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): March 30, 2022

CENTESSA PHARMACEUTICALS PLC

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

England and Wales	**001-04321**	**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 March 30, 2022, Centessa Pharmaceuticals plc (the "Company") announced its financial results for the quarter and year ended December 31, 2021. 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 to the investment community at various industry and other conferences slide presentations to provide updates and summaries of its business. The Company is posting to the "Investors" portion of its website at www.centessa.com a copy of its current corporate slide presentation. 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 99.2.

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 March 30, 2022
99.2	Corporate presentation prepared as of March 30, 2022

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: March 30, 2022

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

Exhibit 99.1

Centessa Pharmaceuticals Reports Fourth Quarter and 2021 Financial Results and Provides Business Update

– Company strengthens strategic focus on rare disease and immuno-oncology assets and details expected upcoming clinical milestones –

– SerpinPC registration studies planned to begin in 2H 2022 following recent FDA meeting; initial focus on Hemophilia B with and without inhibitors –

– LB101 preclinical data expected to be shared at ASCO 2022; IND planned for late 2022 –

– ZF874 Phase 1 update from multiple dose cohorts with PiMZ and PiZZ subjects expected in 2H 2022 –

– Pipeline review led to discontinuation of small molecule EGFR inhibitor discovery program, strategic evaluation of imgatuzumab and discontinuation of funding for lead dual STAT3/5 degrader –

– Cash and cash equivalents of $595.1 million as of December 31, 2021 –

BOSTON and LONDON, March 30, 2022 – Centessa Pharmaceuticals plc (Nasdaq: CNTA), a clinical-stage pharmaceutical company with a Research & Development ("R&D") innovation engine that aims to discover, develop and ultimately deliver impactful medicines to patients, today reported financial results for the fourth quarter and year ended December 31, 2021 and provided a business update.

"We have strengthened our strategic focus on innovative, high impact rare disease and immuno-oncology assets. Lixivaptan for ADPKD and SerpinPC for hemophilia are entering into registrational studies while LB101, our PD-L1xCD47 LockBody®, is advancing toward the clinic," said Saurabh Saha, MD, PhD, Chief Executive Officer. "We are in a strong financial position to make significant clinical progress towards our '4x24' goal of having four programs in registrational trials in 2024."

"We believe that our LockBody® programs have the potential to become the cornerstone for a multi-product immuno-oncology franchise. We look forward to sharing initial preclinical data at ASCO 2022 for the first program, LB101, which is designed to selectively drive potent CD47 effector function activity while avoiding systemic toxicity," said Antoine Yver, MD, MSc, Chairman of Development.

"The breadth of our rare disease programs provides us multiple opportunities to develop drugs which can potentially impact the lives of thousands of patients living with debilitating diseases such as ADPKD, hemophilia, alpha-1-antitrypsin deficiency, pulmonary arterial hypertension, and narcolepsy, among others," added Javad Shahidi, MD, MSc, Chief Medical Officer.

2021 Highlights and Recent Business Updates

Clinical Development Updates

- **SerpinPC:** Recently completed pre-IND interactions with the FDA regarding the planned registrational studies for SerpinPC. Based on the FDA feedback, the Company is proceeding with a streamlined, integrated registrational development plan initially for Hemophilia B, with and without inhibitors. The FDA discussions followed the announcement in September 2021 of positive topline data from a proof-of-concept study of SerpinPC in severe Hemophilia A and B subjects not on prophylaxis.
- **Lixivaptan:** Commenced dosing in the pivotal Phase 3 clinical trial (“ACTION Study”) evaluating lixivaptan as a potential treatment for autosomal dominant polycystic kidney disease (“ADPKD”). In addition, a key US patent was issued on February 8, 2022, which covers the use of lixivaptan for the treatment of ADPKD. The patent term expires June 8, 2038, before considering possible patent term extensions or adjustments.
- **ZF874:** Announced proof-of-mechanism data from the first three PiMZ subjects dosed in the Phase 1 Part B study evaluating ZF874 for the treatment of AATD demonstrating that a pharmacological chaperone has the potential to achieve clinically significant Z-A1AT serum increases in individuals with AATD.

Business Updates

- Further strengthened the leadership team with multiple key appointments, including Antoine Yver, MD, MSc, Executive Vice President and Chairman of Development; Javad Shahidi, MD, MSc, Chief Medical Officer; and David Grainger, PhD, Chief Innovation Officer.
- Dosing of the first subject with lixivaptan in the Phase 3 ACTION Study in February 2022 triggered settlement of the contingent value rights (“CVRs”) originally issued to the former shareholders and option holders of Palladio Biosciences in connection with its acquisition by Centessa in January 2021.
- Entered into financing agreement with funds managed by Oberland Capital Management LLC (“Oberland Capital”) and received initial $75 million funding in October of 2021.
- As part of ongoing portfolio management, the Company has recently decided to discontinue the small molecule EGFR inhibitor discovery program; evaluate strategic options, including potential divestment, for imgatuzumab; and discontinue internal funding for the lead dual-STAT3/5 degrader program.
- Announced ‘4x24’ portfolio goal with the aim of having four registrational programs in 2024.

Upcoming Program Milestones

Registrational: Programs currently in or expected to enter registrational trials this year:

- **Lixivaptan, vasopressin V2 receptor antagonist for ADPKD:** Lixivaptan is currently being administered in the Phase 3 registrational ACTION Study to investigate its potential to treat ADPKD and avoid safety issues associated with the only drug currently approved for the treatment of ADPKD. The ACTION Study is expected to enroll ~1,350 subjects across>200 sites in

over 20 countries. The Company anticipates completing enrollment in the second half of 2023 and, if results are supportive, plans to submit a New Drug Application after completion of the one-year double-blind portion of the study.

- **SerpinPC, an activated protein C inhibitor for Hemophilia:** In the second half of 2022 the Company expects to launch two registrational studies. The first study will enroll ~120 subjects and evaluate the efficacy and safety of prophylactic SerpinPC in subjects with severe Hemophilia B without inhibitors and will include subjects with severe Hemophilia A to add to the safety database. The second registrational study is planned with fewer than 20 subjects to evaluate the efficacy and safety of SerpinPC in subjects with severe Hemophilia B with inhibitors. Registrational plans for Hemophilia A are in development. The Phase 2a open label extension study is ongoing, and we expect to report data on the 48-week flat dose portion of that study and interim results from the following 24-week high dose portion in the fourth quarter of 2022.

Emerging: Programs / platforms with expected clinical proof of concept in the next 18 months

- **LB101 and LB201 in Solid Tumors:** LB101, a PD-L1xCD47 LockBody®, is designed to selectively drive potent CD47 effector function activity while avoiding systemic toxicity. We anticipate sharing foundational preclinical data at ASCO 2022, with an IND for LB101 planned for late 2022. LB201, a PD-L1xCD3 LockBody®, is designed to selectively drive potent CD3 effector function activity while avoiding systemic toxicity. IND for LB201 is planned for 2023.
- **ZF874 in Alpha-1 Antitrypsin Deficiency (AATD):** Small molecule folding corrector of the Z variant of alpha-1-antitrypsin. We expect to share Phase 1 data from multiple dose cohorts with PiMZ and PiZZ subjects in 2H 2022.
- **MGX292 in Pulmonary Arterial Hypertension (PAH):** Recombinant modified BMP9 replacement protein designed to overcome the deficiency in BMP9 signaling in PAH. IND is planned for early 2023.
- **OX2R Agonists (Oral and Intranasal) in Narcolepsy Type 1 (NT1):** Selective orexin receptor 2 agonists targeting the underlying pathophysiology of orexin neuron loss in NT1. INDs/CTAs are planned for 2023.

Exploratory: Programs with expected clinical proof of concept beyond 18 months

- **CBS001 in Inflammatory / Fibrotic Diseases:** High-affinity anti-LIGHT antibody. Phase 1 clinical trial in healthy volunteers is expected to begin in the second quarter of 2022.
- **CBS004 in Autoimmune Diseases:** Humanized mAb targeting BDCA2. IND is planned for late 2022.

