

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Date of Report (date of earliest event reported): November 12, 2024

CENTESSA PHARMACEUTICALS PLC

(Exact name of Registrant, as specified in its charter)

England and Wales

(State or other jurisdiction of incorporation)

001-40445

(Commission File Number)

98-1612294

(I.R.S. Employer Identification Number)

Mailing address:

3rd Floor

1 Ashley Road

Altrincham

Cheshire WA14 2DT

United Kingdom

(Address of principal executive offices) (Zip code)

Registrant's telephone number, including area code: **+1 (617) 468-5770**

Former name or address, if changed since last report:

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Ordinary shares, nominal value £0.002 per share	CNTA	Nasdaq Stock Market, LLC*
American Depositary Shares, each representing one ordinary share, nominal value £0.002 per share	CNTA	Nasdaq Stock Market, LLC

*Not for trading, but only in connection with the listing of the American Depositary Shares on The Nasdaq Stock Market, LLC.

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Item 2.02 Results of Operations and Financial Condition.

On November 12, 2024, Centessa Pharmaceuticals plc (the “Company”) announced its financial results for the quarter ended September 30, 2024. The full text of the press release issued in connection with the announcement is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

Item 7.01 Regulation FD Disclosure.

The Company from time to time presents and/or distributes slide presentations to the investment community at various industry and other conferences to provide updates and summaries of its business. The Company is posting a copy of its current corporate slide presentation to the “Investors” portion of its website at www.centessa.com/events-presentations. These slides are attached to this Current Report on Form 8-K as Exhibit 99.2. The Company undertakes no obligation to update, supplement or amend the materials attached hereto as Exhibit 99.1.

The information in this Current Report on Form 8-K (including Exhibits 99.1 and 99.2) shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

<u>Exhibit No.</u>	
99.1	Press Release dated November 12, 2024
99.2	Corporate Presentation dated November 2024
104	Cover Page Interactive Data (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: November 12, 2024

By:
Name:
Title:

Saurabh Saha, M.D., Ph.D.
Chief Executive Officer

Centessa Pharmaceuticals Reports Financial Results for the Third Quarter of 2024 and Provides Business Update

- *Announced additional interim data from ongoing Phase 1 clinical study of ORX750, a novel orexin receptor 2 (OX2R) agonist, in acutely sleep-deprived healthy volunteers that further support best-in-class potential of ORX750 in narcolepsy type 1 (NT1), narcolepsy type 2 (NT2), and idiopathic hypersomnia (IH); Presentation of Phase 1 data planned for medical congress in Q2 2025*
- *Initiated Phase 2a clinical study of ORX750 in patients with NT1, NT2 and IH; Phase 2a data across all three indications expected in 2025 with first-in-class potential in NT2 and IH*
- *Advancing ORX142 in IND-enabling studies for treatment of neurological, neurodegenerative, and psychiatric disorders; Clinical data in healthy volunteers planned for 2025*
- *Nominated ORX489 as third OX2R agonist development candidate; Entering IND-enabling studies for treatment of additional neurological, neurodegenerative, and psychiatric disorders*
- *Announced strategic decision to discontinue clinical development of SerpinPC; Net savings of approximately \$200 million to be reallocated towards expansion of OX2R agonist franchise*

BOSTON and LONDON, November 12, 2024: [Centessa Pharmaceuticals plc](#) (Nasdaq: CNTA), a clinical-stage pharmaceutical company with a mission to discover, develop and ultimately deliver medicines that are transformational for patients, today reported financial results for the third quarter ended September 30, 2024, and provided a business update.

“The totality of data across our OX2R agonist program continues to reinforce the strength of our discovery engine and the therapeutic potential of these assets across a broad spectrum of disorders,” said Saurabh Saha MD PhD, Chief Executive Officer of Centessa. “The Phase 1 interim data for ORX750, now updated to include over 70 subjects dosed with ORX750, continue to support its best-in-class potential in NT1, NT2 and IH. Based on the strength of these interim data, we recently initiated a Phase 2a clinical study of ORX750 in patients with NT1, NT2 and IH. Similar to our Phase 1 study, which enabled a move from IND clearance to clinical data in the course of a few months, we expect our Phase 2a study design to generate clinical data for all three indications in 2025 and enable dose selection for future pivotal studies with the potential to be first-in-class in NT2 and IH.”

