June 14, 2024

Cabaletta Bio Reports Positive Initial Clinical Data from Phase 1/2 RESET-Myositis™ and RESET-SLE™ Trials of CABA-201

– No CRS, ICANS, infections or serious adverse events observed in either of the first two patients through data cut-off of May 28, 2024 –

– CABA-201 exhibited anticipated profile of CAR T cell expansion and contraction with complete B cell depletion observed in both patients by day 15 post-infusion –

– Improvements in both patients' specific disease measures, consistent with academic experience of a similar 4-1BB CD19-CAR T, suggest emerging clinical benefit with CABA-201 while discontinuing all disease-specific therapies other than a planned steroid taper in one patient –

– Immature, naïve B cell repopulation in first IMNM patient observed at week 8 consistent with a potential immune system reset –

– 18 sites open and recruiting across four Phase 1/2 RESET™ trials with 5 patients enrolled as of June 12, 2024; initial clinical and translational data support continued development of CABA-201 at the current dose –

– Company to host live investor conference call and webcast today at 8:00 a.m. ET –

PHILADELPHIA, June 14, 2024 (GLOBE NEWSWIRE) -- Cabaletta Bio, Inc. (Nasdaq: CABA), a clinical-stage biotechnology company focused on developing and launching the first curative targeted cell therapies designed specifically for patients with autoimmune diseases, today reported positive initial clinical data from each of the first two patients dosed with CABA-201 in the Phase 1/2 RESET-Myositis and RESET-SLE trials. These data will be presented today at 8:15 a.m. CEST (2:15 a.m. ET) at a EULAR European Congress of Rheumatology 2024 Industry Symposia session titled "Immune Reset: The Potential of CAR T Cell Therapy to Transform the Treatment of Patients with Autoimmune Disease" in Vienna, Austria. Slides from the presentation can be found on the company's website here.

"We are encouraged by the initial safety, clinical and translational data from the RESET-Myositis and RESET-SLE trials which we believe provide important early validation regarding the potential of the selected clinical dose of CABA-201 to enable an immune system reset for patients with autoimmune diseases. By demonstrating a potentially well-tolerated safety profile along with initial clinical and translational data consistent with the academic experience of a similar 4-1BB CD19-CAR T construct, we believe CABA-201 may be uniquely positioned to fulfill unmet patient needs across a broad range of autoimmune diseases," said David J. Chang, M.D., Chief Medical Officer of Cabaletta. "With the RESET-SSc™ and RESET-MG™ trials recently opening for enrollment, an additional cohort

evaluating patients with juvenile myositis incorporated into the RESET-Myositis trial and the momentum provided by the promising early clinical data, we are looking forward to accelerating clinical trial enrollment in the RESET clinical program. We continue to expect to report initial clinical data from the Phase 1/2 RESET-SSc and RESET-MG trials as well as additional data from the RESET-Myositis and RESET-SLE trials in the second half of this year."

Cabaletta designed CABA-201, a 4-1BB-containing fully human CD19-CAR T cell investigational therapy, to deeply and transiently deplete CD19-positive B cells following a one-time infusion that may enable a reset of the immune system with the potential for durable remission without chronic therapy in patients with autoimmune diseases. Cabaletta is advancing four Phase 1/2 RESET trials evaluating CABA-201 within a total of ten cohorts with six patients in each cohort. All cohorts are evaluating the same single, weight-based dose of 1 x 10^6 cells/kg, following a preconditioning regimen of fludarabine and cyclophosphamide consistent with the dosing regimen used in the academic experience, without a dose escalation requirement.

As of May 28, 2024, the data cut-off date, one patient treated in the immune-mediated necrotizing myopathy (IMNM) cohort in the RESET-Myositis trial had completed three months of follow-up and one patient enrolled in the systemic lupus erythematosus (SLE) non-renal cohort in the RESET-SLE trial had completed one month of follow-up. The patient with IMNM is a 33-year-old male with a two-year history of disease, positive for anti-SRP antibody and who had prior disease-specific therapy that included IVIg, rituximab, methotrexate and glucocorticoids. The patient with SLE is a 26-year-old male with a six-year history of disease, positive for anti-dsDNA antibody and who had prior disease specific therapy that included cyclophosphamide, voclosporin, belimumab, tacrolimus, mycophenolate mofetil, hydroxychloroquine and glucocorticoids. Both patients were administered a one-time infusion of CABA-201 at 1 x 10^6 cells/kg, following a preconditioning regimen of fludarabine and cyclophosphamide. The primary endpoint of each trial is safety and tolerability within 28 days of infusion. Secondary endpoints include translational assessments and clinical outcomes.

