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): August 14, 2023

CENTESSA PHARMACEUTICALS PLC

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

England and Wales	**001-40445**	**98-1612294**
(State or other jurisdiction of incorporation)	(Commission File Number)	(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: **+44 7391 789784**

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 August 14, 2023, Centessa Pharmaceuticals plc (the "Company") announced its financial results for the quarter ended June 30, 2023. 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

Exhibit No.	
99.1	Press Release dated August 14, 2023
99.2	Corporate Presentation prepared as of August 14, 2023
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: August 14, 2023

By:	/s/ Saurabh Saha
Name:	Saurabh Saha, M.D., Ph.D.
Title:	Chief Executive Officer

Exhibit 99.1

Centessa Pharmaceuticals Reports Financial Results and Business Highlights for the Second Quarter of 2023

- *Enrollment and dosing ongoing in registrational study of SerpinPC for the treatment of hemophilia B*
- *Enrollment and dosing ongoing in Phase 1/2a Study of LB101, a PD-L1xCD47 LockBody® for the treatment of solid tumors*
- *IND-enabling activities advancing for ORX750, an oral selective orexin receptor 2 (OX2R) agonist for the treatment of narcolepsy and other sleep disorders; Announces ORX750 preclinical data to be presented at World Sleep Congress in October 2023*
- *Nominates second LockBody candidate, LB206, a conditionally bivalent PD-L1xCD3 bispecific monoclonal antibody*

BOSTON and LONDON, August 14, 2023: Centessa Pharmaceuticals plc (Nasdaq: CNTA), a clinical-stage pharmaceutical company focused on discovering and developing medicines that are transformational for patients, today reported financial results and business highlights for the second quarter ended June 30, 2023.

“This is an exciting time for Centessa as we continue to execute across our portfolio with the goal of bringing transformative medicines to patients with unmet needs,” said Saurabh Saha MD PhD, Chief Executive Officer of Centessa. “We recently commenced dosing in our registrational PRESent-2 study of SerpinPC for the treatment of hemophilia B without inhibitors and are now enrolling subjects across multiple global sites. To date, clinical data support SerpinPC's potential to be a first-in-class subcutaneously administered therapy with a differentiated safety profile for persons with hemophilia B. In the months ahead, we plan to share new data from subjects with approximately 3 years of continuous treatment with SerpinPC from the ongoing Phase 2a study.”

“We are also making great progress with our LockBody technology platform, enrolling and dosing subjects in the ongoing Phase 1/2a clinical trial of LB101, a PD-L1xCD47 LockBody molecule for the treatment of solid tumors. In addition, we are excited to announce LB206, a conditionally bivalent PD-L1xCD3 bispecific monoclonal antibody, as our second LockBody development candidate for the treatment of solid tumors, and share encouraging preclinical data for LB206 which demonstrated the potential of our LockBody technology to selectively drive potent CD3 activity within solid tumors in a difficult-to-treat mouse xenograft model with no apparent observed toxicity. We believe this progress marks an important milestone in advancing our novel LockBody technology platform,” said Dr. Saha.

“In parallel with progress on our two clinical programs, we are advancing ORX750, our first oral selective orexin receptor 2 (OX2R) agonist development candidate, through IND enabling studies for the treatment of narcolepsy, and are thrilled to present preclinical data for ORX750 at the World Sleep Congress in October 2023,” said Dr. Saha. “We are also excited to be exploring follow-up orexin agonists for potential expansion opportunities into a range of high value sleep disorders and broader neurological indications. With a team comprised of experienced and insightful scientists in the orexin field, we believe Centessa is well-positioned to play a leading role in orexin agonist development.”

Dr. Saha concluded, “We have line of sight to multiple potential clinical milestones expected over the next several quarters and with a cash runway into 2026, we believe we are well positioned to advance our pipeline of potentially transformative medicines and deliver value for our stakeholders.”

Recent Highlights

- Today, the Company shared new preclinical data for LB206, a PD-L1xCD3 LockBody development candidate, which demonstrated single agent regressions of large tumors in a difficult-to-treat mouse xenograft model. The preclinical data is shown in the Company’s corporate overview for August 2023 which is available at https://investors.centessa.com/events-presentations.
- In July, the Company announced the dosing of the first subject in its registrational PRESent-2 clinical study of SerpinPC for the treatment of hemophilia B without inhibitors. SerpinPC is an investigational subcutaneously administered novel inhibitor of activated protein C (APC).
- In May, the Company announced that the U.S. Food and Drug Administration (FDA) has granted Fast Track designation to SerpinPC for the treatment of hemophilia B, with or without inhibitors.

Anticipated Upcoming Program Milestones

- **Hemophilia (SerpinPC) -** The global registrational program for hemophilia B is ongoing. PRESent-5, an observational feeder study, continues enrolling subjects and the Company has commenced dosing in the registrational PRESent-2 clinical study of hemophilia B without inhibitors. Dosing in the registrational PRESent-3 clinical study of hemophilia B with inhibitors, is expected to begin this year. In addition, the Company expects to share data from Part 5 of the ongoing Phase 2a study of SerpinPC at a scientific meeting later this year.
- **Solid Tumors**
    - **PD-L1xCD47 LockBody (LB101) -** The Phase 1/2a first-in-human clinical study is ongoing.
    - **PD-L1xCD3 LockBody (LB206) -** LB206 has been named as a development candidate.