Dr. Saha continued, “In addition to ORX750, we are advancing a growing pipeline of OX2R agonists targeting excessive daytime sleepiness (EDS) in neurological, neurodegenerative, and psychiatric disorders, as well as other potential symptoms including impaired attention, cognitive deficits, and fatigue. ORX142 is currently in IND-enabling studies, and subject to IND clearance, we expect to initiate clinical development and share clinical data in acutely sleep-deprived healthy volunteers in 2025. We’re also pleased to be kicking off our next wave of candidates with ORX489, our most potent OX2R agonist to date based on preclinical data, which is entering IND-enabling studies.”

Interim Data from Ongoing Phase 1 Clinical Study of ORX750

The additional interim data from the ongoing Phase 1 clinical trial of ORX750 in healthy volunteers includes results from two single-ascending dose (SAD) cohorts at 3.5 mg (n=12: 9 active, 3 placebo) and 5.0 mg (n=12: 9 active, 3 placebo), a cohort of acutely sleep-deprived healthy volunteers within the cross-over assessment at 3.5 mg (n=10) administered as a single oral dose, and two multiple-ascending dose (MAD) cohorts at 2.0 mg (n=10: 8 active, 2 placebo) and 3.0 mg (n=10: 8 active, 2 placebo). The interim data showed:

- Significantly increased wakefulness in acutely sleep-deprived healthy volunteers compared to placebo at all doses tested, with a clear dose dependent response. Treatment with ORX750 resulted in statistically significant (p<0.05) and clinically meaningful increased sleep latency in the Maintenance of Wakefulness Test (MWT) (time to sleep onset over the four sessions performed at ~2, 4, 6, and 8 hours after dosing at 11 p.m., maximum 40 minutes per session) compared to placebo at all doses tested. The 3.5 mg dose was shown to restore normative wakefulness¹ with a mean sleep latency of 34 minutes and a placebo-adjusted mean sleep latency of 20 minutes, as measured by the MWT.

**Interim Data from Ongoing Phase 1 Clinical Study of ORX750
(as of October 31, 2024 data cutoff date)**

	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

- A favorable safety and tolerability profile with all observed treatment-emergent adverse events (AEs) being mild and transient with none leading to treatment discontinuation. No cases of hepatotoxicity or visual disturbances were observed. Additionally, there were no clinically significant treatment-emergent changes in hepatic and renal parameters, vital signs, or electrocardiogram (ECG) parameters.

Interim Safety Data from Ongoing Phase 1 Clinical Study of ORX750
(as of October 31, 2024 data cutoff date)

	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

Treatment-emergent adverse event (TEAE). Safety data from Sleep Study Cohorts was consistent with SAD. Nonrelated includes unlikely related and not related. Related includes probably and possibly related.

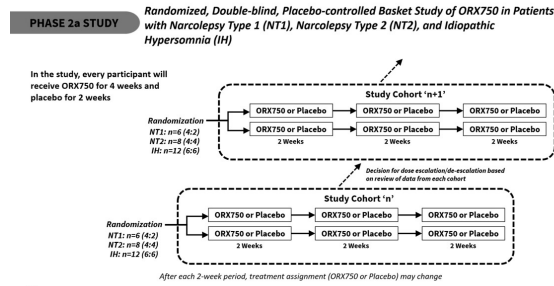
- An encouraging linear pharmacokinetic (PK) profile that supports the use of ORX750 as a once-daily oral dosing regimen with rapid absorption (plasma concentrations of ORX750 peaked 2h after the first dose). The systemic exposure of ORX750 increased in a dose-proportional manner.

The Phase 1 study is ongoing as dose escalation is continuing in the acutely sleep-deprived cross-over assessment, SAD and MAD portions of the study.

Phase 2a Clinical Study of ORX750

The Phase 2a study is a randomized, double-blind, placebo-controlled, cross-over basket study to evaluate the safety, tolerability, and PK of ORX750 in patients with NT1, NT2, and IH. There will be separate cohorts for each indication. Initial dosing for NT1 will be 1.0 mg and for NT2 and IH will be 2.0 mg with sequential dose escalation/

de-escalation between cohorts. Each dosing cohort consists of a 6-week treatment duration with crossover study design. During the 6 weeks of treatment, each participant will be randomized to one of two blinded treatment sequences and receive a total of 4 weeks of treatment with ORX750 and 2 weeks of treatment with placebo. Efficacy assessments will evaluate the effect of ORX750 on excessive daytime sleepiness (using the MWT and Epworth Sleepiness Scale (ESS)), cataplexy (NT1 patients only), and overall symptom improvement (measured by Narcolepsy Severity Scale (NSS) and Idiopathic Hypersomnia Severity Scale (IHSS)). Other exploratory assessments include measures of sleep, cognition, attention, memory, and general health.