Initial Clinical Data Summary

Safety and Tolerability

- CABA-201 was administered during a four-day hospital stay, as currently required by the protocol, and was generally well-tolerated with no serious adverse events reported for either patient through the follow-up period.
- No evidence of cytokine release syndrome (CRS) or immune effector cell-associated neurotoxicity syndrome (ICANS) of any grade was observed for either patient through the follow-up period. Tocilizumab was not administered for either patient.
- No infections were observed for either patient through the follow-up period.
- All chronic maintenance therapy or concomitant medications were discontinued for both patients through the follow-up period, other than a planned prednisone taper for the SLE patient.

Clinical and Translational Profile

- Complete B cell depletion was observed within 15 days post-infusion with CABA-201 in

both patients. Both patients had early, transient leukopenia, as expected with the preconditioning regimen.

- CAR T cell expansion associated with CABA-201 reached its peak magnitude at day 15 post-infusion in both patients and the magnitude of expansion was consistent with the academic experience with a similar 4-1BB CD19-CAR T construct.
- At week 12 of follow-up for the IMNM patient, the data show a decline in creatinine kinase from 617 at infusion to 308 and a total improvement score (TIS) of 30, which is consistent with the clinically meaningful improvement seen in the academic experience of a similar 4-1BB CD19-CAR T construct that also recently reported data from an IMNM patient.
- At week 4 of follow-up for the SLE patient, the data demonstrated an improvement in the SLEDAI-2K (systemic lupus erythematosus disease activity index) score from 26 at baseline to 10.
- B cell repopulation was observed in the IMNM patient at week 8 with immature, naïve B cell phenotypes as demonstrated by flow cytometry, suggesting potential immune system reset with confirmatory analyses ongoing.

Investor Conference Call and Webcast Information

Cabaletta will host a conference call and webcast today, June 14, 2024, at 8:00 a.m. ET to review the initial clinical data presented at the satellite symposium at the EULAR 2024 Congress and provide an update on the RESET clinical development program. A webcast of the live call can be accessed on the News and Events section of the Company's website at www.cabalettabio.com. An archived replay will be available on the Company's website.

About the RESET-Myositis™ Trial

The RESET-Myositis™ trial is a Phase 1/2 open-label study of CABA-201 in subjects with active idiopathic inflammatory myopathy (IIM, or myositis), including the subtypes of dermatomyositis (DM), anti-synthetase syndrome (ASyS), immune-mediated necrotizing myopathy (IMNM) and juvenile myositis (JM), each evaluated in individual cohorts. Subjects will receive a one-time infusion of CABA-201 at a dose of 1 x 10^6 cells/kg, following a preconditioning regimen of fludarabine and cyclophosphamide. Key inclusion criteria for the DM, ASyS and IMNM cohorts include patients between ages 18 to 75 (inclusive), evidence of active disease and disease activity despite prior or current treatment with standard of care treatments. Key exclusion criteria for the DM, ASyS and IMNM cohorts include cancer-associated myositis, significant lung or cardiac impairment, treatment with a B cell depleting agent within the prior approximately six months or treatment with a biologic agent within the prior approximately three months.

About the RESET-SLE™ Trial

The RESET-SLE™ trial is a Phase 1/2 open-label study of CABA-201 in subjects with systemic lupus erythematosus (SLE) and lupus nephritis (LN), each evaluated in individual cohorts. Subjects will receive a one-time infusion of CABA-201 at a dose of 1 x 10^6 cells/kg, following a preconditioning regimen of fludarabine and cyclophosphamide. Key inclusion criteria include patients between ages 18 to 65 (inclusive), evidence of active disease and disease activity despite prior or current treatment with standard of care treatments. Key exclusion criteria include treatment with a B cell depleting agent within the prior approximately six months or treatment with a biologic agent within the prior approximately three months.

About CABA-201
CABA-201 is designed to deeply and transiently deplete CD19-positive cells following a one-time infusion, which may enable an “immune system reset” with the potential for durable remission without chronic therapy in patients with autoimmune diseases. Cabaletta is evaluating CABA-201 in multiple autoimmune conditions within five disease-specific company sponsored INDs including myositis (idiopathic inflammatory myopathy, or IIM), systemic lupus erythematosus (SLE), systemic sclerosis (SSc), generalized myasthenia gravis (gMG) and pemphigus vulgaris (PV; a sub-study to evaluate CABA-201 without preconditioning).