Fourth Quarter and 2021 (period January 30 through December 31, 2021) Successor Financial Results

- **Cash and Cash Equivalents:** $595.1 million as of December 31, 2021 which the Company expects will fund operations, based on current non-risk adjusted plans, into early 2024, without drawing on the remaining available tranches under the Oberland facility.

- **R&D Expenses:** $41.5 million for the Company for the quarter ended December 31, 2021, $95.7 million for the Successor for 2021.
- **General & Administrative Expenses:** $13.0 million for the Company for the quarter ended December 31, 2021, $42.9 million for the Successor for 2021.
- **Net Loss Attributable to Ordinary Shareholders:** $60.8 million for the quarter ended December 31, 2021, $381.1 million for the Successor for 2021 (which includes two special, non-cash expenses: a $220 million charge for acquired in-process R&D associated with the Centessa subsidiary acquisitions; and a $15 million fair value adjustment to the CVRs).

About Centessa Pharmaceuticals

Centessa Pharmaceuticals plc ("Centessa") is a clinical-stage pharmaceutical company with a Research & Development ("R&D") innovation engine that aims to discover, develop and ultimately deliver impactful medicines to patients. Our programs span discovery-stage to late-stage development and cover a range of high-value indications in rare diseases and immuno-oncology. Our management team has extensive R&D experience, and provides direct guidance to our program teams as they advance candidates from research through all stages of development. For more information, visit www.centessa.com.

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 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 lixivaptan, SerpinPC and ZF874; strategy; regulatory matters, including the timing and likelihood of success of obtaining approvals to initiate or continue clinical trials or market any products; market size and opportunity for our product candidates; and our anticipated cash runway. Any forward-looking statements in this press release are based on our current expectations, estimates 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 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/or commercialized; the risk that the results of preclinical studies or clinical studies will not be predictive of future results in connection with future studies; geo-political risks such as the Russia-Ukraine conflict and risks related to the COVID-19 pandemic including the effects of the Delta, Omicron and any other variants. These and other risks concerning our programs and operations are described in additional detail in our Form 10-K, and our other reports, which are on file with the SEC. We explicitly disclaim any obligation to update any forward-looking statements except to the extent required by law.

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Media:

media@centessa.com

Centessa Pharmaceuticals plc (Successor) and Centessa Predecessor Group (Predecessor)

Consolidated and Combined Statements of Operations and Comprehensive Loss

(unaudited)

(amounts in thousands except share and per share data)

	Successor		Predecessor		
	Three months ended December 31, 2021	Period from January 30, 2021 through December 31, 2021	Period from January 1, 2021 through January 29, 2021	Three months ended December 31, 2020	Twelve months ended December 31, 2020
Operating expenses:					
Research and development	$ 41,534	$ 95,660	$ 662	$ 2,697	$ 9,301
General and administrative	12,988	42,888	121	308	1,139
Change in fair value of contingent value rights	3,770	15,082	—	—	—
Acquired in-process research and development	—	220,454	—	—	—
Loss from operations	(58,292)	(374,084)	(783)	(3,005)	(10,440)
Interest income (expense), net	(1,272)	(1,172)	(9)	(12)	(68)
Amortization of debt discount	—	—	(37)	(90)	(310)
Debt issuance costs	(1,331)	(1,331)	—	—	—
Other income (expense), net	235	(4,370)	—	(180)	155
Loss before income taxes	(60,660)	(380,957)	(829)	(3,287)	(10,663)
Income tax charge	114	114	—	—	—
Net loss	(60,774)	(381,071)	(829)	(3,287)	(10,663)
Other comprehensive loss:					
Foreign currency translation adjustment	(2,050)	778	107	119	(240)
Total comprehensive loss	$ (62,824)	$ (380,293)	$ (722)	$ (3,168)	$ (10,903)
Net loss per ordinary share - basic and diluted	$ (0.68)	$ (5.07)			
Weighted average ordinary shares outstanding - basic and diluted	89,935,902	75,166,456			

Centessa Pharmaceuticals plc (Successor) and Centessa Predecessor Group (Predecessor)

Condensed Consolidated and Combined Balance Sheets

(unaudited)

(amounts in thousands except share and per share data)

	Successor	Predecessor
	December 31, 2021	December 31, 2020
Total assets:		
Cash and cash equivalents	$ 595,082	$ 7,227
Other assets	34,553	4,490
Total assets	$ 629,635	$ 11,717
Total liabilities		
Other liabilities	$ 24,681	$ 8,619
Long term debt	75,700	—
Contingent value rights	37,700	—
Total liabilities	$ 138,081	$ 8,619
Total convertible preferred shares, shareholders' equity and combined deficit	$ 491,554	$ 3,098
Total liabilities, convertible preferred shares, shareholders' equity and combined deficit	$ 629,635	$ 11,717

CENTESSA PHARMACEUTICALS

Corporate Overview

MARCH 2022

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 lixivaptan, SerpinPC and ZF874; strategy; regulatory matters, including the timing and likelihood of success of obtaining approvals to initiate or continue clinical trials or market any products; 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. 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.


We are an **R&D innovation engine** that aims to discover, develop and ultimately deliver **impactful medicines to patients**

Centessa management team with deep R&D experience

CENTESSA

“4 x 24”: Our goal is to have 4 registrational programs in 2024

CURRENT PORTFOLIO

1 REGISTRATIONAL (Programs in registrational trials this year)

Lixivaptan in Autosomal Dominant Polycystic Kidney Disease
SerpinPC in Hemophilia (Hemophilia B for initial registrational trial)

2 EMERGING (Programs with clinical proof of concept anticipated in next 18 months)

LB101 and LB201 in Solid Tumors
ZF874 in Alpha-1 Antitrypsin Deficiency
MGX292 in Pulmonary Arterial Hypertension
Orexin Agonists in Narcolepsy and other Sleep-Wake Disorders

3 EXPLORATORY (Programs with proof of concept beyond 18 months)

CBS001 in Inflammatory/Fibrotic Diseases
CBS004 in Systemic Sclerosis, Lupus Erythematosus

Substantial portfolio of programs targeting multi-billion dollar markets

CENTESSA PHARMACEUTICALS

External market validation for our Registrational and Emerging programs

Asset	Disease	Reason to believe	Market validation
1 REGISTRATIONAL (Programs in registrational trials this year)			
Lixivaptan	**ADPKD**	Potential to **avoid safety issues** associated with the only approved drug (product-specific tox with black box / REMS)	**$770M** 2021 US sales for Otsuka's flagship product, JYNARQUE®, only one approved for ADPKD
SerpinPC	**Hemophilia A and B**	Associated with **promising ABR reduction** and infrequent **subcutaneous** dosing **with limited risk of thrombosis**	**$2B+** licensing deal in 2020 for Hemophilia B gene therapy in Phase 3 clinical trials
2 EMERGING (Programs with clinical proof of concept anticipated in next 18 months)			
LB101 / LB201	**Solid Tumors**	Platform of LockBody® programs designed to **selectively drive effector function activity** while avoiding systemic tox	**$2.5B** acquisition for pipeline of bispecific / multi-specific antibody technologies
ZF874	**AATD**	**Small molecule** pharmacological chaperone folding corrector intended to address **lung and liver manifestations** of AATD	**$20B** total market cap loss after two clinical failures for small molecule approaches in AATD
MGX292	**PAH**	**Replacement BMP9 protein** designed to overcome signaling deficiency and directly target underlying disease mechanism	**$11.5B** acquisition, lead candidate sotatercept indirectly impacting BMPR2 pathway in PAH
Orexin Agonists	**Narcolepsy**	Designed to leverage unique structural insights and to **directly target underlying pathophysiology** of orexin neuron loss	**$5B** market cap loss after clinical failure of orexin agonist program in Narcolepsy Type 1 (NT1)

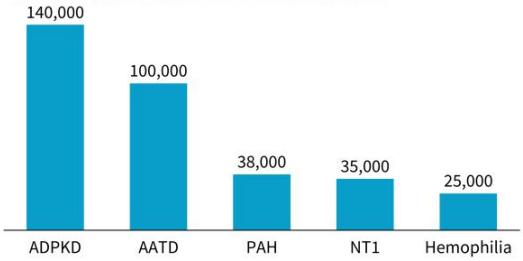
Source: Otsuka Holdings FY2021 Financial Results Presentation; uniQure 8-K (May 6, 2021); Amgen PR (July 27, 2021); Vertex market cap loss based on share price changes from Oct 14, 2020 ($271.46) to Oct 15, 2020 ($215.28) and June 10, 2021 ($216.77) to June 11, 2021 ($193.02); Acceleron PR (Sept 30, 2021); Takeda market cap loss based on share price changes from Oct 5, 2021 ($16.08) to Oct 6, 2021 ($14.31).