“The Phase 2a study of ORX750 is intended to accelerate overall timelines and inform future registrational studies,” said Mario Alberto Accardi PhD, President of Centessa’s Orexin Program. “This well-powered study leverages highly innovative design elements which we believe have the potential to enable efficient data generation with an optimal number of patients in each indication. With this design, all participating patients will receive ORX750 for at least 4 weeks. We aim to generate data across all three indications in 2025, which could enable ORX750 to be first-in-class in NT2 and IH.”

SerpinPC Clinical Program Update

The Company has made a strategic and data-driven decision to discontinue the global clinical development of SerpinPC, a novel inhibitor of activated protein C that was being evaluated for the treatment of hemophilia B. This action was driven by the Company’s decision to prioritize capital toward the development of its OX2R agonist program and the outcome of a planned interim analysis of Part 1 of the PRESENT-2 study of SerpinPC. Within the interim analysis, SerpinPC was observed to have a favorable safety and tolerability profile; however, the Company determined that additional time and investment would be required to further develop SerpinPC with a more

competitive profile for the treatment of hemophilia B in light of the evolving treatment and market landscape for hemophilia B, including the recent FDA approval of a competing product. The Company would like to thank the hemophilia community and all the patients, caregivers and physicians who participated in the SerpinPC clinical trials. The Company is now exploring potential strategic alternatives for SerpinPC.

“Moving forward, we intend to prioritize our resources and reallocate net savings of approximately \$200 million associated with the planned commercial launch of SerpinPC towards expanding our potential best-in-class OX2R agonist franchise, where we see significant opportunities to both address unmet patient needs and create shareholder value,” stated John Crowley, Chief Financial Officer. “With a cash runway that extends into mid-2027, we believe Centessa is well positioned to support our OX2R agonist franchise through multiple, potential value-creating milestones.”

Recent Highlights

- In September, the Company presented preclinical data from non-human primate studies of ORX142 at the 27th Congress of the European Sleep Research Society (Sleep Europe 2024).
- In September, the Company completed an upsized underwritten public offering of 17,542,372 American Depositary Shares (ADSs) in the aggregate, at a price to the public of \$14.75 per ADS, resulting in net proceeds of approximately \$242.7 million, which included the underwriters’ over-allotment option to purchase additional shares.
- In September, the Company announced positive interim data from the ongoing Phase 1 clinical trial of ORX750 in acutely sleep-deprived healthy volunteers as of an August 26, 2024 data cutoff date.

Anticipated Upcoming Program Milestones

- **OX2R Agonist Program** –
 - **ORX750:** Subject to acceptance, a presentation of Phase 1 clinical data is planned at a medical conference in the second quarter of 2025. The Company expects to share Phase 2a data for NT1, NT2 and IH in 2025.
 - **ORX142:** Advancing through IND-enabling studies. The Company is focused on obtaining IND clearance and initiating clinical development with the goal of sharing clinical data in acutely sleep-deprived healthy volunteers in 2025.
 - **ORX489:** Entering IND-enabling studies.

- **OX2R Agonist Pipeline:** Progressing additional OX2R agonists as well as research efforts on differentiated pharmacology associated with the activation of the orexin system.
- **LockBody Technology Platform** – LB101 (PD-L1xCD47 LockBody) is in an ongoing Phase 1/2a first-in-human clinical study for the treatment of solid tumors.

Third Quarter 2024 Financial Results

- **Cash, Cash Equivalents and Short-term Investments:** \$518.4 million as of September 30, 2024. The Company expects its cash, cash equivalents and short-term investments as of September 30, 2024 will fund operations into mid-2027.
- **Research & Development Expenses:** \$33.9 million for the third quarter ended September 30, 2024, compared to \$28.2 million for the third quarter ended September 30, 2023.
- **General & Administrative Expenses:** \$12.5 million for the third quarter ended September 30, 2024, compared to \$12.0 million for the third quarter ended September 30, 2023.
- **Net Loss Attributable to Ordinary Shareholders:** \$42.6 million for the third quarter ended September 30, 2024, compared to \$38.6 million for the third quarter ended September 30, 2023.

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

About Centessa Pharmaceuticals

Centessa Pharmaceuticals plc is a clinical-stage pharmaceutical company that aims to discover and develop medicines that are transformational for patients. We are developing potential best-in-class orexin receptor 2 (OX2R) agonists intended to be orally administered for the treatment of sleep-wake disorders including narcolepsy type 1 (NT1), narcolepsy type 2 (NT2) and idiopathic hypersomnia (IH), and excessive daytime sleepiness (EDS) in neurological, neurodegenerative, and psychiatric conditions. We also anticipate that our orexin agonists may have utility in treating impaired attention, cognitive deficits, fatigue, and other symptoms. Our lead OX2R agonist, ORX750, is currently being evaluated in Phase 1 and Phase 2 clinical trials for NT1, NT2 and IH. ORX750 has not been approved by the FDA or any other regulatory authority. Centessa's proprietary LockBody technology platform aims to redefine immuno-oncology treatment for patients with cancer. LockBody drug candidates are designed to selectively drive potent effector function activity, such as CD47 or CD3, to the tumor micro-environment (TME) while avoiding systemic toxicity. LB101 has not been approved by the FDA or any other regulatory authority.

