a Highly Potent and Selective OX2R Agonist



***EC_{50} 0.035 nM** for hOX2R*

***8,800-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; ORX489 EC50 at hOX1R = 310 nM.

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

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

3 Safety 47 and GPCRMax from >60 receptor families.

CENTESSA PHARMACEUTICALS

Building a Multi-Asset Orexin Agonist Franchise

ORX750

Sleep-Wake Disorders

NT1, NT2 & IH

$5B+

potential market opportunity

ORX142 & ORX489

Neurological, Neurodegenerative and Psychiatric Disorders

$10B+

potential market opportunity

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

CENTESSA PHARMACEUTICALS

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

OREXIN AGONIST PROGRAM

ORX750

Initiated Phase 2a study in patients with NT1, NT2, and IH; Data expected in **2025**

Presentation of Phase 1 data planned for **Q2 2025**

ORX142

IND-enabling studies ongoing; Clinical data in acutely sleep-deprived healthy volunteers expected in **2025**

ORX489

Entering IND-enabling studies

Orexin Agonist Program

LockBody Technology Platform

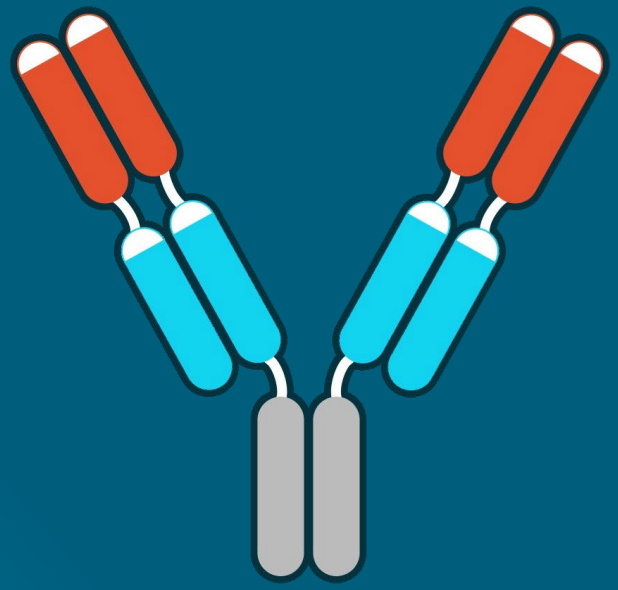
***LockBody* Technology Platform aims to *redefine* immuno-oncology treatment**

- **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).