Our portfolio spans high value Rare Disease programs and IO platform

RARE DISEASE

- Exciting **Rare Disease pipeline** targeting large opportunities with high unmet patient need

Estimated US prevalence for our disease areas



IMMUNO-ONCOLOGY

- Platform of novel LockBody® compounds designed to **selectively drive potent effector function activity** (such as CD47 or CD3) while avoiding systemic toxicity
- Potential for the first two LockBody® programs to become the cornerstone for a **multi-product immuno-oncology franchise**
- Broad potential application in solid tumors

Note: Alpha-1 Antitrypsin Deficiency prevalence based on estimate of PiZZ individuals in the US
Sources: Acquavella et al, 2020; Willey, 2019; Alpha-1 Foundation; Leber et al, 2021; Soucie, 2020

CENTESSA PHARMACEUTICALS

Upcoming 2022 catalysts with cash runway into early 2024

$595 million cash and cash equivalents as of December 31, 2021

2022 data

- **LB101 in Solid Tumors:** Expect to report preclinical data at ASCO in June 2022
- **ZF874 in AATD:** Ph 1 data from multiple dose cohorts anticipated in 2H 2022
- **SerpinPC in Hemophilia:** Open-label extension (OLE) data expected in 4Q 2022

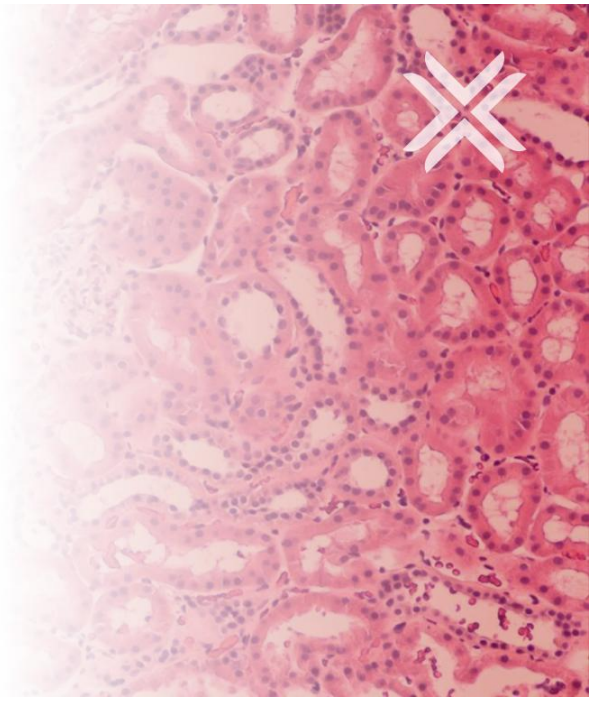
2022 program updates

- **CBS001 in Inflammatory / Fibrotic Diseases:** Start of Ph1 in Healthy Volunteers expected in 2Q 2022
- **SerpinPC in Hemophilia B:** Start of Hem B registrational trials planned in 2H 2022
- **LB101 in Solid Tumors:** IND anticipated in late 2022
- **CBS004 in autoimmune diseases:** IND anticipated in late 2022

Within our current cash runway, we expect to have clinical PoC readouts on all of our Emerging programs

Note: Cash runway does not include potential draws on the remaining available tranches under the Oberland facility. Currently $75m drawn under facility.

Lixivaptan in ADPKD



Lixivaptan is uniquely positioned to deliver a differentiated profile in ADPKD

LARGE RARE DISEASE MARKET WITH HIGH UNMET NEED FOR A SAFER TREATMENT

- ~140,000 ADPKD patients in the US and only one FDA approved product (tolvaptan), which has a boxed warning about its serious and potentially fatal liver injury

SIMILAR MECHANISM OF ACTION WITH DIFFERENTIATED CHEMISTRY

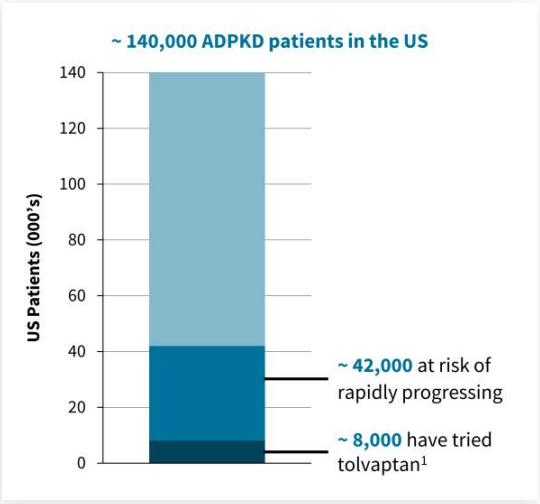
- Lixivaptan does not have the metabolite believed to cause drug-induced liver injury with tolvaptan, and lixivaptan did not exhibit signs of DILI when tested in tolvaptan intolerant subjects

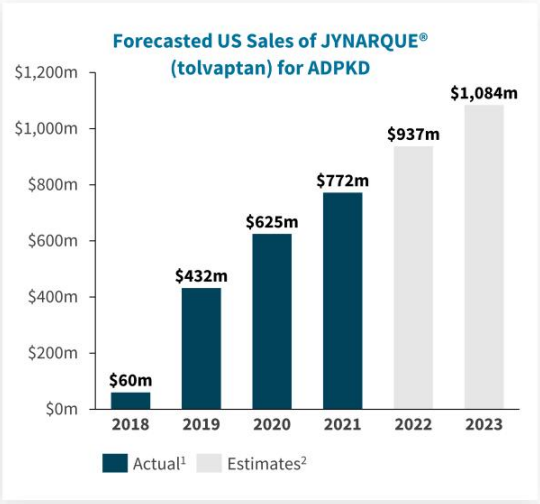
HIGH MARKET POTENTIAL WITH LIMITED PIPELINE AGENTS

- Only one other treatment in late-stage development

Source: Willey et al., 2019

The ADPKD market represents a multi-billion dollar rare disease opportunity

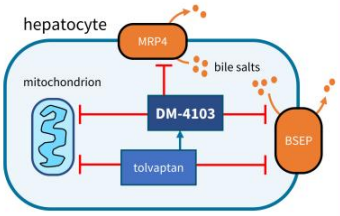




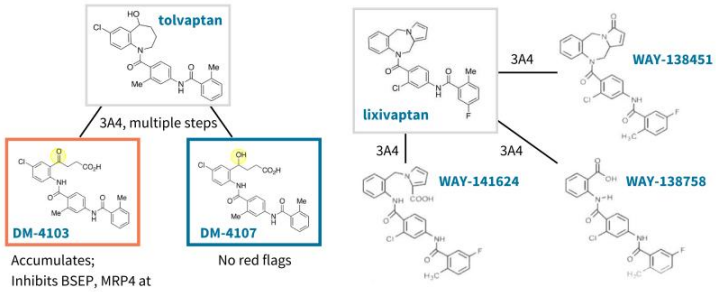
Sources: Willey et al., 2019; primary market research 1. Otsuka Holdings FY2021 Financial Results Presentation 2. Evaluate Pharma