Forward Looking Statements

This press release contains forward-looking statements. These statements may be identified by 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 that are intended to identify forward-looking statements. Any such statements in this press release that are not statements of historical fact may be deemed to be forward-looking statements, including statements related to the Company’s ability to discover and develop transformational medicines for patients; its expectations for executing on the Company’s pipeline; its expectations on its anticipated cash runway; the timing of commencement of new studies or clinical trials or clinical and preclinical data related to ORX750, ORX142, ORX489 and other OX2R agonist molecules, LB101, other LockBody candidates, and the LockBody technology platform; its ability to identify, screen, recruit and maintain a sufficient number of or any subjects in its existing and anticipated studies or clinical trials of ORX750, ORX142, ORX489 and other OX2R agonist molecules, LB101 and any other LockBody candidates; its expectations on executing its research and clinical development plans and the timing thereof; its expectations as to the potential results and impact of each of its clinical programs and trials; the Company’s ability to differentiate ORX750, ORX142, ORX489 and other OX2R agonist molecules, LB101, other LockBody candidates from other treatment options; the development, design and therapeutic potential of ORX750, ORX142, ORX489 and other OX2R agonist molecules, LB101, other LockBody candidates and the LockBody technology platform; the anticipated net savings associated with the discontinuation of the

SerpinPC program; and regulatory matters, including the timing and likelihood of success of obtaining regulatory clearance, obtaining authorizations to initiate or continue clinical trials. Any forward-looking statements in this press release are based on our current expectations, estimates, assumptions and projections only as of the date of this release and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to, risks related to the safety and tolerability profile of our product candidates; our ability to identify, screen and recruit a sufficient number of or any subjects in our existing and anticipated new studies or clinical trials of ORX750, ORX142, ORX489 or LB101 or within anticipated timelines; our expectations relating to the clinical trials of ORX750, including the predicted timing of enrollment, the predicted efficacious doses of ORX750 and our ability to successfully conduct our clinical development of ORX750, our ability to protect and maintain our intellectual property position; business (including commercial viability), regulatory, economic and competitive risks, uncertainties, contingencies and assumptions about the Company; risks inherent in developing product candidates 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; our operating costs and use of cash, including cash runway, cost of development activities and conducting clinical trials, future expenditures risks; the risk that any one or more of our product candidates will not be successfully developed and/or commercialized; the risk that the historical results of preclinical studies or clinical studies will not be predictive of future results in ongoing or future studies; economic risks to the United States and United Kingdom banking systems; and geo-political risks such as the Russia-Ukraine war or the Middle East conflicts. These and other risks concerning our programs and operations are described in additional detail in our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and our other reports, which are on file with the U.S. Securities and Exchange Commission (SEC). We explicitly disclaim any obligation to update any forward-looking statements except to the extent required by law.

Contact:

Kristen K. Sheppard, Esq.
SVP of Investor Relations
investors@centessa.com

Centessa Pharmaceuticals plc
Consolidated Statements of Operations and Comprehensive Loss
(unaudited)
(amounts in thousands except share and per share data)

	Three Months Ended September 30, 2024	Three Months Ended September 30, 2023	Nine Months Ended September 30, 2024	Nine Months Ended September 30, 2023
Operating expenses:				
Research and development	\$ 33,903	\$ 28,190	\$ 89,370	\$ 94,689
General and administrative	12,502	12,019	37,105	41,416
Loss from operations	(46,405)	(40,209)	(126,475)	(136,105)
Interest income	3,340	2,953	9,171	7,543
Interest expense	(2,557)	(2,541)	(7,611)	(7,336)
Other income (expense), net	3,664	(1,677)	2,281	(4,550)
Loss before income taxes	(41,958)	(41,474)	(122,634)	(140,448)
Income tax expense (benefit)	608	(2,826)	1,794	(26,200)
Net loss	(42,566)	(38,648)	(124,428)	(114,248)
Other comprehensive income (loss):				
Foreign currency translation adjustment	(412)	(419)	(498)	1,241
Unrealized gain on available for sale securities, net of tax	912	252	1,100	1,035
Other comprehensive income (loss)	500	(167)	602	2,276
Total comprehensive loss	\$ (42,066)	\$ (38,815)	\$ (123,826)	\$ (111,972)
Net loss per ordinary share - basic and diluted	\$ (0.37)	\$ (0.40)	\$ (1.15)	\$ (1.20)
Weighted average ordinary shares outstanding - basic and diluted	116,253,902	96,648,110	108,571,742	95,589,181