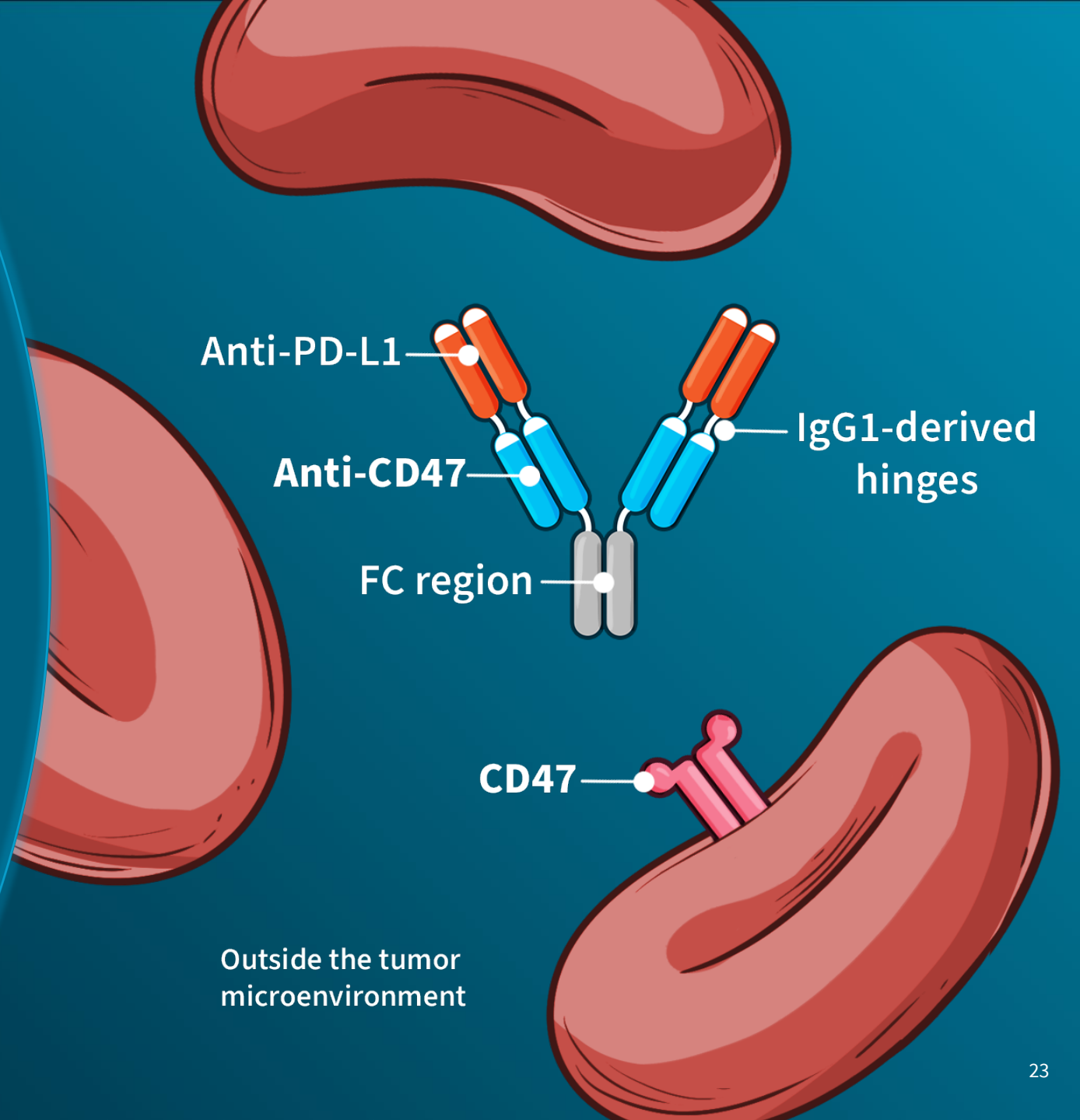
MOA

Locked Configuration



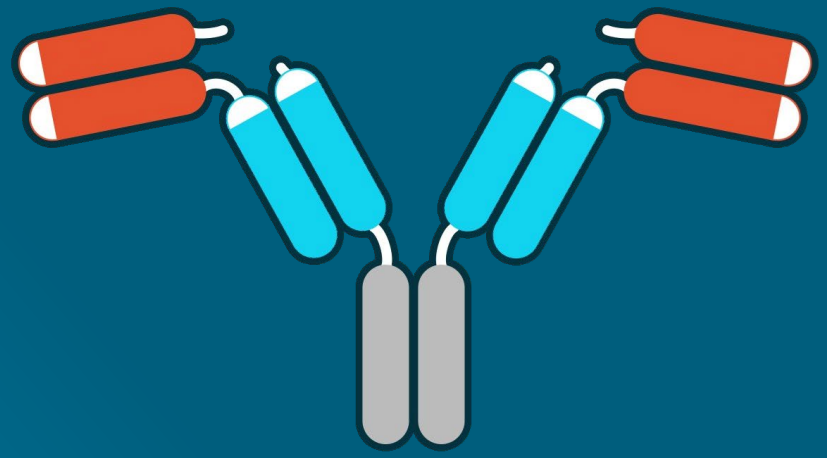
LockBody LB101

Conditionally tetravalent PD-L1xCD47 bispecific monoclonal antibody



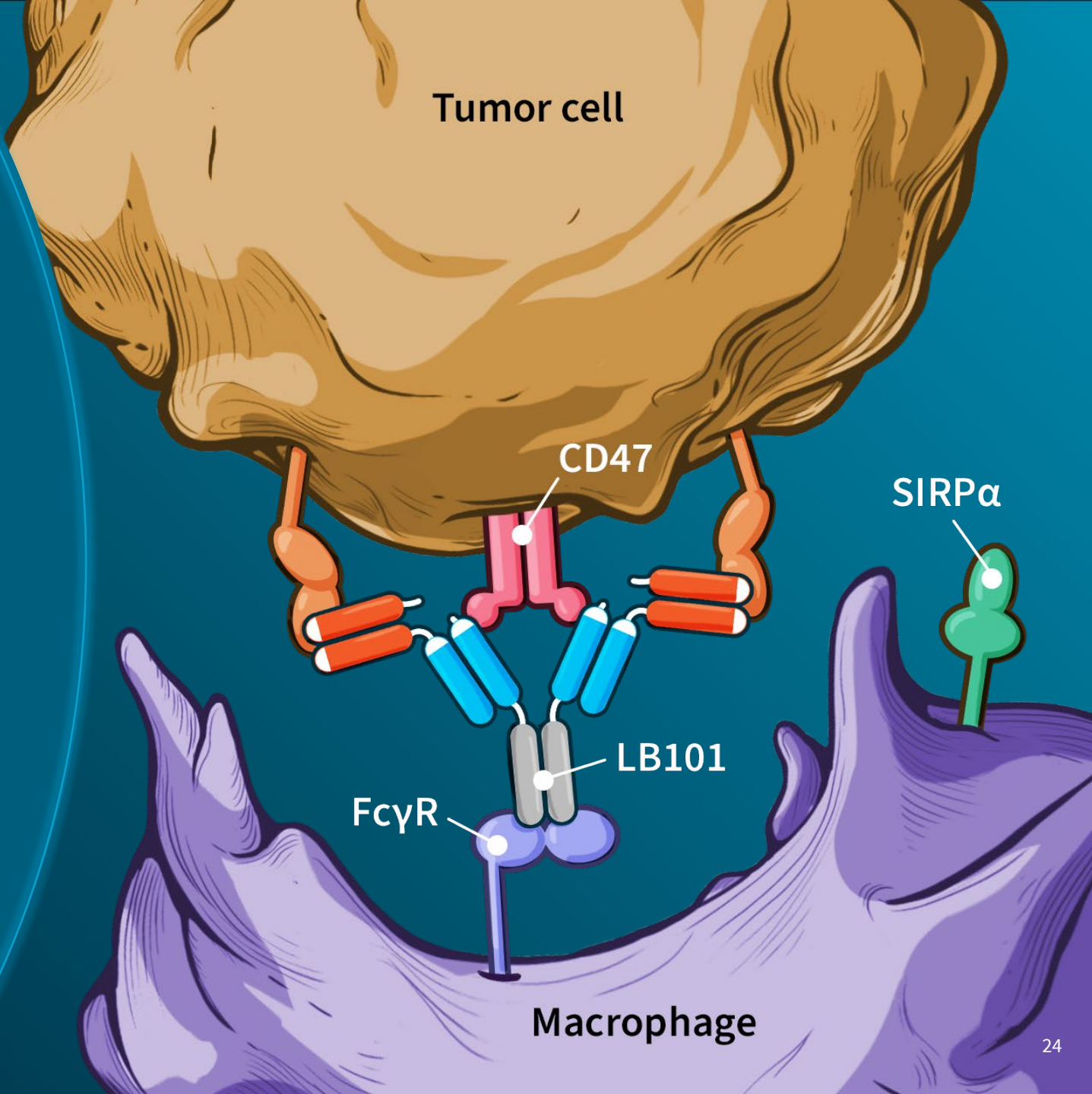
MOA

Unlocked Configuration



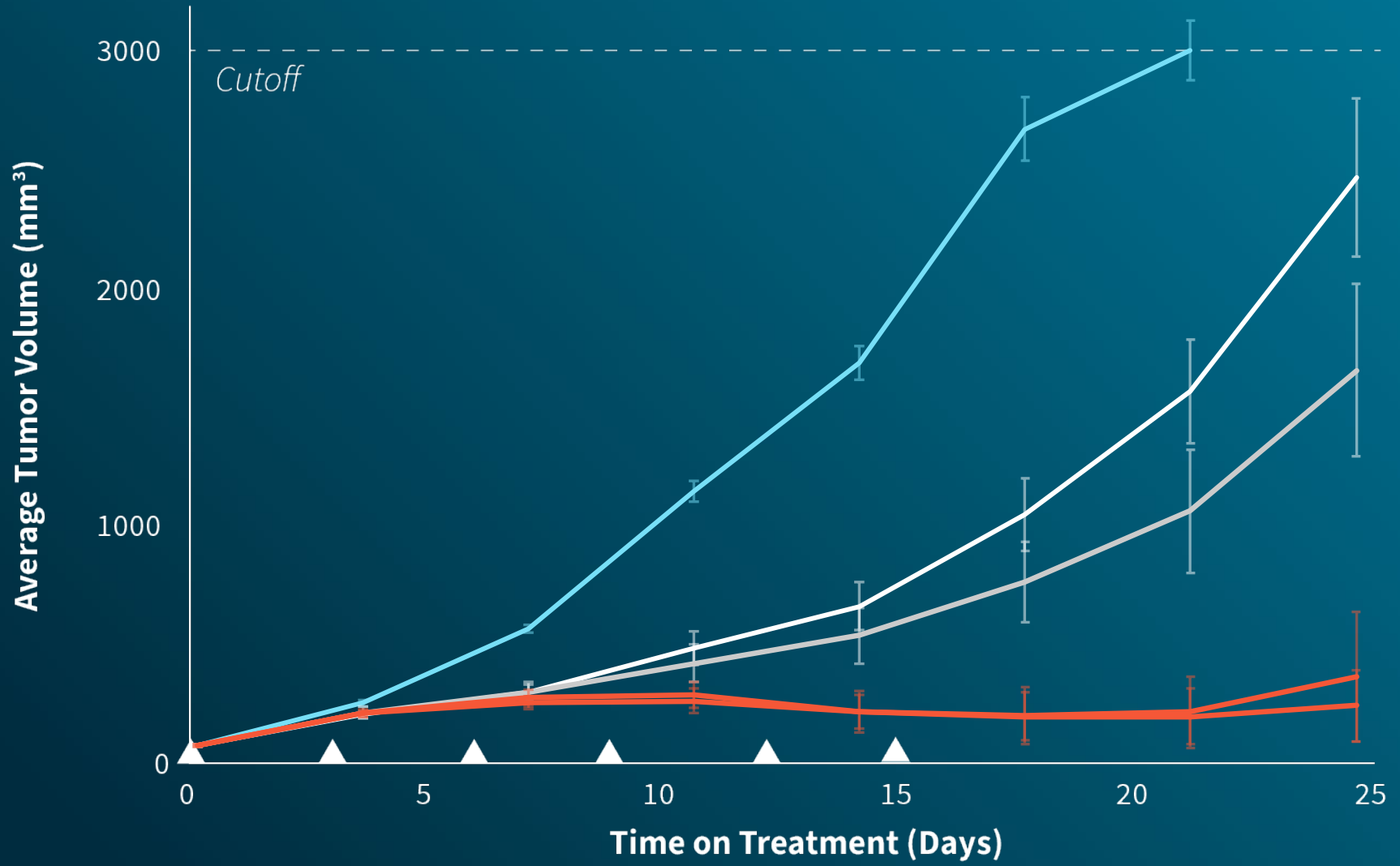
LockBody LB101