CENTESSA PHARMACEUTICALS

Potential to avoid liver risk with unique structure and differential chemistry



DM-4103 is a **tolvaptan-specific metabolite** believed to cause liver toxicity



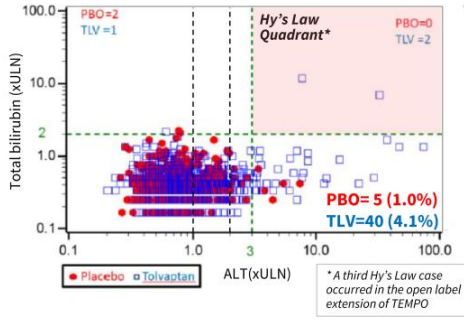
Chemical species	Tolvaptan	DM-4103	DM-4107	Lixivaptan	141624	138451	138758
Parent dose	120 mg	TEMPO doses	60 mg	200 mg BID	200 mg BID	200 mg BID	200 mg BID
Ratio C_{ss} / BSEP IC_{50}	0.04	3.7	0.00	0.08	0.02	0.02	0.32
Ratio C_{ss} / MRP4 IC_{50}	0.01	3.7	0.00	0.02	0.05	0.00	0.45

CENTESSA PHARMACEUTICALS

Drug-induced liver injury observed in tolvaptan clinical trials

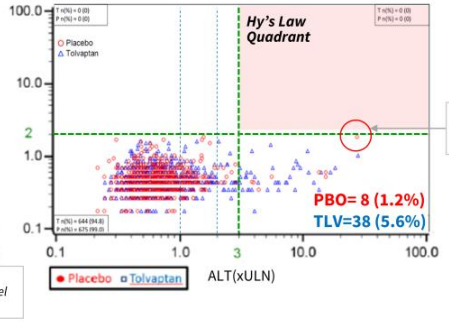
Evaluation of Drug-Induced Serious Hepatotoxicity (eDISH plots)

Tolvaptan TEMPO Study[1]
36 months with quarterly monitoring



*A third Hy's Law case occurred in the open label extension of TEMPO

Tolvaptan REPRISE Study[2]
12 months with monthly monitoring



Quasi-Hy's Law case caused by tolvaptan during run-in period

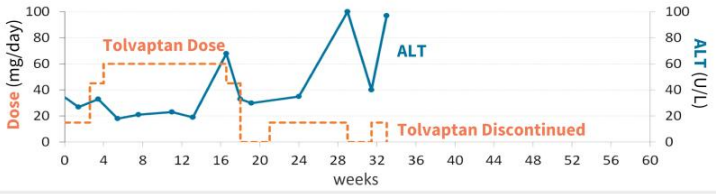
[1] Watkins PB, et al. Clinical Pattern of Tolvaptan-Associated Liver Injury in Subjects with Autosomal Dominant Polycystic Kidney Disease: Analysis of Clinical Trials Database. 2015; [2] Torres VE, et al. Tolvaptan in Later-Stage Autosomal Dominant Polycystic Kidney Disease. *N Engl J Med*. 2017

CENTESSA PHARMACEUTICALS

No liver tox observed to date with lixivaptan in tolvaptan-intolerant subjects

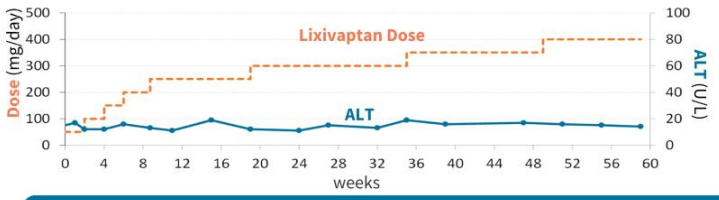
Initial tolvaptan experience

Young subject with ADPKD developed DILI on each of three unsuccessful attempts to initiate tolvaptan.



Subsequent lixivaptan experience

Lixivaptan did not cause any signs of liver toxicity in this highly susceptible subject during *14* months of therapy.

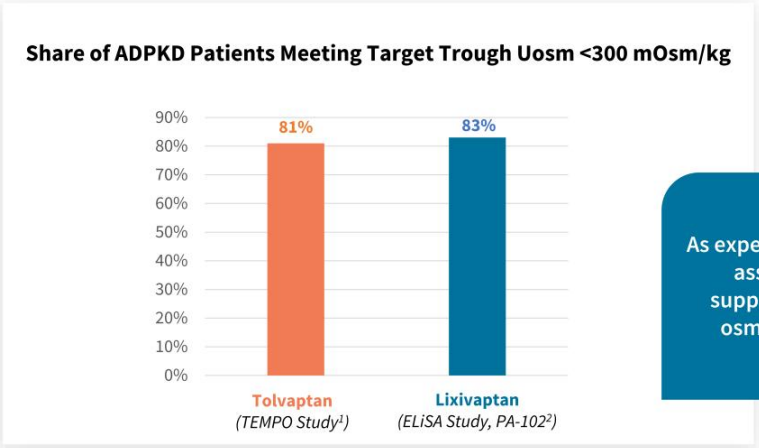


Four additional tolvaptan-intolerant subjects have now been successfully dosed with lixivaptan with no DILI in the ALERT Study *

* ALERT is an ongoing open-label, non-registrational repeat-dose study designed to assess hepatic and non-hepatic safety in subjects who previously experienced liver chemistry test abnormalities while treated with tolvaptan and were permanently discontinued from the drug for that reason. NCT04152837

CENTESSA PHARMACEUTICALS

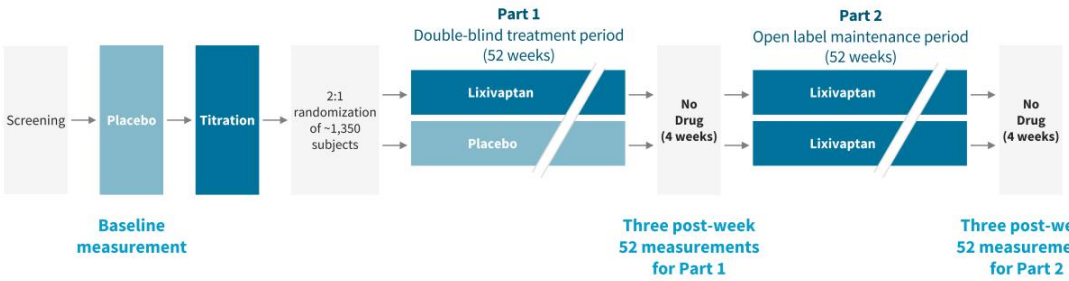
Urine osmolality is the key physiologic marker for drug activity in ADPKD



1. Devuyst, Olivier, et al. "Urine osmolality, response to tolvaptan, and outcome in autosomal dominant polycystic kidney disease: results from the TEMPO 3: 4 trial." *Journal of the American Society of Nephrology* 28.5 (2017): 1592-1602. 2. The ELiSA Study was a Phase 2 open-label, parallel-group, multiple dose, multi-center study to directly characterize the safety and tolerability, PK, and PD of lixivaptan in ADPKD subjects. A total of 31 subjects received either 50 mg or 200 mg twice daily for seven days.
Note: Results were not generated in a head-to-head clinical study and may not represent comparable results.