Centessa Pharmaceuticals plc
Condensed Consolidated Balance Sheets
(unaudited)
(amounts in thousands)

	September 30, 2024	December 31, 2023
Total assets:		
Cash and cash equivalents	\$ 395,026	\$ 128,030
Short-term investments	123,423	128,519
Other assets	91,266	103,697
Total assets	\$ 609,715	\$ 360,246
Total liabilities		
Other liabilities	\$ 34,878	\$ 48,302
Long term debt	75,700	75,700
Total liabilities	110,578	124,002
Total shareholders' equity	499,137	236,244
Total liabilities and shareholders' equity	\$ 609,715	\$ 360,246



CENTESSA
P H A R M A C E U T I C A L S

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

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

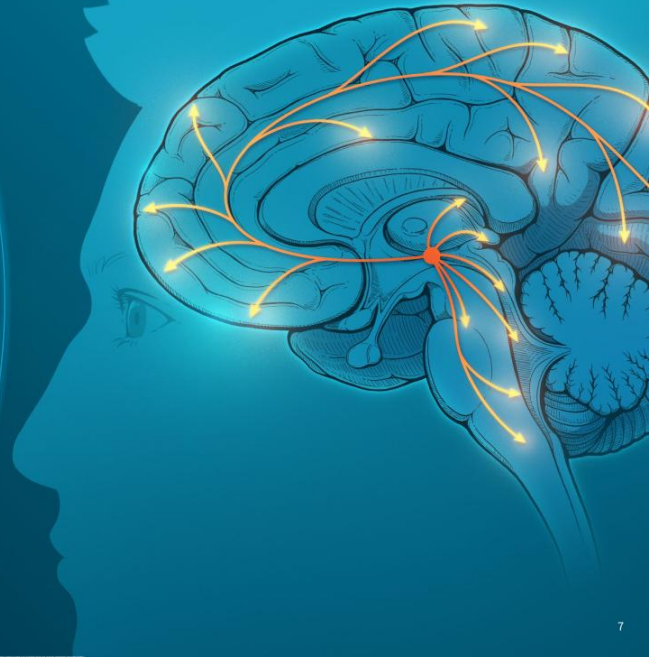
LB101

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***

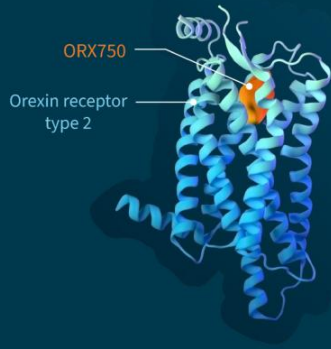


Centessa is Developing a Pipeline of Potential Best-in-Class / First-in-Class Orexin Receptor 2 (OX2R) Agonists

- **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 absorption¹
- ✓ 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 date¹

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

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

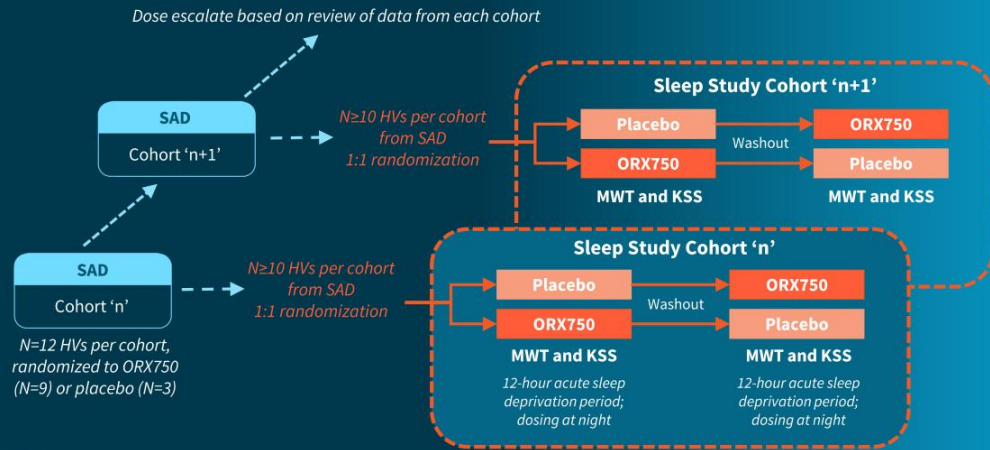
In parallel

- 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.