- **Narcolepsy and Other Sleep Disorders (ORX750)** - ORX750 is undergoing IND-enabling activities. The Company plans to share preclinical data on ORX750 at the World Sleep Congress taking place from October 20-25, 2023, in Rio de Janeiro, Brazil.

The Company has multiple earlier-stage preclinical assets including additional orexin agonists and discovery-stage programs. Where applicable, the Company plans to provide updates on preclinical programs as they advance toward clinical studies.

Second Quarter 2023 Financial Results

- **Cash, Cash Equivalents and Short-term Investments:** $303.6 million as of June 30, 2023. In addition, the Company received approximately $15.0 million in gross proceeds through ATM sales in August 2023. The Company expects its current cash, cash equivalents and short-term investments will fund operations into 2026, without drawing on the remaining available tranches under the Oberland credit facility.
- **Research & Development Expenses:** $33.7 million for the second quarter ended June 30, 2023, compared to $53.7 million for the second quarter ended June 30, 2022.
- **General & Administrative Expenses**: $13.3 million for the second quarter ended June 30, 2023, compared to $14.8 million the second quarter ended June 30, 2022.
- **Net Loss Attributable to Ordinary Shareholders:** $24.9 million for the second quarter ended June 30, 2023, compared to $64.7 million for the second quarter ended June 30, 2022. The net loss for the second quarter of 2023 included a tax benefit of $24.1 million, which primarily relates to a release of a valuation allowance on certain U.S. deferred tax assets in the quarter.

About Centessa Pharmaceuticals

Centessa Pharmaceuticals plc is a clinical-stage pharmaceutical company that aims to discover and develop medicines that are transformational for patients. Our programs span discovery-stage to late-stage development and cover a range of high-value indications. We operate with the conviction that each one of our programs has the potential to change the current treatment paradigm and establish a new standard of care. For more information, visit http://www.centessa.com/, which does not form part of this release.

About SerpinPC

SerpinPC is a subcutaneously administered novel inhibitor of APC being developed as a potential treatment for hemophilia, regardless of severity or inhibitor status, and which may also be developed to prevent bleeding associated with other bleeding disorders. The ongoing registrational program for

SerpinPC in hemophilia B includes a set of clinical studies with multiple components. PRESent-5 is an observational feeder study to collect prospective observational data for minimum defined periods before switching to dosing subjects in the interventional studies. The interventional studies include PRESent-2 (moderately severe to severe hemophilia B without inhibitors, and severe hemophilia A with or without inhibitors) and PRESent-3 (hemophilia B with inhibitors). Additional information on the trials can be accessed at www.clinicaltrials.gov (NCT05605678, NCT05789524, NCT05789537). The U.S. Food and Drug Administration (FDA) has granted Fast Track designation to SerpinPC for the treatment of hemophilia B, with or without inhibitors. SerpinPC is an investigational agent that has not been approved by the FDA or any other regulatory authority.

About the LockBody Technology Platform and LB101

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. The first LockBody candidate is LB101, a conditionally tetravalent PD-L1xCD47 bispecific monoclonal antibody which has two anti-CD47 domains blocked by two anti-PD-L1 domains, with proprietary human IgG-derived hinges linking the anti-CD47 and anti-PD-L1 domains. The cell-killing mechanism of action, CD47, is designed to be blocked by the PD-L1 tumor targeting domain until the IgG-derived hinges are naturally degraded in the TME, thus unlocking and activating the CD47 effector function activity in the tumor. LB101 is in a Phase 1/2a clinical trial. Additional information on the trial can be accessed at www.clinicaltrials.gov (NCT05821777). LB101 is an investigational agent that 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 cash runway into 2026; the timing of commencement of new studies or clinical trials or clinical and preclinical data related to SerpinPC, LB101, LB206, other LockBody candidates, the LockBody technology platform, ORX750 and other orexin agonist molecules; its ability to identify, screen and recruit a sufficient number of or any subjects in its existing and anticipated studies or clinical trials including PRESent-5, the observational feeder study, PRESent-2 and PRESent-3 and studies or trials of LB101, LB206, and any other LockBody candidates, ORX750 and other orexin agonist molecules and its expectations on executing its research and clinical development plans and the timing thereof; the Company's ability to differentiate SerpinPC, LB101, LB206, ORX750, other orexin agonist molecules, and other LockBody candidates from other treatment options; the development and therapeutic potential of SerpinPC, LB101, LB206, other LockBody candidates, the LockBody technology platform, ORX750 and other orexin agonist molecules; and regulatory matters, including the timing and likelihood of success of 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 anticipated new studies or clinical trials including PRESent-2, PRESent-3, PRESent-5, and studies or trials of LB101 or within anticipated timelines; our ability to execute IND-enabling activities in a timely manner or at all, including with respect to ORX750 and LB206; 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; future expenditures risks related to our asset-centric corporate model; the risk that any one or more of our product candidates will not be successfully developed and/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.

