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): June 16, 2025

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: **+1 (617) 468-5770**

Former name or address, if changed since last report:

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

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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

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

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

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

Emerging growth company ☒

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

Item 8.01 Other Events.

On June 16, 2025, Centessa Pharmaceuticals plc (the "Company") issued a press release announcing that the U.S. Food and Drug Administration (the "FDA") has cleared the Investigational New Drug application (the "IND") to initiate a Phase 1 clinical study of ORX142 in healthy volunteers for the treatment of select neurological and neurodegenerative disorders. A copy of the press release is attached as Exhibit 99.1 to this Current Report on Form 8-K and incorporated herein by reference.

The Phase 1 study will evaluate the safety, tolerability and pharmacokinetics of single-ascending doses (SAD) and multiple-ascending doses (MAD) of ORX142 in healthy volunteers. In parallel to the SAD, a placebo-controlled crossover pharmacodynamic (PD) assessment will be performed utilizing the Maintenance of Wakefulness Test (MWT) and Karolinska Sleepiness Scale (KSS) in acutely sleep-deprived healthy adult subjects. The Company plans to initiate the first-in-human Phase 1 clinical study imminently, with clinical data expected this year.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	
99.1	Press Release dated June 16, 2025
104	Cover Page Interactive Data (embedded within the Inline XBRL document)

Forward Looking Statements

This Current Report on Form 8-K 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 Current Report on Form 8-K that are not statements of historical fact may be deemed to be forward-looking statements, including statements related to the Company's ability to discover and develop transformational medicines for patients; its expectations for executing on the Company's pipeline; its expectations on its anticipated cash runway; the timing of commencement of new studies or clinical trials or clinical and preclinical data related to ORX750, ORX142, ORX489 and other OX2R agonist molecules, and the LockBody technology platform; its ability to identify, screen, recruit and maintain a sufficient number of or any subjects in its existing and anticipated studies or clinical trials of ORX750, ORX142, ORX489 and other OR2R agonist molecules, and any LockBody candidates; its expectations on executing its research and clinical development plans and the timing thereof; its expectations as to the potential results and impact of each of its clinical programs and trials; the Company's ability to differentiate ORX750, ORX142, ORX489 and other OX2R agonist molecules, any LockBody candidates from other treatment options; the development, design and therapeutic potential of ORX750, ORX142, ORX489 and other OX2R agonist molecules, and the LockBody technology platform; and regulatory matters, including the timing and likelihood of success of obtaining regulatory clearance, obtaining authorizations to initiate or continue clinical trials. Any forward-looking statements in this Current Report on Form 8-K are based on the Company's 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 the safety and tolerability profile of the Company's product candidates; the Company's ability to identify, screen and recruit a sufficient number of or any subjects in its existing and anticipated new studies or clinical trials of ORX750, ORX142, ORX489 or within anticipated timelines; the Company's expectations relating to the clinical trials of ORX750 and ORX142, including the predicted timing of enrollment, the predicted efficacious doses of ORX750 and/or ORX142 and its ability to successfully conduct its clinical development of ORX750 and ORX142, the Company's ability to protect and maintain its 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 the Company's ongoing and planned clinical trials; the Company's ability to obtain adequate financing, including through its financing facility with Oxford Finance, to fund its 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; its operating costs and use of cash, including cash runway, cost of development activities and conducting clinical trials, future expenditures risks; the risk that any one or more of its product candidates will not be successfully developed and/or commercialized; the risk that the historical results of preclinical studies or clinical studies will not be predictive of future results in ongoing or future studies; economic risks to the United States and United Kingdom banking systems,; and geo-political risks such as the Russia-Ukraine war or the Middle East conflicts. These and other risks

concerning the Company's programs and operations are described in additional detail in the Company's Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and its other reports, which are on file with the U.S. Securities and Exchange Commission. The Company's explicitly disclaims any obligation to update any forward-looking statements except to the extent required by law.

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: June 17, 2025

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

Exhibit 99.1

Centessa Pharmaceuticals Announces Clearance of Investigational New Drug Application (IND) for ORX142, a Novel Orexin Receptor 2 (OX2R) Agonist; Clinical Data in Acutely Sleep-Deprived Healthy Volunteers Planned for this Year

BOSTON and LONDON, June 16, 2025 -- Centessa Pharmaceuticals plc (Nasdaq: CNTA), a clinical-stage pharmaceutical company, today announced that the U.S. Food and Drug Administration (FDA) has cleared the IND to initiate a Phase 1 clinical study of ORX142 in healthy volunteers. ORX142 is an investigational, novel, highly potent and selective OX2R agonist being developed for the treatment of select neurological and neurodegenerative disorders. ORX142 is the second drug candidate from the Company's multi-asset orexin franchise.

"The clearance of our IND to initiate clinical studies of ORX142 represents a significant milestone, signaling the beginning of an exciting new phase in the clinical development of our OX2R agonist pipeline for indications beyond rare hypersomnias," said Saurabh Saha MD PhD, Chief Executive Officer of Centessa. "With our most advanced OX2R agonist, ORX750, advancing in the Phase 2a *CRYSTAL-1* study for the treatment narcolepsy type 1 (NT1), narcolepsy type 2 (NT2) and idiopathic hypersomnia (IH), we are eager to leverage our insights from this new drug class and explore ORX142's potential to treat a broad range of neurological and neurodegenerative disorders with significant unmet needs. We are excited to begin executing our ORX142 Phase 1 clinical study in acutely sleep-deprived healthy volunteers which is aimed at generating early proof-of-concept data for ORX142 this year which we expect to enable a dose selection for planned studies evaluating ORX142 in patients."