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.

	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



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 pharmacokinetics 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)

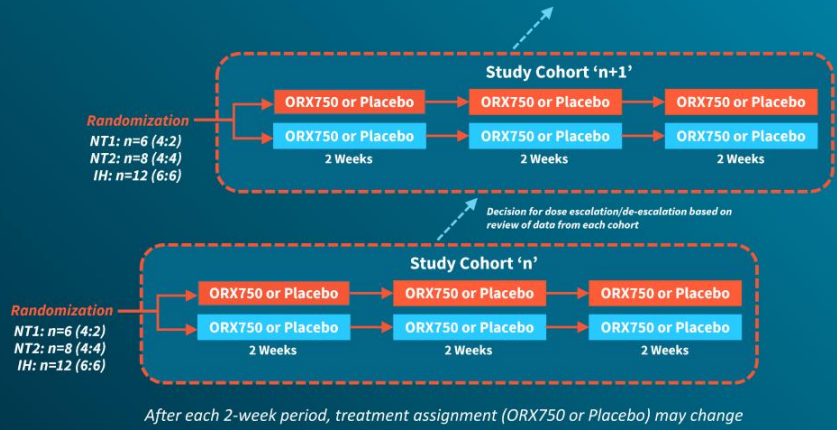


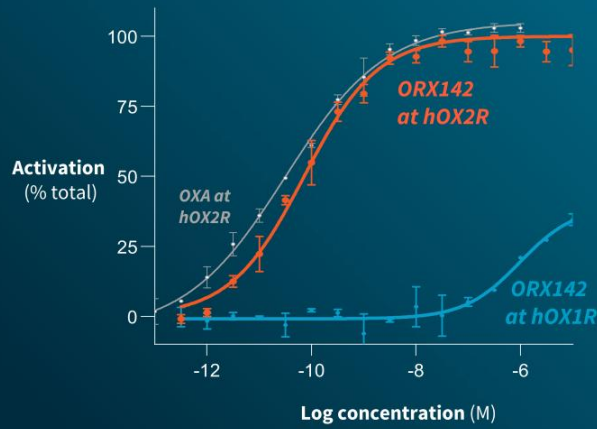
PHASE 2a STUDY

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





EC_{50} 0.069 nM for hOX2R
>13,000-fold selectivity vs. hOX1R

- Activation pattern was comparable to OXA with lack of biased agonism¹
- No significant differences in OX2R potency were observed across species²
- No significant pharmacological activity observed in GPCR selectivity and in vitro safety panels³

Fluorescent imaging plate reader (FLIPR) assay with Chinese hamster ovary (CHO) cells stably expressing recombinant human OX1R or OX2R; OXA

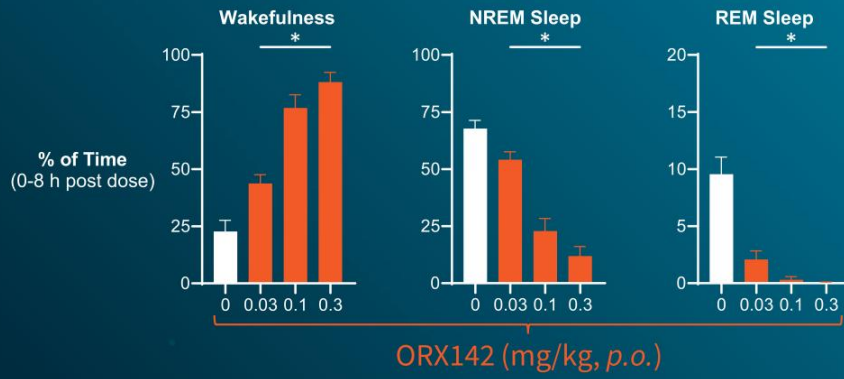
EC_{50} at hOX2R = 0.035 nM; ORX142 EC_{50} at hOX1R = 930 nM.

¹ Calculated from FLIPR Ca^{2+} mobilization and Pathhunter β -arrestin recruitment assays

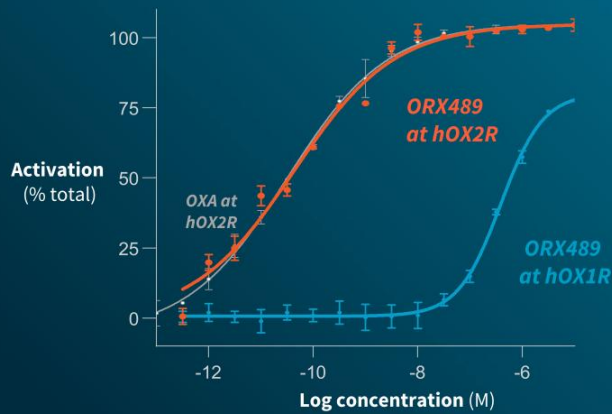
² Human, mouse, rat, dog, monkey recombinant receptors *in vitro*.