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 June 30, 2023	Three Months Ended June 30, 2022	Six Months Ended June 30, 2023	Six Months Ended June 30, 2022
Operating expenses:				
Research and development	$ 33,673	$ 53,651	$ 66,499	$ 90,504
General and administrative	13,346	14,763	29,397	29,148
Change in fair value of contingent value rights	—	—	—	1,980
Loss from operations	(47,019)	(68,414)	(95,896)	(121,632)
Interest income	2,059	25	4,590	129
Interest expense	(2,450)	(1,653)	(4,795)	(3,153)
Other (expense) income, net	(1,527)	5,359	(2,873)	5,555
Loss before income taxes	(48,937)	(64,683)	(98,974)	(119,101)
Income tax (benefit) expense	(24,051)	(22)	(23,374)	58
Net loss	(24,886)	(64,661)	(75,600)	(119,159)
Other comprehensive income (loss):				
Foreign currency translation adjustment	762	(1,124)	1,660	(1,830)
Unrealized gain on available for sale securities, net of tax	783	—	783	—
Other comprehensive income (loss)	1,545	(1,124)	2,443	(1,830)
Total comprehensive loss	$ (23,341)	$ (65,785)	$ (73,157)	$ (120,989)
Net loss per ordinary share - basic and diluted	$ (0.26)	$ (0.69)	$ (0.80)	$ (1.29)
Weighted average ordinary shares outstanding - basic and diluted	95,162,734	94,109,089	95,050,940	92,317,172

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

	June 30, 2023	December 31, 2022
Total assets:		
Cash and cash equivalents	$ 145,220	$ 393,644
Short-term investments	158,367	—
Other assets	89,334	50,663
Total assets	$ 392,921	$ 444,307
Total liabilities		
Other liabilities	$ 43,015	$ 38,338
Long term debt	73,300	69,800
Total liabilities	$ 116,315	$ 108,138
Total shareholders’ equity	$ 276,606	$ 336,169
Total liabilities and shareholders' equity	$ 392,921	$ 444,307


CENTESSA
PHARMACEUTICALS
Corporate
Overview
Asset-Centric. Patient-Centric.
AUGUST 2023

Disclaimer

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

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

Discovering and developing medicines that are transformational for patients

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

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

DIFFERENTIATION

We are a transformational pharmaceutical company fueling an innovative pipeline

MULTIPLE PATHWAYS TO SIGNIFICANT VALUE CREATION

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

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

*Source: [1]Evaluate Pharma 2021 and internal estimates

INNOVATIVE PIPELINE

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

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

CASH RUNWAY INTO 2026 ENABLES MULTIPLE CLINICAL READOUTS

CENTESSA PHARMACEUTICALS

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

LEADERSHIP

Team with deep R&D experience and focused on execution

SAURABH SAHA MD PhD
Chief Executive Officer
Bristol Myers Squibb · NOVARTIS · Delinia · ATLAS VENTURE · McKinsey&Company

ANTOINE YVER MD MSc
EVP & Chairman of Development
Johnson&Johnson · AstraZeneca · Schering-Plough · MERCK · RHÔNE-POULENC · Aventis

DAVID GRAINGER PhD
Chief Innovation Officer
medicxi · RxCelerate · totalscientific · Index Ventures

IQBAL HUSSAIN
General Counsel
ReedSmith · SLAUGHTER AND MAY · ROPES&GRAY · Johnson&Johnson

GREG WEINHOFF MD MBA
Chief Financial Officer
ARVELLE THERAPEUTICS · CHL HEALTHCARE PARTNERS · Morgan Stanley · Amicus Therapeutics · AXOVANT

TIA BUSH
Chief Technology & Quality Officer
AMGEN

DAVID CHAO PhD
Chief Administrative Officer
BIOMED VALLEY DISCOVERIES · XO · McKinsey&Company · NOVARTIS

