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

November 18, 2024
Date of Report (Date of earliest event reported)

CABALETTA BIO, INC.
(Exact name of Registrant as Specified in its Charter)

Delaware	**001-39103**	**82-1685768**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

2929 Arch Street, Suite 600, Philadelphia, PA	**19104**
(Address of principal executive offices)	**(Zip Code)**

(267) 759-3100
(Registrant's telephone number, including area code)

Not Applicable
(Former name or former 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:

☐ 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**
Common Stock, par value $0.00001 per share	CABA	The Nasdaq Global Select Market

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 7.01 Regulation FD Disclosure

On November 18, 2024, Cabaletta Bio, Inc. ("Cabaletta" or the "Company") posted an investor presentation (the "Investor Presentation") to the "News & Media" section of the Company's website at *www.cabalettabio.com*. The Investor Presentation will be used in connection with a conference call and webcast today, November 18, 2024, at 8:00 a.m. ET, to review the clinical data presented at the American College of Rheumatology (ACR) Convergence 2024 conference ("ACR Convergence 2024") and provide an update on the RESET clinical development program. A copy of the Investor Presentation is furnished herewith as Exhibit 99.1 to this Current Report on Form 8-K.

On November 18, 2024, the Company also issued a Press Release reporting 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 (the "Press Release"). A copy of the Press Release is furnished herewith as Exhibit 99.2 to this Current Report on Form 8-K.

The information contained in Item 7.01 of this Current Report on Form 8-K, including Exhibits 99.1 and 99.2 attached hereto, is being furnished and shall not be deemed to be "filed" for the purposes of Section 18 of the Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section and shall not be incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

Item 8.01 Other Events.

On November 16, 2024, the Company presented translational updates from the RESET clinical trials at the ACR Convergence 2024 conference. A copy of the poster, which has been published to the "Technology - Posters & Presentations" section of the Company's website is filed as Exhibit 99.3 to this Current Report on Form 8-K and is incorporated herein by reference.

On November 17, 2024, the Company presented a clinical update at the ACR Convergence 2024 conference. A copy of the slides, which has been published to the "News & Media" section of the Company's website, is filed as Exhibit 99.4 to this Current Report on Form 8-K and is incorporated herein by reference.

On November 18, 2024, the Company issued the Press Release reporting 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.

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.

Forward-Looking Statements

The information under this Item 8.01 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 Item 8.01 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 Item 8.01 is as of the date of this Current Report on Form 8-K, and the Company undertakes no duty to update this information unless required by law.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

99.1	Investor Presentation, dated November 18, 2024, furnished herewith.
99.2	Press Release issued by the registrant on November 18, 2024, furnished herewith.
99.3	Poster presentation from Cabaletta Bio, Inc., dated November 16, 2024
99.4	Slides from Cabaletta Bio, Inc.'s ACR Convergence 2024 Conference Presentation, dated November 17, 2024.
104	Cover Page Interactive Data File (embedded within the Inline XBRL Document).

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, hereunto duly authorized.

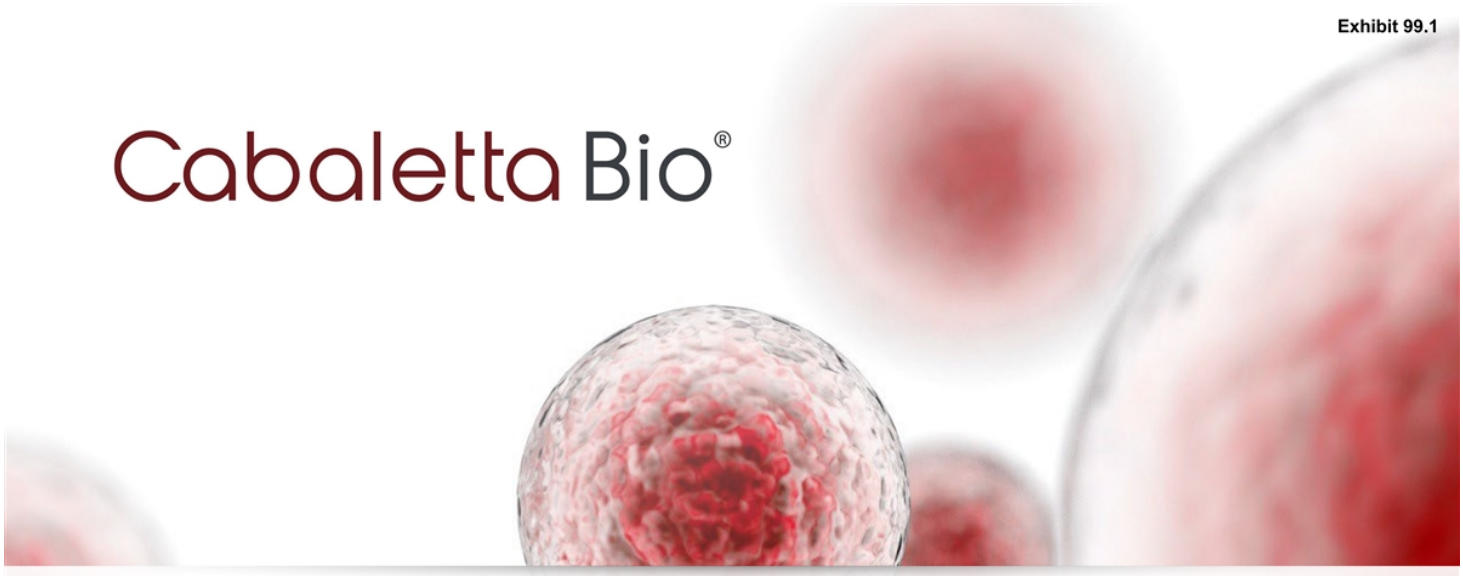
CABALETTA BIO, INC.