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

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)



EC_{50} 0.035 nM for hOX2R
8,800-fold selectivity vs. hOX1R

- Activation pattern was indistinguishable from OXA with lack of biased agonism¹
- No significant differences in OX2R potency were observed across species²
- No significant pharmacological activity observed in GPCR selectivity and in vitro safety panels³

Fluorescent imaging plate reader (FIPR) assay with Chinese hamster ovary (CHO) cells stably expressing recombinant human OX1R or OX2R; OXA

EC_{50} at hOX2R = 0.035 nM; ORX489 EC_{50} 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.

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



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**

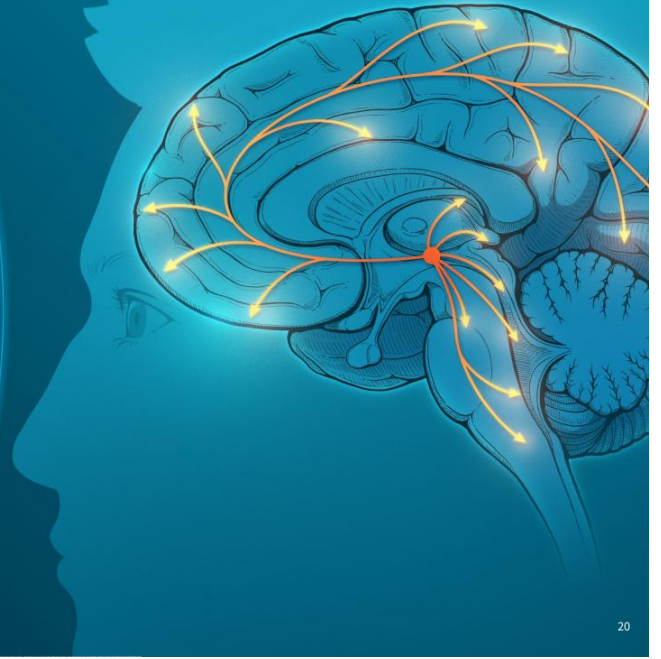
Presentation of Phase 1 data planned for **Q2 2025**

ORX142

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

ORX489

Entering IND-enabling studies



Orexin Agonist
Program

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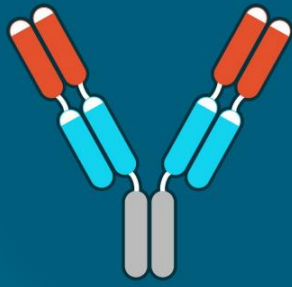
**LockBody Technology
Platform aims to *redefine*
immuno-oncology
treatment**

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



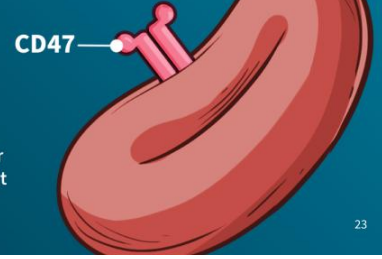
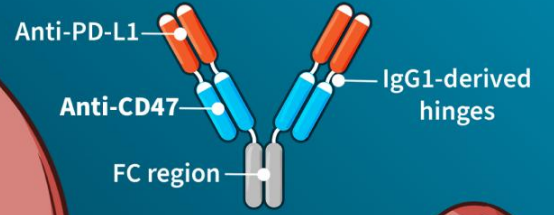
LB101 is an investigational agent that has not been approved by the FDA or any other regulatory authority. Information on the Phase 1/2a trial of LB101 can be accessed at www.clinicaltrials.gov (NCT05821777). 1. LB101 *in-vivo* preclinical data: MC38 hPD-L1+ syngeneic model in mouse, and in non-human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

Locked Configuration



LockBody LB101

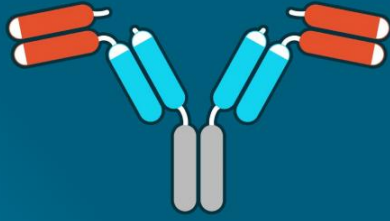
Conditionally tetravalent PD-L1xCD47 bispecific monoclonal antibody