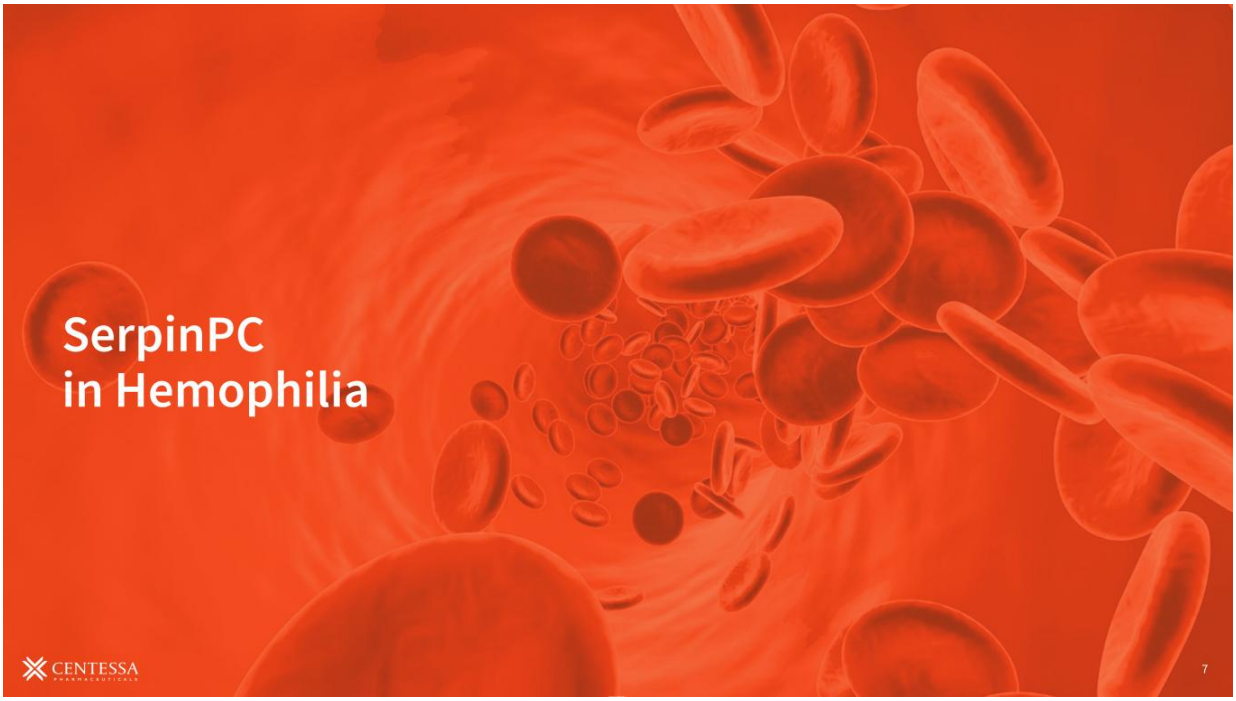
KAREN ANDERSON
Chief People Officer
Baxter · BAYER · Alnylam · Biogen · mimecast

KRISTEN SHEPPARD ESQ
SVP, Investor Relations & Corp. Comm.
Dicerna · STAGE · Akebia · EQUALLOGIC · enteromics

HARRIS ROTMAN PhD
SVP, Regulatory Affairs
SANOFI · Shire · Wyeth · endo · SwanBio

PATRICK YUE MD
SVP, Clinical Development
GBT · GILEAD · PORTOLA

CENTESSA PHARMACEUTICALS


SerpinPC
in Hemophilia
CENTESSA
PHARMACEUTICALS
7

SerpinPC: Novel, subcutaneously administered biologic inhibitor of APC

In registrational studies for the treatment of hemophilia B

HEMOPHILIA B UNMET NEED

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

Data for potentially competitive agents has shown potential risk of thrombosis

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

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

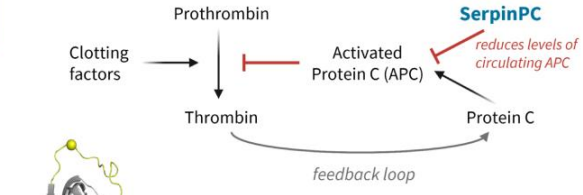
Shown to have a **favorable safety and well tolerated profile**[2]; **No thrombosis** observed[2]

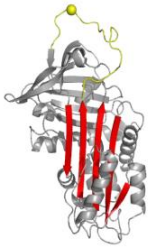
Designed as **convenient subcutaneous injection**

SerpinPC is an investigational serine protease inhibitor (SERPIN) engineered to specifically inhibit activated protein C (APC), that has not been approved by the FDA or any other regulatory authority. MoA is mechanism of action. Source: 1. Evaluate Pharma 2021. 2. Ongoing Phase 2a Study (AP-0101) being conducted in Georgia and Moldova to evaluate safety, tolerability, pharmacokinetics and efficacy of SerpinPC in a population of severe hemophilia A and B subjects not on previous prophylaxis and with a history of frequent bleeding.

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

Primary APC is the target of SerpinPC





3D-model of SerpinPC

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

SerpinPC

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

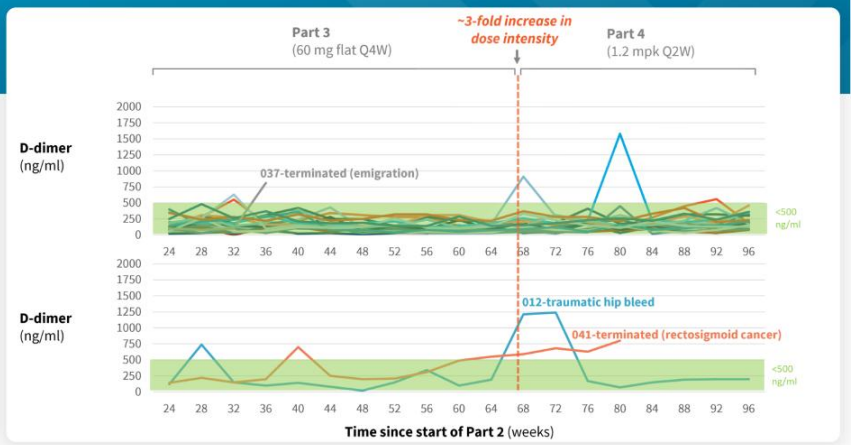
SerpinPC Phase 2a Study

Robust and highly differentiating clinical data

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

Favorable Safety Profile[1,2]

