November 18, 2024

Cabaletta Bio Presents Positive Clinical Safety and Efficacy Data on CABA-201 at ACR Convergence 2024

– CABA-201 safety profile suggests favorable risk-benefit with no CRS or ICANS in the majority of patients; low-grade CRS in three of eight patients and one previously reported ICANS event –

– Compelling clinical responses observed in lupus and myositis patients with up to six months of follow-up; first SSc patient demonstrated an emerging, drug-free clinical response –

– All eight patients with active, refractory autoimmune disease discontinued all immunosuppressants prior to CABA-201 infusion and through the follow-up period –

– Consistent and complete B cell depletion observed in all patients within the first month after CABA-201 infusion; evidence of transitional naïve B cell repopulation as early as eight weeks in the first two patients –

– 40 U.S. clinical sites actively recruiting across the RESET™ clinical development program, with 16 patients enrolled and 10 patients dosed with CABA-201 as of November 12, 2024 –

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

PHILADELPHIA, Nov. 18, 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 announced new and updated clinical data on CABA-201 demonstrating the potential to achieve drug-free, compelling clinical responses based on eight patients dosed across the ongoing Phase 1/2 RESET-Myositis™, RESET-SLE™ and RESET-SSc™ clinical trials. These data were presented in oral and poster presentations at the American College of Rheumatology (ACR) Convergence 2024, which is being held at the Walter E. Washington Convention Center in Washington, D.C. from November 14-19, 2024. Presentation materials featured at ACR Convergence 2024 can be accessed on the Company's website here.

"The clinical data reported at ACR Convergence this weekend support the potential of the current dose of CABA-201 to provide immunosuppressant-free, compelling clinical responses in patients with active, refractory autoimmune disease. Data presented from the previously reported patient with lupus nephritis who experienced ICANS and had acute inflammatory events shortly before CABA-201 treatment demonstrated an abnormal, pro-inflammatory cytokine profile prior to and after CABA-201 infusion, suggestive of an occult infection. As a result of these data, subjects in the RESET clinical program who develop a fever prior to scheduled infusion will wait a minimum of two weeks before administration of CABA-201. Other than this patient with a second, later peak expansion, CABA-201 displayed

a consistent PK and PD profile in all other patients," said David J. Chang, M.D., Chief Medical Officer of Cabaletta. "In addition to our promising clinical and translational data set from the RESET program, we believe our efficient clinical trial design, growing footprint of 40 actively recruiting U.S. clinical sites and anticipated expansion into Europe in 2025 provide us with a differentiated opportunity to accelerate development of CABA-201 for patients. Data permitting, we anticipate meeting with the FDA in 2025 to discuss potential registrational trial designs for CABA-201 that will allow us to bring the therapeutic potential of this investigational therapy closer to autoimmune patients."

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 immunosuppressive therapies in patients with autoimmune diseases. Cabaletta is currently evaluating CABA-201 in the RESET clinical development program across five company-sponsored clinical trials that each have disease-specific cohorts with six patients per cohort. All cohorts are evaluating the same single, weight-based dose of CABA-201 at 1 x 10^6 cells/kg without a dose escalation requirement. Treatment with CABA-201 in each clinical trial includes a preconditioning regimen of fludarabine and cyclophosphamide, consistent with the dosing regimen used in the third-party academic studies, except for the RESET-PV™ trial which is evaluating CABA-201 without preconditioning.

New and Updated Clinical Data Summary

As of the data cut-off date of November 1, 2024, eight patients had been dosed with CABA-201 with sufficient follow-up to be evaluable across the RESET clinical development program. In the RESET-Myositis trial, one patient in the immune-mediated necrotizing myopathy (IMNM) cohort completed six months of follow-up and two patients, one in the IMNM cohort and one in the dermatomyositis (DM) cohort, each completed one month of follow-up. In the RESET-SLE trial, one patient in the non-renal systemic lupus erythematosus (SLE) cohort completed six months of follow-up, one patient in the lupus nephritis (LN) cohort completed four months of follow-up and two patients in the non-renal SLE cohort each completed one month of follow-up. Translational assessments from the third patient in the non-renal SLE cohort were not available for inclusion at the time of the data cut-off. In the RESET-SSc trial, one patient in the severe skin cohort completed six weeks of follow-up.

Across these eight patients treated with CABA-201, 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.

Safety and Tolerability Profile: CABA-201 has shown a favorable risk-benefit profile in patients with active and refractory autoimmune disease

- Through 28 days of follow-up, no evidence of cytokine release syndrome (CRS) of any grade was observed in five of the eight patients. Low-grade CRS (Grades 1-2) was observed in three patients, all of which recovered following standard care. Tocilizumab

was not administered for any cases of CRS.
- No evidence of immune effector cell-associated neurotoxicity syndrome (ICANS) of any grade has been observed in any patient since reporting the initial safety data on the first LN patient in August 2024. This patient had acute inflammatory events shortly before CABA-201 treatment and demonstrated an abnormal, pro-inflammatory cytokine profile prior to infusion that continued after CABA-201 infusion, suggestive of a possible occult infection.

Translational Assessments: CABA-201 induced consistent and complete B cell depletion, with early naïve B cell repopulation suggesting the potential to generate an immune system reset

- CAR T cell expansion associated with CABA-201 reached its peak between day 8 and day 15. Translational assessments from the first patient in the LN cohort indicated a second peak at day 29.
- Complete B cell depletion was observed by day 22 after CABA-201 infusion.
- B cell repopulation occurred in the first two patients treated with CABA-201 as early as 8 weeks and exhibited a transitional naïve phenotype, reflecting the production of new B cells after deep systemic depletion.
- Two of the three patients with follow-up beyond three months demonstrated a reduction in disease-associated antibodies. Clinical responses in all three of these patients were observed independent of autoantibody levels.
- Vaccine and infectious pathogen antibodies remained generally stable.