Outside the tumor microenvironment

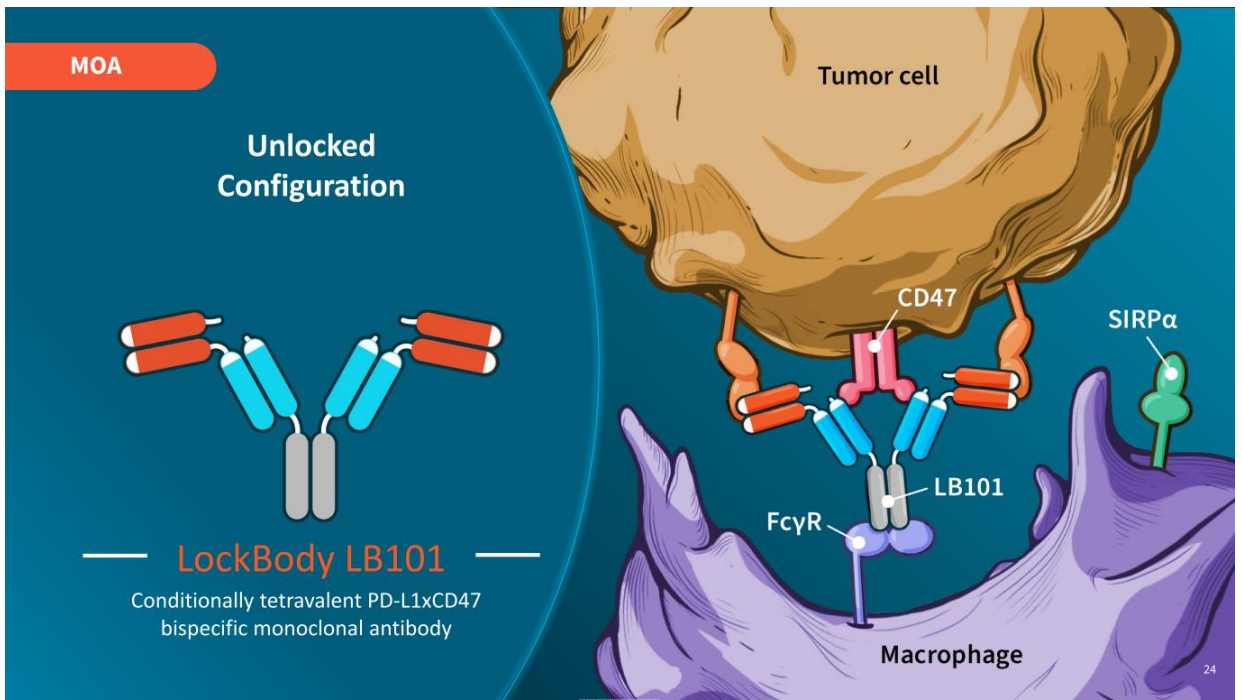
MOA

Unlocked
Configuration



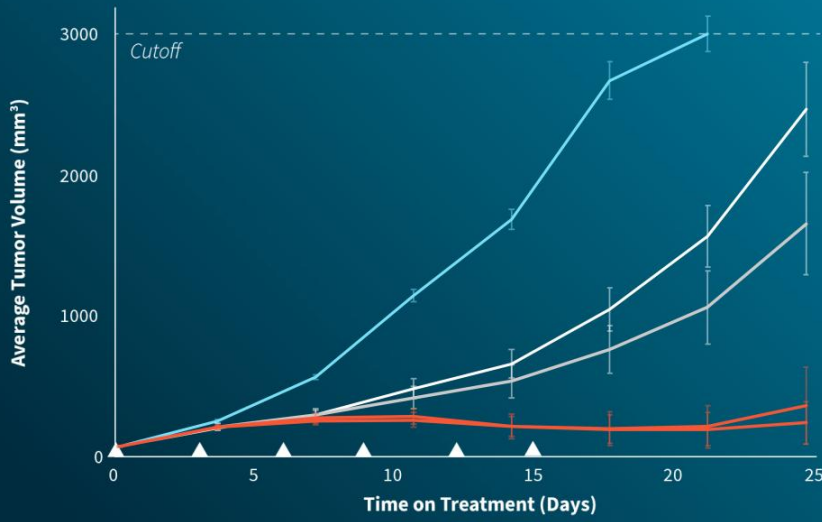
LockBody LB101

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



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**

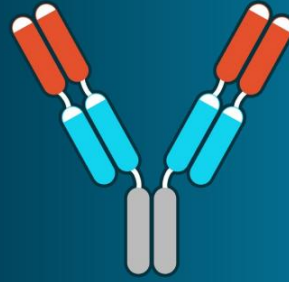


No weight loss



**No change in red blood
cell or hemoglobin**

*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 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