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



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

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

SerpinPC Phase 2a Study

Robust and highly differentiating clinical data

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

Favorable Tolerability Profile[1]

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

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

* Determined by Safety Review Group

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

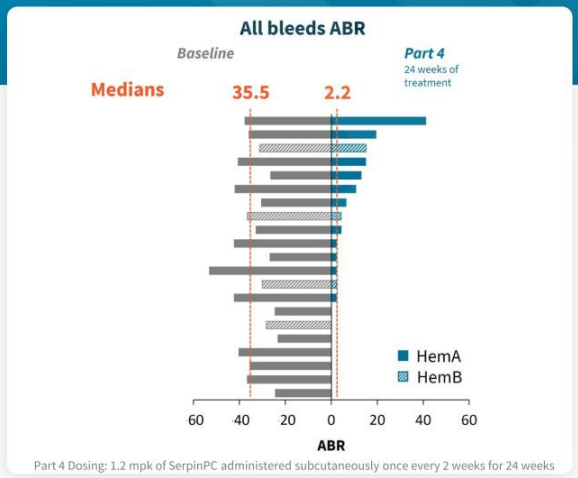
SerpinPC Phase 2a Study

Robust and highly differentiating clinical data

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

Reduction in Bleeding[1]

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



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

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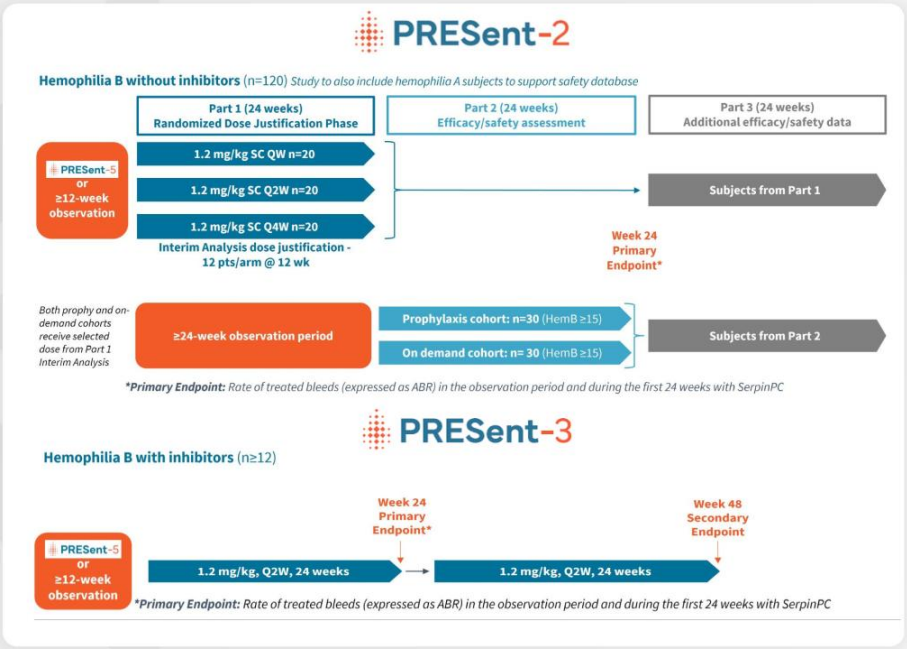
ABR is annualized bleeding rate.

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

SerpinPC

In registrational studies for hemophilia B, with or without inhibitors

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



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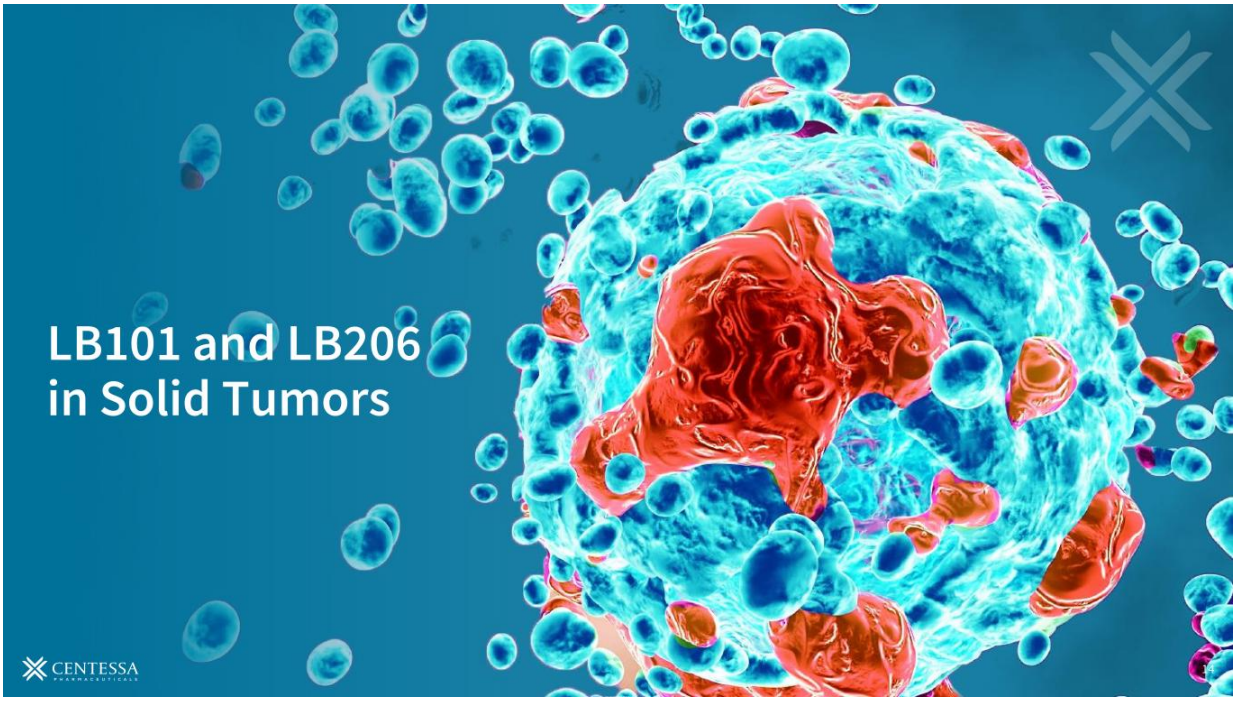
SerpinPC has not been approved by the FDA or any other regulatory authority.