About Cabaletta Bio
Cabaletta Bio (Nasdaq: CABA) is a clinical-stage biotechnology company focused on the discovery and development of engineered T cell therapies that have the potential to provide a deep and durable, perhaps curative, treatment for patients with autoimmune diseases. The CABA™ platform encompasses two strategies: the CARTA (chimeric antigen receptor T cells for autoimmunity) strategy, with CABA-201, a 4-1BB-containing fully human CD19-CAR T, as the lead product candidate being evaluated in the RESET™ (REstoring SElf-Tolerance) clinical trials in systemic lupus erythematosus, myositis, systemic sclerosis and generalized myasthenia gravis and in the RESET-PV™ sub-study within the DesCAARTes™ clinical trial in pemphigus vulgaris, along with the CAART (chimeric autoantibody receptor T cells) strategy, with multiple clinical-stage candidates, including DSG3-CAART for mucosal pemphigus vulgaris and MuSK-CAART for MuSK-associated myasthenia gravis. The expanding CABA™ platform is designed to develop potentially curative therapies that offer deep and durable responses for patients with a broad range of autoimmune diseases. Cabaletta Bio’s headquarters and labs are located in Philadelphia, PA.

Forward-Looking Statements
This press release contains “forward-looking statements” of Cabaletta Bio within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including without limitation, express or implied statements regarding: Cabaletta’s ability to grow its autoimmune pipeline; Cabaletta’s future plans and strategies for its CAAR T and CARTA technologies and the company’s business plans and objectives as a whole; Cabaletta’s expectations around the potential safety and therapeutic benefits of CABA-201, including its belief that CABA-201 may enable an “immune system reset” with the potential for durable remission without chronic therapy in patients with autoimmune diseases; the Company’s advancement of separate Phase 1/2 clinical trials of CABA-201 in patients with SLE, myositis, SSc and gMG and advancement of a RESET-PV sub-study within the ongoing DesCAARTes trial in PV, including the Company’s expectations for the efficiency of the trial designs and updates related to status, safety data, or otherwise and the expected timing of the related data read-outs; Cabaletta’s ability to accelerate its pipeline, develop meaningful therapies for patients and leverage its research and translational insights; the clinical significance of the initial clinical data read-out at the EULAR 2024 Congress in June 2024 for patients with myositis and SLE treated with CABA-201; Cabaletta’s additional planned initial clinical data read-outs for patients with SSc and gMG treated with CABA-201 or otherwise; Cabaletta’s advancement of the process to activate clinical trial sites and pursue patient enrollment; and Cabaletta’s planned assessment of its DesCAARTes™ and MusCAARTes™ trials.

Any forward-looking statements in this press release are based on management's current expectations and beliefs of future events 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 regulatory filings and potential clearance; the risk that signs of biologic activity or persistence may not inform long-term results; Cabaletta's ability to demonstrate sufficient evidence of safety, efficacy and tolerability in its preclinical studies and clinical trials of CABA-201; the risk that the results observed with the similarly-designed construct employed in academic publications, including due to the dosing regimen, are not indicative of the results we seek to achieve with CABA-201; risks related to clinical trial site activation, delays in enrollment generally or enrollment rates that are lower than expected; delays related to assessment of clinical trial results; risks related to unexpected safety or efficacy data observed during clinical studies; risks related to volatile market and economic conditions and public health crises; Cabaletta's ability to retain and recognize the intended incentives conferred by Orphan Drug Designation and Fast Track Designation or other designations for its product candidates, as applicable; risks related to Cabaletta's ability to protect and maintain its intellectual property position; risks related to fostering and maintaining successful relationships with Cabaletta's collaboration and manufacturing partners, including in light of recent legislation; uncertainties related to the initiation and conduct of studies and other development requirements for its product candidates; the risk that any one or more of Cabaletta's product candidates will not be successfully developed and/or commercialized; and the risk that the initial or interim results of preclinical studies or clinical studies will not be predictive of future results in connection with future studies. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause Cabaletta's actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in Cabaletta's most recent annual report on Form 10-K as well as discussions of potential risks, uncertainties, and other important factors in Cabaletta's other filings with the Securities and Exchange Commission. All information in this press release is as of the date of the release, and Cabaletta undertakes no duty to update this information unless required by law.

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