CENTESSA PHARMACEUTICALS

Ongoing ACTION Phase 3 clinical trial for lixivaptan in ADPKD



- **Primary endpoint:** Annualized change in eGFR from baseline to end of Part 1 (post-52 weeks)
- **Key secondary endpoint:** Incidence of serum ALT levels >3x ULN in participants randomized to lixivaptan vs. to placebo in Part 1

- Target completing enrollment by 2H 2023
- Plan to submit NDA based on one-year data from Part 1 *(pending positive data)*

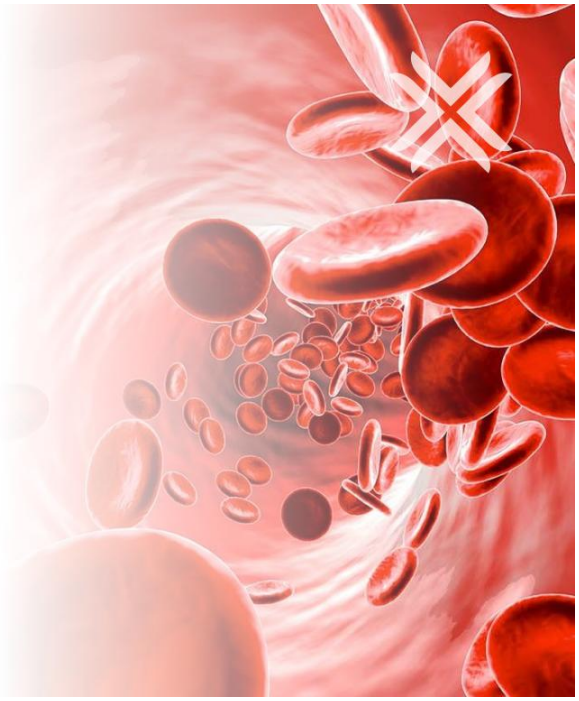
CENTESSA PHARMACEUTICALS

Lixivaptan is expected to have limited potential competition

ASSET NAME	COMPANY	MECHANISM OF ACTION	PHASE
JYNARQUE®	Otsuka	Vasopressin V2 Receptor Antagonist	**Marketed**
Lixivaptan	CENTESSA PHARMACEUTICALS	Vasopressin V2 Receptor Antagonist	**3**
~~**Venglustat**~~	~~SANOFI GENZYME~~	~~GCS Inhibitor~~	~~**Discontinued**~~
Bardoxolone	REATA PHARMACEUTICALS	KEAP1-Nrf2 Activation	**3**
GLPG-2737	Galapagos	C2 Corrector	**2**
RGLS-4326	REGULUS	miR-17 Inhibition	**1**

- JYNARQUE® Orange Book exclusivity through April 2030
- Lixivaptan recent patent with expiration in 2038 before considering patent term extensions or adjustments
- Sanofi announced the discontinuation of the venglustat ADPKD program in June 2021
- Bardoxolone is the only other pipeline agent in Phase 3; CRL from the FDA in February 2022 for bardoxolone in Alport Syndrome

SerpinPC in Hemophilia



SerpinPC has the potential to shift Hemophilia B treatment paradigm

GENETIC VALIDATION AND CLINICAL PROOF OF CONCEPT FOR NEW MECHANISM

- Human genetic target validation in individuals who co-inherit Factor V Leiden mutation and either FVIII or FIX mutations reinforced with positive proof-of-concept Phase 2 data

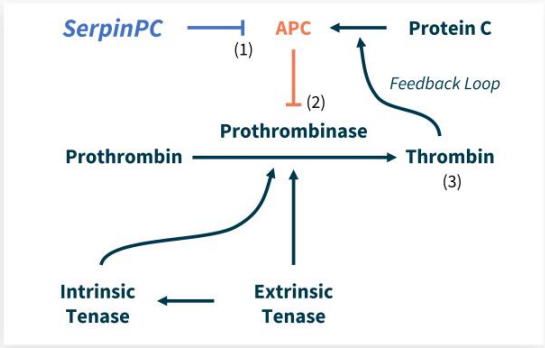
UNIQUE MECHANISM THAT IS NOT BELIEVED TO CONFER RISK FOR THROMBOSIS

- No sustained elevations in D-dimer and no evidence of thrombosis observed in clinical trials in healthy volunteers and persons with hemophilia

PROMISING REDUCTIONS IN BLEEDING WITH INFREQUENT SUBCUTANEOUS DOSING

- Observed a median 88% reduction in all bleed ABR in the highest dose cohort in the Phase 2 study, with PK suitable for an infrequent dosing schedule

SerpinPC is believed to have a unique MoA supported by human genetics



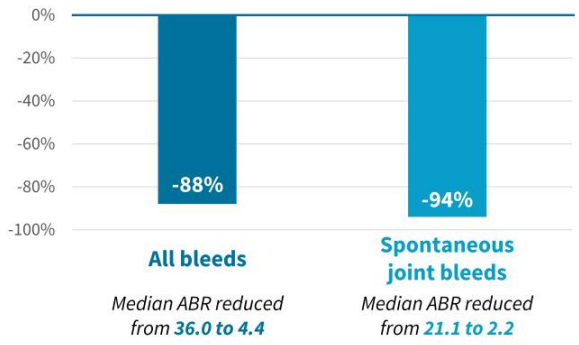
SerpinPC reduces levels of circulating APC (1), thereby prolonging activity of prothrombinase (2) and directly increasing the amount of thrombin (3) at the site of tissue damage

Genetically validated target based on coinheritance of Factor V Leiden mutation with hemophilia

CENTESSA PHARMACEUTICALS

SerpinPC showed promising reductions in bleeding rates and was observed to be well-tolerated in the Phase 2a study

Median ABR reduction for highest dose cohort (1.2 mg/kg)



*Median ABR reduced from **36.0 to 4.4***

*Median ABR reduced from **21.1 to 2.2***

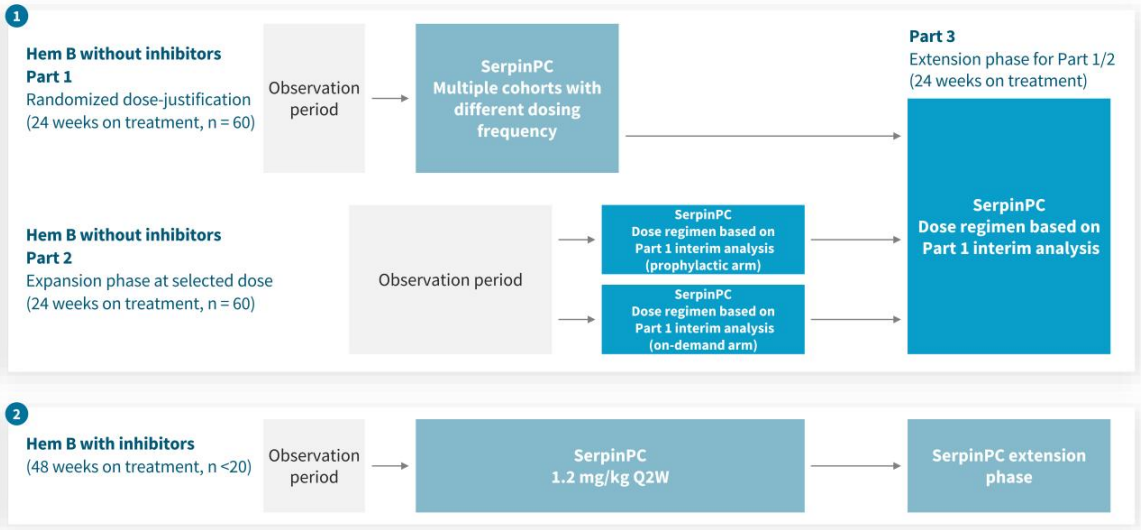
Across all dose levels:

- **No thrombosis**
- **No instances of sustained elevations in D-dimer**
- 1 moderate skin reaction led to withdrawal of a subject with history of a skin disorder
- Two subjects with ADAs, with no apparent impact on ABRs
- No other SerpinPC-related AEs

Initial registration studies focused on Hem B (+/- inhibitors) given high unmet need and market opportunity