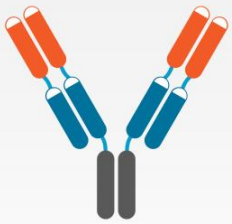

LB101 and LB206
in Solid Tumors
CENTESSA

LockBody Technology Platform: Aims to redefine immuno-oncology treatment

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

LockBody®

"It's all about the hinge"



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

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

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

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

LB206 (PD-L1xCD3) development candidate

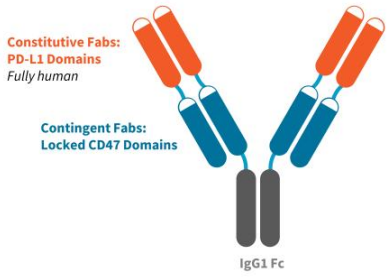
CENTESSA PHARMACEUTICALS

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

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

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

LOCKED

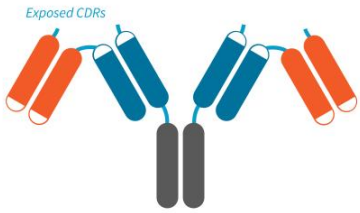


Peripheral Stability: IgG1 hinges naturally resistant to cleavage in serum

1. Constitutive Fabs drive tumor enrichment

2. Natural cleavage of IgG-derived hinges in tumors

UNLOCKED

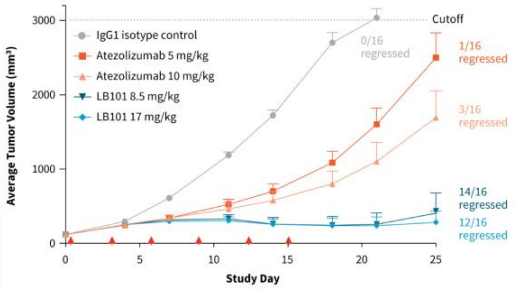


Tumor Unlocking: IgG1 hinges susceptible to cleavage in diseased tissue by various natural processes

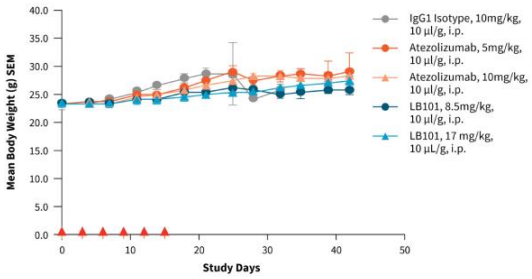
TME is tumor micro-environment

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

In vivo study showed systemically delivered LB101 exhibited significant tumor regression



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



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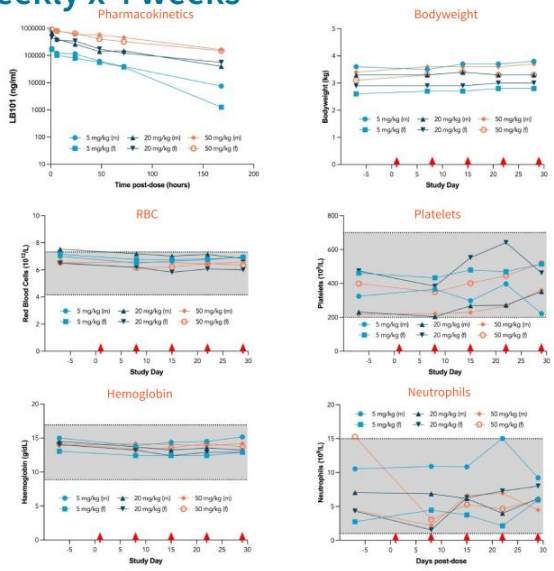
Note: MC38 hPD-L1+ syngeneic model in mouse; Arrows indicate dosing every 3 days (Q3d x 6) at Days 0, 3, 6, 9, 12, and 15. 5 mg/kg of atezolizumab is equivalent to 8.5 mg/kg of LB101.