The Phase 1 study will evaluate the safety, tolerability and pharmacokinetics of single-ascending doses (SAD) and multiple-ascending doses (MAD) of ORX142 in healthy volunteers. In parallel to the SAD, a placebo-controlled crossover pharmacodynamic (PD) assessment will be performed utilizing the Maintenance of Wakefulness Test (MWT) and Karolinska Sleepiness Scale (KSS) in acutely sleep-deprived healthy adult subjects. The Company plans to initiate the first-in-human Phase 1 clinical study imminently, with clinical data expected this year.

About Centessa's Orexin Receptor 2 (OX2R) Agonist Program Orexin is a neuropeptide that regulates the sleep-wake cycle, leading to arousal and promoting wakefulness. Targeting the orexin pathway with novel orexin receptor 2 (OX2R) agonists represents a promising approach to address excessive daytime

sleepiness (EDS), impaired attention, cognitive deficits and fatigue associated with a broad range of neurological, neurodegenerative and neuropsychiatric disorders. Centessa is developing a pipeline of potential best-in-class OX2R agonists, including ORX750 for the treatment of sleep-wake disorders including narcolepsy type 1 (NT1), narcolepsy type 2 (NT2) and idiopathic hypersomnia (IH), ORX142 for the treatment of select neurological and neurodegenerative disorders, and ORX489 for the treatment of neuropsychiatric disorders. ORX750 is being evaluated in the Phase 2a *CRYSTAL-1* study. ORX750, ORX142 and ORX489 are investigational candidates and have not been approved by the FDA or any other regulatory authority.

About Centessa Pharmaceuticals Centessa Pharmaceuticals, plc is a clinical-stage pharmaceutical company with a mission to discover, develop and ultimately deliver medicines that are transformational for patients. We are pioneering a new class of potential therapies within our orexin receptor 2 (OX2R) agonist program for the treatment of excessive daytime sleepiness (EDS), impaired attention, cognitive deficits, fatigue and other symptoms across neurological, neurodegenerative and neuropsychiatric disorders. We also have an early-stage immuno-oncology program focused on our novel LockBody® technology platform. For more information, visit www.centessa.com, which does not form part of this release.

Forward Looking Statements

This press release contains forward-looking statements. These statements may be identified by words such as “may,” “might,” “will,” “could,” “would,” “should,” “expect,” “intend,” “plan,” “objective,” “anticipate,” “believe,” “estimate,” “predict,” “potential,” “continue,” “ongoing,” “aim,” “seek,” and variations of these words or similar expressions that are intended to identify forward-looking statements. Any such statements in this press release that are not statements of historical fact may be deemed to be forward-looking statements, including statements related to the Company’s ability to discover and develop transformational medicines for patients; its expectations for executing on the Company's pipeline; its expectations on its anticipated cash runway; the timing of commencement of new studies or clinical trials or clinical and preclinical data related to ORX750, ORX142, ORX489 and other OX2R agonist molecules, and the LockBody technology platform; its ability to identify, screen, recruit and maintain a sufficient number of or any subjects in its existing and anticipated studies or clinical trials of ORX750, ORX142, ORX489 and other OX2R agonist molecules, and any LockBody candidates; its expectations on executing its research and clinical development plans and the timing thereof; its expectations as to the potential results and impact of each of its clinical programs and trials; the Company’s ability to differentiate ORX750, ORX142, ORX489 and other OX2R agonist molecules, any LockBody candidates

from other treatment options; the development, design and therapeutic potential of ORX750, ORX142, ORX489 and other OX2R agonist molecules, and the LockBody technology platform; and regulatory matters, including the timing and likelihood of success of obtaining regulatory clearance, obtaining authorizations to initiate or continue clinical trials. Any forward-looking statements in this press release are based on our current expectations, estimates, assumptions and projections only as of the date of this release and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to, risks related to the safety and tolerability profile of our product candidates; our ability to identify, screen and recruit a sufficient number of or any subjects in our existing and anticipated new studies or clinical trials of ORX750, ORX142, ORX489 or within anticipated timelines; our expectations relating to the clinical trials of ORX750, including the predicted timing of enrollment, the predicted efficacious doses of ORX750 and our ability to successfully conduct our clinical development of ORX750, our ability to protect and maintain our intellectual property position; business (including commercial viability), regulatory, economic and competitive risks, uncertainties, contingencies and assumptions about the Company; risks inherent in developing product candidates and technologies; future results from our ongoing and planned clinical trials; our ability to obtain adequate financing, including through our financing facility with Oxford Finance, to fund our planned clinical trials and other expenses; trends in the industry; the legal and regulatory framework for the industry, including the receipt and maintenance of clearances to conduct or continue clinical testing; our operating costs and use of cash, including cash runway, cost of development activities and conducting clinical trials, future expenditures risks; the risk that any one or more of our product candidates will not be successfully developed and/or commercialized; the risk that the historical results of preclinical studies or clinical studies will not be predictive of future results in ongoing or future studies; economic risks to the United States and United Kingdom banking systems; and geo-political risks such as the Russia-Ukraine war or the Middle East conflicts. These and other risks concerning our programs and operations are described in additional detail in our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and our other reports, which are on file with the U.S. Securities and Exchange Commission (SEC). We explicitly disclaim any obligation to update any forward-looking statements except to the extent required by law.

Contact:

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SVP of Investor Relations

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