CENTESSA PHARMACEUTICALS

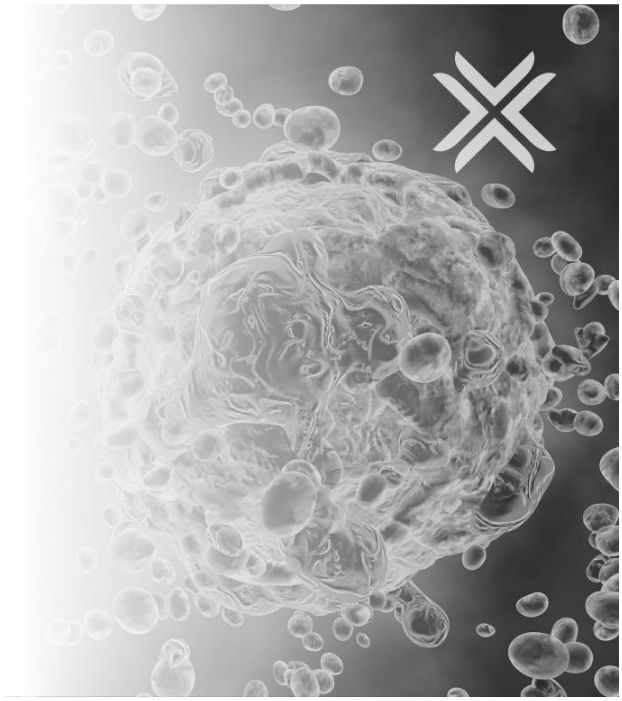
Two registrational trials planned to start in 2H 2022 in Hemophilia B



Note: The first registrational study will also enroll subjects with severe HA, with and without inhibitors, to add to the safety database

CENTESSA PHARMACEUTICALS

LB101 & LB201 in Solid Tumors



LockBody® programs aim to redefine immuno-oncology treatment

DESIGNED TO ADDRESS IMMUNO-ONCOLOGY THERAPY CHALLENGES

- LockBody® mechanism aims to bypass typical "sink" effect, minimize peripheral toxicity, and drive maximal effector function activity, such as CD47, directly into the tumor

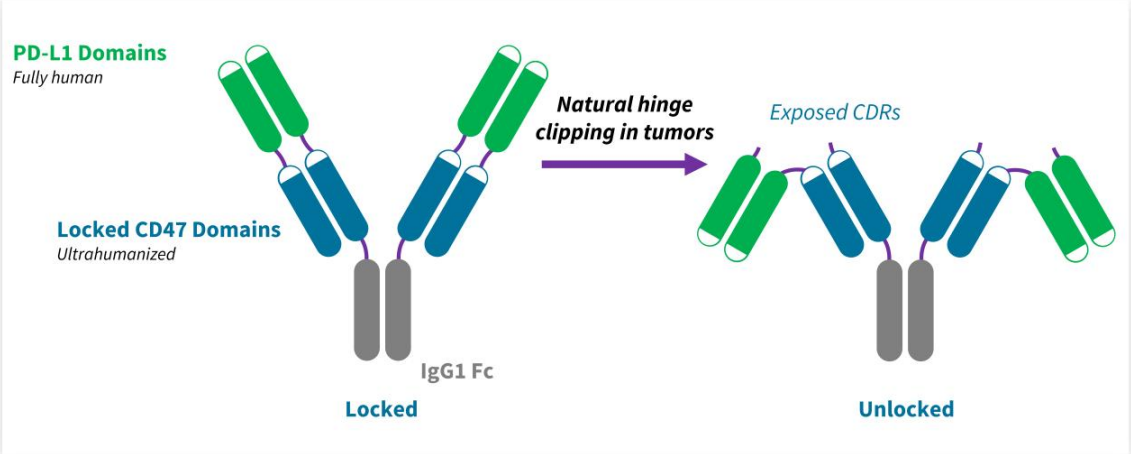
UNIQUE TECHNOLOGY DESIGNED TO UNLOCK CELL KILLING IN THE TUMOR

- Effector function activity, such as CD47 or CD3, is blocked by the PD-L1 tumor targeting domain until the human IgG-derived hinges are naturally degraded in the tumor microenvironment (TME)

POTENTIAL FOR SINGLE AGENT SYSTEMIC ACTIVITY

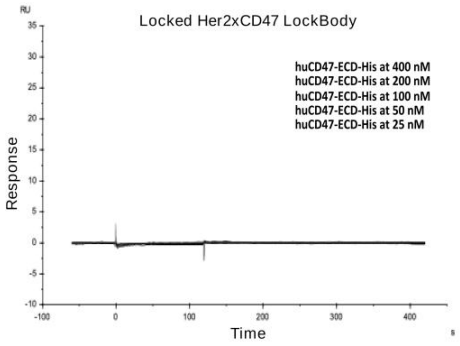
- LB101 is designed as a single agent combining PD-L1 targeting, CD47 blockade and with a fully functional IgG1 Fc region

LB101 is designed to allow for anti-PD-L1 activity plus CD47 activity in the TME

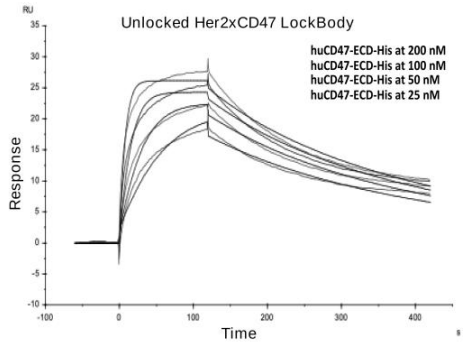


CENTESSA PHARMACEUTICALS

In vitro data using Her2xCD47 LockBody® demonstrated effector function locking



Locked form: No measurable binding to CD47



Unlocked form: Clear, high-affinity, concentration-dependent binding

CENTESSA PHARMACEUTICALS

In vivo data showed Her2xCD47 LockBody® was generally well tolerated and stable, with antibody-like pharmacokinetics (PK)

Her2xCD47 LockBody®

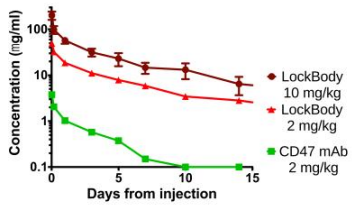
- Long, mAb-like distribution
- Up to 100-fold increase in AUC
- No evidence of target-driven clearance, no anaemia, no reticulocyte amplification

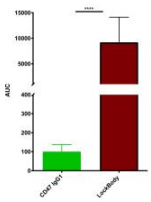
CD47 IgG1

- Lethal at 10 mg/kg after 24h
- Rapid clearance at 2 mg/kg

LockBody® exhibited mAb-like distribution, IgG1 rapidly cleared

PK





AUC

CENTESSA PHARMACEUTICALS

LockBody® development plan and upcoming milestones

- Plan to present foundational preclinical data at ASCO (June 2022) evaluating the activity and tolerability of LB101 monotherapy in a hPD-L1+ syngeneic model in mice, in comparison with atezolizumab
- Plan to submit an IND for LB101 (PD-L1xCD47) in late 2022
- Plan to submit an IND for LB201 (PD-L1xCD3) in 2023

ZF874
in AATD

ZF874 has the potential to be a disease-modifying treatment for AATD

DESIGNED AS A CATALYTIC, NON-COVALENT SMALL MOLECULE FOLDING CORRECTOR

- ZF874 is designed to bind to the stalled folding intermediate specific to Z-A1AT with no detectable binding to fully folded Z-A1AT *in vitro*

POTENTIAL TO INCREASE FUNCTIONAL A1AT LEVELS TO PROTECT THE LUNG

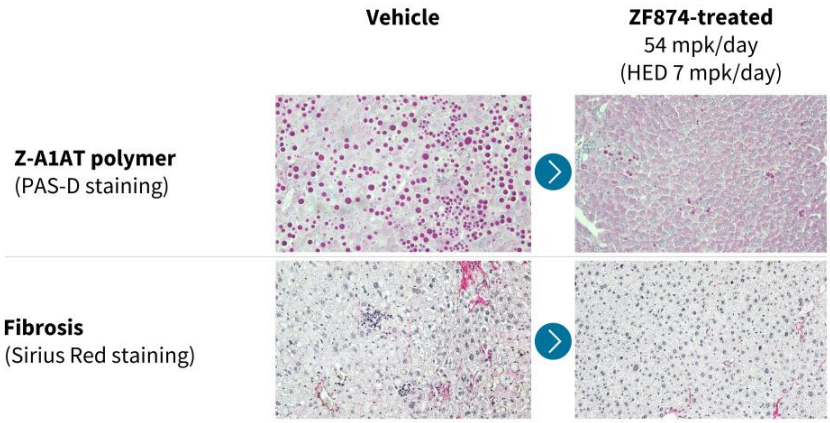
- Initial ZF874 clinical data was the first demonstration that a pharmacological chaperone could provide sufficient functional Z-A1AT increases in serum to potentially achieve >11µm levels in PiZZ individuals