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

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

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



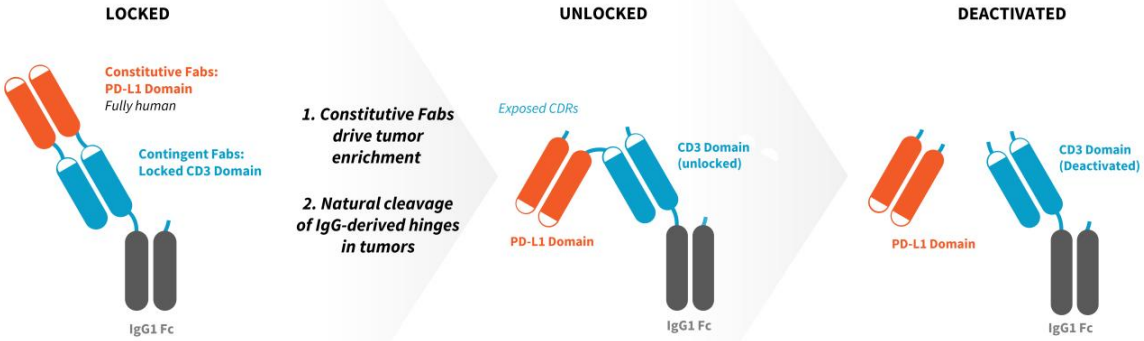
LB101 LockBody in Phase 1/2a Clinical Trial

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

Phase 1/2a Clinical Trial

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

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



Peripheral Stability: IgG1 hinges naturally resistant to cleavage in serum

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

Deactivation: Second cleaving event terminates CD3 activity

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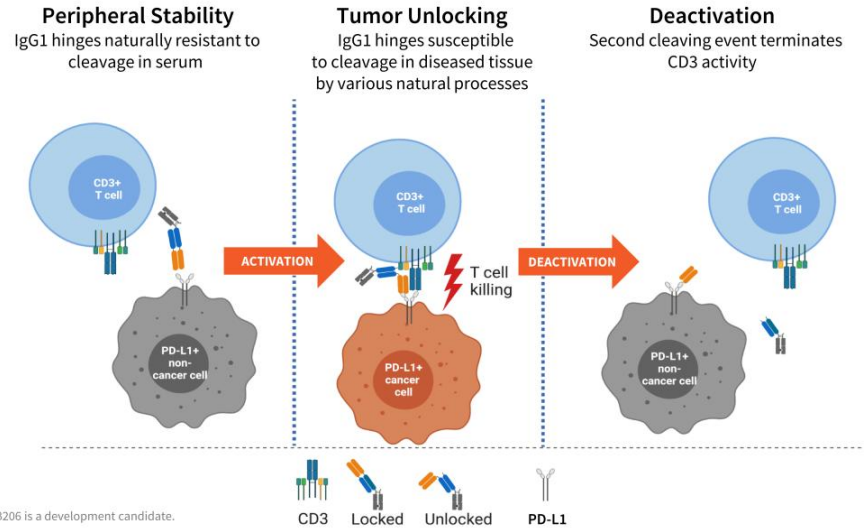
LB206 is a development candidate.

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



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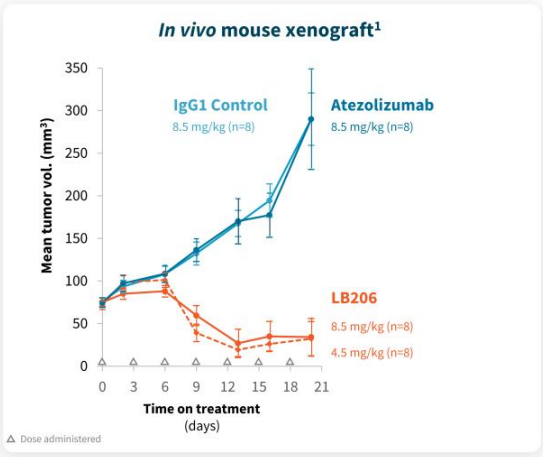
LB206 is a development candidate.

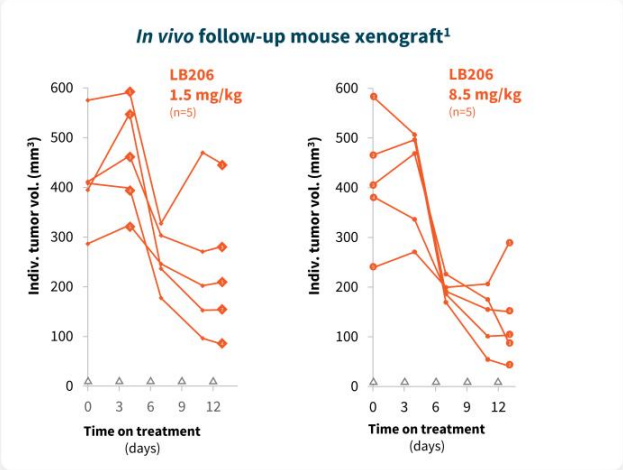
LB206: *In vivo* data demonstrated significant tumor regressions with LB206 in a difficult-to-treat mouse model