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

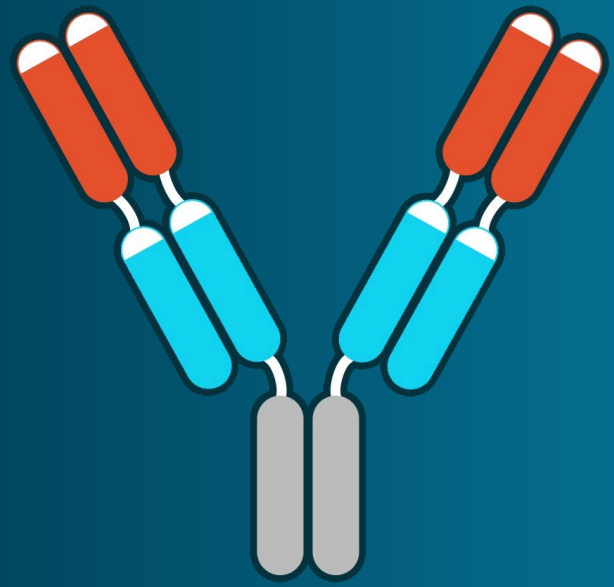
No anemia/ thrombocytopenia

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



OUR MISSION

Discovering and Developing Medicines that are Transformational for Patients

- Potential best-in-class / first-in-class orexin agonist franchise
- Ongoing momentum in 2024 with clinical milestones anticipated across our orexin agonist pipeline in 2025
- Strong balance sheet

CENTESSA PHARMACEUTICALS

Centessa reported **$518.4 million** in cash, cash equivalents and short-term investments as of September 30, 2024. Cash runway estimated into mid-2027.

CENTESSA

PHARMACEUTICALS