POTENTIAL TO CLEAR POLYMERS FROM THE LIVER

- Preclinical data showed both increased blood levels of Z-A1AT and clearance of Z-A1AT polymer from the liver in mice over-expressing human Z-A1AT at lower doses than in human studies

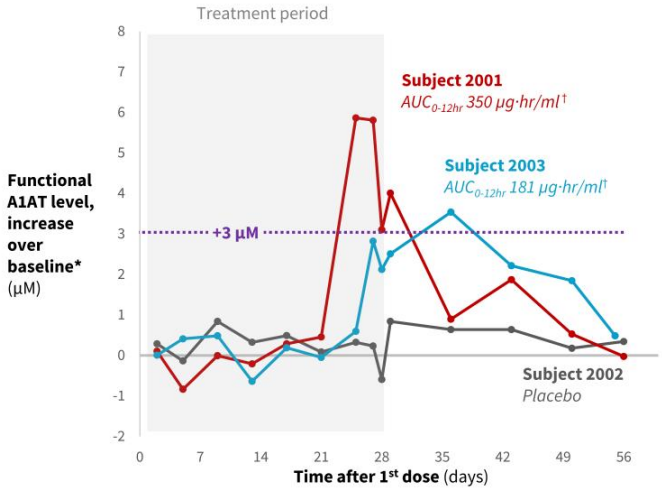
Preclinical data showed low doses of ZF874 clear polymer & reduced fibrosis

Liver histology from 84-day treatment of mice expressing human Z-A1AT (PiZ mice)



Abbreviations: mpk = milligrams per kilogram; PAS-D = Periodic Acid-Schiff staining with diastase; HED = human equivalent dose

Clinical data in PiMZ subjects dosed with placebo or ZF874 15 mpk BID



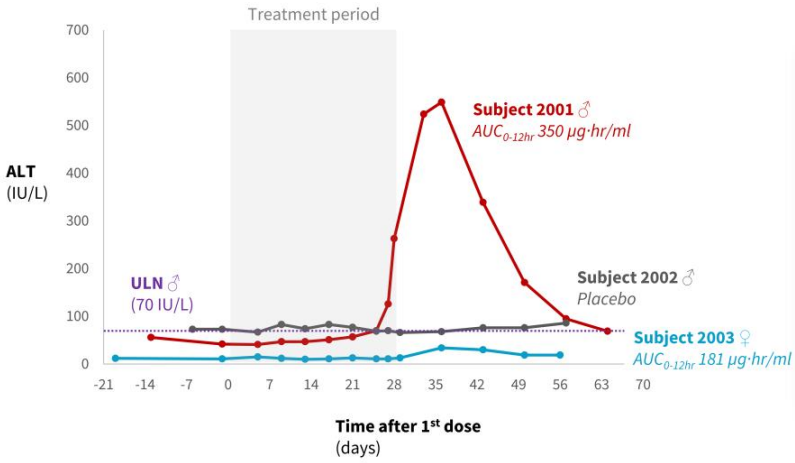
Demographics and data
First 3 subjects in Part B

Subj.	Treatment	Genotype	Baseline A1AT*	Peak A1AT
2001	15 mpk BID (1.6 g BID)	MZ	17.6 µM	23.5 µM
2002	Placebo (N/A)	MZ	12.7 µM	13.5 µM
2003	15 mpk BID (1.1 g BID)	MZ	14.8 µM	18.3 µM

* Activity level equivalent to molar amount of M A1AT reference standard. Baseline for each subject = average of Pre-Screen , Day -1, and Day 1 Pre-Dose values for each subject
† Trapezoidal AUC for the first 12 hours after the first dose on Day 28
* Baseline = average of Pre-Screen, Day -1 and Day 1 Pre-Dose values from A1AT functional assay

CENTESSA PHARMACEUTICALS

Liver signal in one PiMZ subject with highest exposure in Part B



- Subject 2001 showed increases in ALT (8X ULN) and AST (3.5X ULN) after the treatment period
- In the same subject, BILI, GGT and ALP stayed in the reference range throughout the observation period
- No liver signal was observed in SAD with PiMM healthy volunteers in Part A (n = 42, dose range 1.5 mpk to 50 mpk)
- All other observed AEs were mild

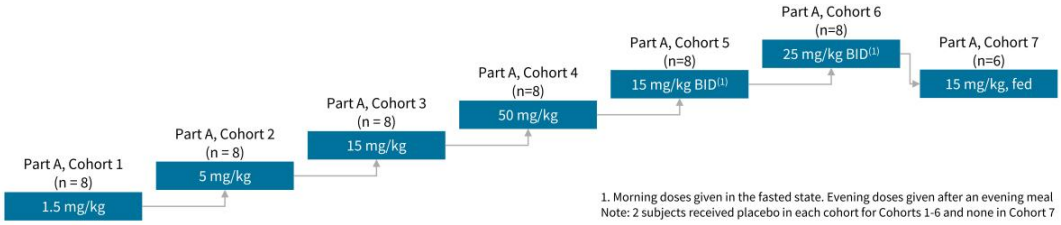
* ULN ♀ (33 IU/L)
† Trapezoidal AUC for the first 12 hours after the first dose on Day 28

Abbreviations: ULN = upper limit of normal; IU/L = international units per liter; BILI = bilirubin; GGT = gamma-glutamyl transferase; ALP = alkaline phosphatase

CENTESSA PHARMACEUTICALS

Overview of ongoing Phase 1 trial of ZF874 in AATD

Part A (completed): Single Ascending Dose Study in **Healthy Volunteers**



1. Morning doses given in the fasted state. Evening doses given after an evening meal
Note: 2 subjects received placebo in each cohort for Cohorts 1-6 and none in Cohort 7

Part B (ongoing): 28-day Repeat Dosing in **PiXZ Subjects (Including PiZZ and PiMZ Subjects)**

Pending receipt of satisfactory long-term animal tox data, protocol may be amended to extend duration of dosing in Part B to up to 3 months

CENTESSA PHARMACEUTICALS

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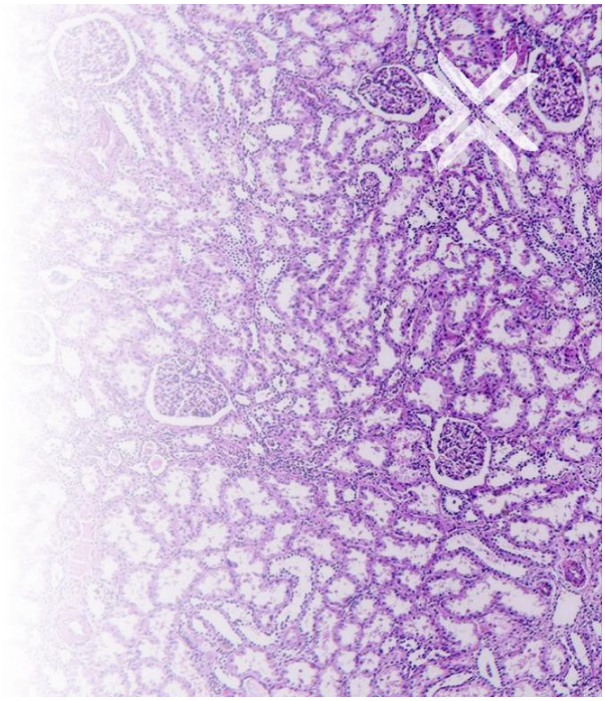
MGX292 in PAH



MGX292 has the potential for disease reversal / modification in PAH

DESIGNED TO DIRECTLY TARGET CENTRAL UNDERLYING DISEASE MECHANISM IN PAH

- Recombinant modified BMP9 replacement protein designed to directly target BMPR2/ALK1 pathway vs. experimental therapies which inhibit Activin signaling with only indirect effects on this pathway