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

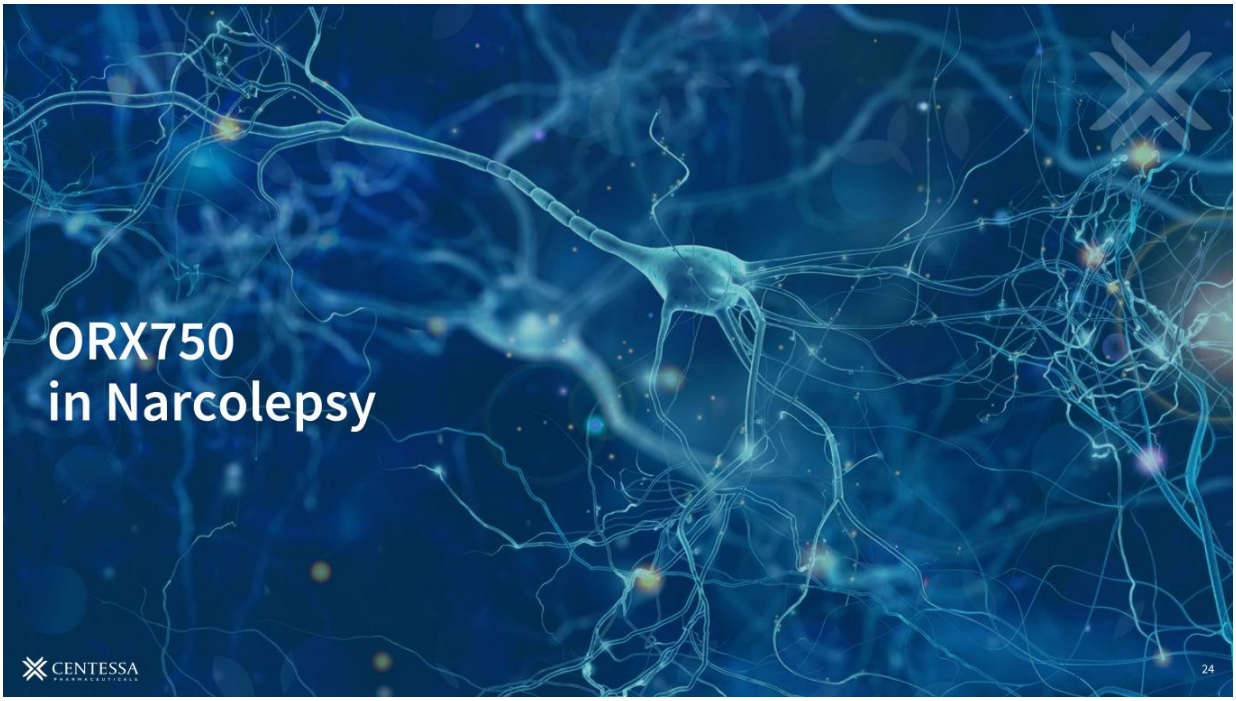


[1] Mean body weight values for Day 0 and Day 20 within +/- 6% range for each of the four groups. LB206 is a PD-L1xCD3 development candidate.

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



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


ORX750
in Narcolepsy
CENTESSA
PHARMACEUTICALS
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ORX750: Orally administered, selective orexin receptor-2 (OX2R) agonist

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

Narcolepsy Type 1 (NT1)

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

Caused by a profound loss of orexin neurons in the brain

High unmet need

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

75% patients experience EDS[1]

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

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

Highly validated human target with clinical proof of concept in NT1

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

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

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

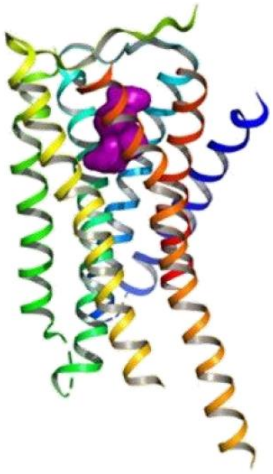

Illustration of OX2R structure
bound to prototype small molecule orexin agonist
(shown in purple)

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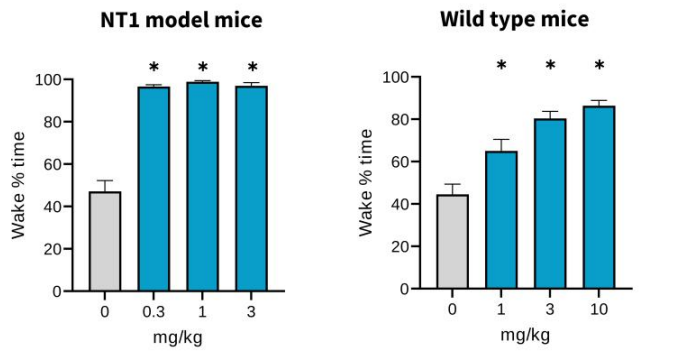
ORX750 increased wakefulness in NT1 model and wild type mice



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

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

*P < 0.05 vs. 0 mg/kg

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

Centessa is fueling multiple pathways to value creation

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

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