Clinical Outcomes: CABA-201 provided compelling signs of early efficacy, supporting the potential for drug-free clinical responses

- Initial clinical responses in the RESET-Myositis trial were consistent with published data with response kinetics appearing to differ between myositis subtypes.
    - The first known adult DM patient dosed with CAR T in the form of CABA-201 demonstrated an improvement in muscle strength to normal and a major total improvement score (TIS) response off all immunosuppressants at one month of follow-up. The Cutaneous Dermatomyositis Disease Area and Severity Index – Activity (CDASI-A) improved from 25 to 9.
    - At six months of follow-up, the first IMNM patient demonstrated a continued and improved clinical response off immunosuppressants and without flares. At one month of follow-up, the second IMNM patient demonstrated a total improvement score consistent with the first IMNM patient at one month after CABA-201 infusion off immunosuppressants.
- All four patients in the RESET-SLE trial demonstrated clinical responses off immunosuppressants.
    - All three patients in the non-renal SLE cohort demonstrated no clinical symptoms on SLEDAI-2K as of the latest follow-up and the first patient has completed a prednisone taper to discontinuation.
    - The first patient in the LN cohort, who experienced the previously reported ICANS event, had a SLEDAI that improved from 22 at baseline to 8 at month four of follow-up. The patient's proteinuria improved more than 90%, approaching normal levels, while off all immunosuppressants and with an ongoing prednisone taper.

- The first patient in the severe skin cohort in the RESET-SSc trial demonstrated early clinical improvements after discontinuation of disease-specific therapy.
    - The modified Rodnan Skin Score of the first patient in the severe skin cohort improved from 42 at baseline (potential maximum of 51) to 36 at day 42, suggesting the potential emergence of a drug-free clinical response.

Investor Conference Call and Webcast Information
Cabaletta will host a conference call and webcast today, November 18, 2024, at 8:00 a.m. ET to review the new and updated clinical data presented at ACR Convergence 2024 and provide an update on the RESET clinical development program. A webcast of the live call can be accessed here or 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 non-renal 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 the RESET-SSc™ Trial
The RESET-SSc™ trial is a Phase 1/2 open-label study of CABA-201 in subjects with systemic sclerosis (SSc), including the subtypes of severe skin involvement and organ involvement regardless of skin involvement, 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 and 70 (inclusive), evidence of significant skin, pulmonary, renal or cardiac involvement and significant organ involvement despite use of immunosuppressants. Key exclusion criteria include a primary diagnosis of another rheumatic autoimmune disease, 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 a 4-1BB-containing fully human CD19-CAR T cell investigational therapy for patients with autoimmune diseases where B cells contribute to the initiation and/or maintenance of disease. Following a one-time infusion, CABA-201 is designed to transiently and completely deplete all CD19-positive cells. This approach has the potential to reset the immune system and result in compelling clinical responses without chronic therapy requirements in patients. Cabaletta is currently evaluating CABA-201 in the RESET™ (REstoring SElf-Tolerance) clinical development program which includes multiple disease-specific, company-sponsored clinical trials across growing portfolios of autoimmune diseases in a broad range of therapeutic areas, including rheumatology, neurology and dermatology.

About Cabaletta Bio
Cabaletta Bio (Nasdaq: CABA) is a clinical-stage biotechnology company focused on developing and launching the first curative targeted cell therapies designed specifically for patients with autoimmune diseases. The CABA™ platform encompasses two complementary strategies which aim to advance the discovery and development of engineered T cell therapies with the potential to become deep and durable, perhaps curative, treatments for a broad range of autoimmune diseases. The lead CARTA (Chimeric Antigen Receptor T cells for Autoimmunity) strategy is prioritizing the development of CABA-201, a 4-1BB-containing fully human CD19-CAR T cell investigational therapy. CABA-201 is currently being evaluated in the RESET™ (REstoring SElf-Tolerance) clinical development program spanning multiple therapeutic areas, including rheumatology, neurology and dermatology. Cabaletta Bio's headquarters and labs are located in Philadelphia, PA. For more information, please visit www.cabalettabio.com and connect with us on LinkedIn.

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 business plans and objectives as a whole; Cabaletta's ability to realize its vision of launching the first curative targeted cell therapy designed specifically for patients with autoimmune diseases; Cabaletta's ability to successfully complete research and further development and commercialization of its drug candidates in current or future indications, including the timing and results of Cabaletta's clinical trials and its ability to conduct and complete clinical trials; expectation that clinical results will support CABA-201's safety and activity profile; statements regarding the expectations of trial modifications and prophylactic measures, continued trial operations; statements regarding the timing of interactions with regulatory authorities, including such authorities' review of safety information from Cabaletta's ongoing clinical trials and potential registrational program designs for CABA-201; Cabaletta's expectations around the potential success and therapeutic benefits of CABA-201, including its belief that CABA-201 has the potential to reset the immune system and result in compelling clinical responses without chronic therapy requirements in patients; 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 trial, including updates related to status, safety data, efficiency of clinical trial design or otherwise; the clinical significance of the clinical data read-out at the ACR Convergence 2024 in November 2024

for patients with myositis, SLE and SSc treated with CABA-201; Cabaletta's ability to increase enrollment from its rapidly expanding clinical network in the RESET clinical program in the United States and beyond and Cabaletta's ability to leverage such growing clinical trial network to accelerate development of its therapy for patients.

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 that modifications to trial design or approach may not have the intended benefits and that the trial design may need to be further modified; 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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