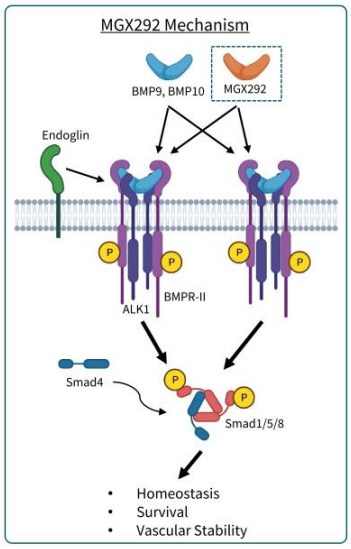
***IN VIVO* DATA DEMONSTRATED POTENTIAL TO RESTORE VASCULAR FUNCTION**

- MGX292 was observed to reverse established advanced pulmonary vascular remodeling in the Sugen-hypoxia rat model, with almost complete reversal of disease at high dose

POTENTIAL FOR RAPID DEVELOPMENT IN GENETICALLY DEFINED PAH

- Potential development plan to address ~25% of idiopathic PAH patients with loss-of-function mutations in the BMP9 signaling axis

MGX292 is designed to directly target central underlying disease mechanism

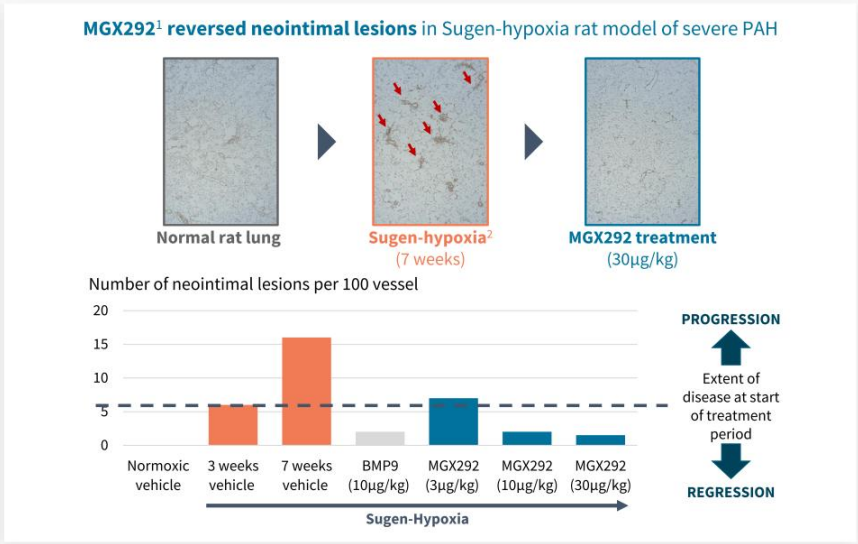


In PAH, reduced **BMP9 signaling** results in the pathological changes underlying PAH.

With MGX292 treatment, supplementation with exogenous recombinant BMP9 protein (MGX292) leads to **restored signaling** and normalization of endothelial cell functions.

CENTESSA PHARMACEUTICALS

MGX292 demonstrated dose-dependent reversal of established lung vascular pathology in Sugen-hypoxia rat model



1. MGX292 treatment was given daily for 4 weeks; 2. Red arrows depict vascular lesions

Development plan for MGX292 in PAH

- Preclinical development ongoing, currently in the IND-enabling stage
- Plan to conduct pre-IND meeting with the FDA in the second half of 2022
- Plan to submit an IND for MGX292 in early 2023

OX2R Agonists in NT1

Our novel orexin agonist approaches have the potential to change the global standard of care in narcolepsy

DESIGNED TO DIRECTLY TARGET UNDERLYING PATHOPHYSIOLOGY OF DISEASE

- Lead molecules are designed to selectively target the Orexin Receptor-2 (OX2R) based on structure-based drug design

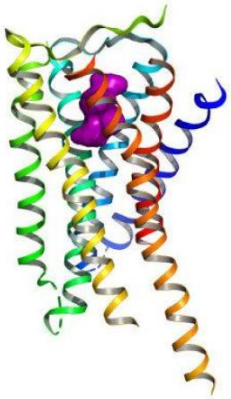
***IN VIVO* DATA DEMONSTRATED DOSE DEPENDENT EFFECTS IN INCREASING WAKEFULNESS**

- Observed significant increases in wakefulness in the NT1 model mice and wild type mice for the exemplar small molecule agonists and in wild type mice for the exemplar peptide agonists

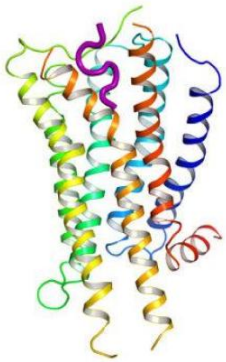
TEAM AND EXCLUSIVE PARTNERSHIPS ENABLE DIFFERENTIATED DRUG DISCOVERY

- Program led by former Takeda orexin team leadership; exclusive license to Sosei Heptares's StaR® technology and exclusive collaboration with Schrödinger to support novel discovery efforts

Our small molecule and peptide orexin agonists are designed to provide a potential replacement therapy approach in NT1



Example X-ray structure of OX2R with small molecule orexin agonist (shown in purple)



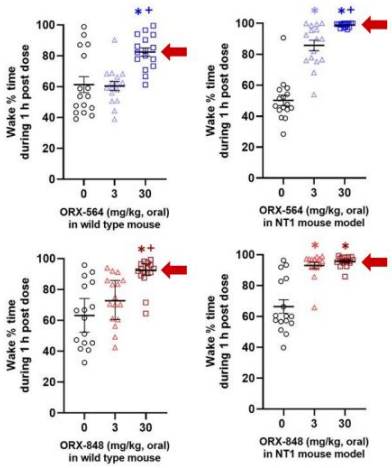
Example Cryo-EM structure of OX2R with peptide agonist (shown in purple)

Our small molecule and peptide orexin agonist molecules have demonstrated **sub-nanomolar potency** in *in vitro* assays *

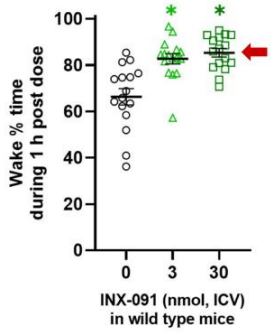
* Based on EC50, *in vitro* functional profiles of exemplar small molecule agonists and exemplar peptide agonists in a calcium mobilization FLIPR assay with cells expressing recombinant human OX2R

Novel small molecule and peptide orexin agonists demonstrated dose-dependent effects in increasing wakefulness in mice

Exemplar small molecule agonists



Exemplar peptide agonist



Wakefulness detected by piezoelectric monitoring, which is a rapid, non-invasive method for classifying sleep and wakefulness by unsupervised machine learning

CENTESSA PHARMACEUTICALS

Development plan for orexin agonists in NT1

- Plan to submit IND / CTA for lead oral program in 2023
- Plan to submit IND / CTA for intranasal program in 2023
- Intend to explore additional indications beyond NT1

Centessa: the assets, resources and talent to drive patient impact

Substantial product portfolio targeting multi-billion dollar markets

- Exciting pipeline of rare disease programs, led by Registrational programs lixivaptan (ADPKD) and SerpinPC (Hemophilia), and a potential multi-product IO franchise driven by LockBody® programs

Cash runway into early 2024 with PoC data anticipated on all Emerging programs

- Anticipate readouts from our Emerging programs within current cash runway
- "4 x 24": Goal is to have 4 programs in registrational studies in 2024

Management team with deep R&D experience from leading biotech & pharma companies

- Provide direct R&D guidance through our integrated one-team structure aimed at rapidly advancing programs with a relentless focus on data-driven decision-making

Note: Cash runway does not include potential draws on the remaining available tranches under the Oberland facility
Definitions: Registrational - Programs in registrational trials this year; Emerging - Programs with potential for clinical proof of concept anticipated in next 18 months

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