Date: November 18, 2024

By: /s/ Steven Nichtberger
Steven Nichtberger, M.D.
President and Chief Executive Officer

Exhibit 99.1

Cabaletta Bio®



CABA-201 Clinical and Translational Data from the RESET™ Phase 1/2 Trials

NOVEMBER 2024

Disclaimer

The following presentation, including any printed or electronic copy of these slides, the talks given by the presenters, the information communicated during any delivery of the presentation and any question and answer session and any document or material distributed at or in connection with the presentation (collectively, the "Presentation") has been prepared by Cabaletta Bio, Inc. ("we," "us," "our," "Cabaletta" or the "Company") and is made for informational purposes only. This Presentation does not purport to be a prospectus, to be complete or to contain all of the information you may desire. Statements contained herein are made as of the date of this Presentation unless stated otherwise, and this Presentation shall not under any circumstances create an implication that the information contained herein is correct as of any time after such date or that information will be updated or revised to reflect information that subsequently becomes available or changes occurring after the date hereof. This Presentation may contain "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 relating to our business, operations, and financial conditions, and include, but are not limited to, express or implied statements regarding our current beliefs, expectations and assumptions regarding: our business, future plans and strategies for our CAAR T and CARTA technologies; our ability to grow our autoimmune-focused pipeline; the ability to capitalize on and potential benefits resulting from our research and translational insights; including those related to any similarly-designed constructs or dosing regimens; the anticipated market opportunities for CABA-201 in patients with autoimmune diseases; our ability to successfully complete research and further development and commercialization of our candidates, including the timing and results of our clinical trials and our 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 regulatory filings and interactions, including timing of such interactions, with regulatory authorities, including such authorities' review of information from Cabaletta's ongoing clinical trials and potential registrational program designs for CABA-201; our business plans and objectives; our expectations around the potential success and therapeutic benefits of CABA-201, our advancement of separate Phase 1/2 clinical trials of CABA-201 in patients with systemic lupus erythematosus (SLE), myositis, SSc, and generalized myasthenia gravis (gMG), and advancement of a RESET-PV trial, including the timing thereof, including our anticipated progress, timing of enrollment, expectations for the efficiency of the clinical trial designs, updates related to status, safety data, or otherwise and the expected timing of the related data read-outs, and ability to leverage our experience in autoimmune cell therapy; 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; our planned initial clinical data read-out for patients with gMG treated with CABA-201 in the first half of 2025; our ability to increase enrollment from our rapidly expanding clinical network in the RESET clinical program in the United States and beyond; our ability to activate clinical trial sites and pursue patient enrollment for the RESET-SLE trial in Europe and leverage our recent CTA; the expectation that Cabaletta may improve outcomes for patients suffering from SLE, SSc, myositis, gMG, mucosal pemphigus vulgaris, or other autoimmune diseases; the ability of our clinical strategy to reduce risk, maximize reach and accelerate timelines of our Phase 1/2 clinical trials of CABA-201; statements related to the differentiation of CAR T in the autoimmune setting; our ability to successfully complete our preclinical and clinical studies for our product candidates, including our ability to enroll the requisite number of patients, dose each dosing cohort in the intended manner, and progress the trial; our ability to obtain and maintain regulatory approval of our product candidates, including our expectations regarding the intended incentives conferred by and ability to retain Orphan Drug Designation and Fast Track Designations for our product candidates, as applicable; our ability to accelerate our pipeline and to develop meaningful therapies for patients, including in collaboration with academic and industry partners and the ability to optimize such collaborations on our development programs; and our expectations regarding our use of capital and other financial results, including our ability to fund operations into the first half of 2026. Words such as, but not limited to, "look forward to," "believe," "expect," "anticipate," "estimate," "intend," "plan," "would," "should" and "could," and similar expressions or words, identify forward-looking statements.

Various risks, uncertainties and assumptions could cause actual results to differ materially from those anticipated or implied in our forward-looking statements. Such risks and uncertainties include, but are not limited to, risks related to the success, cost, and timing of our product candidate development activities and preclinical studies and clinical trials, risks related to our ability to demonstrate sufficient evidence of safety, efficacy and tolerability in our preclinical studies and clinical trials of CABA-201, DSG3-CAART and MuSK-CAART, the risk that the results observed with the similarly-designed construct, including, but not limited to, due to dosing regimen, are not indicative of the results we seek to achieve with CABA-201, ethe risk that signs of biologic activity or persistence may not inform long-term results, the risk that interim results do not always inform later results, the risk that piersistence observed with effective CD19-CAR T oncology studies in combination with lymphodepletion is not indicative of, or applicable to, clinical responses in patients with mPV, risks related to clinical trial site activation or enrollment rates that are lower than expected, our ability to protect and maintain our intellectual property position, risks related to our relationships with third parties, uncertainties related to regulatory agencies' evaluation of regulatory filings and other information related to our product candidates, our ability to retain and recognize the intended incentives conferred by any Orphan Drug Designations and Fast Track Designations, risks related to regulatory filings and potential clearance, 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 volatile market and economic conditions and public health crises. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Accordingly, you are cautioned not to place undue reliance on these forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause our actual results to differ materially from those contained in the forward-looking statements, see the section entitled "Risk Factors" in our most recent annual report on Form 10-K, as well as discussions of potential risks, uncertainties, and other important factors in our other and subsequent filings with the Securities and Exchange Commission. 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 the Company believes these third-party sources to be reliable as of the date of this Presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. The Company is the owner of various trademarks, trade names and service marks. Certain other trademarks, trade names and service marks appearing in this Presentation are the property of third parties. Solely for convenience, the trademarks and trade names in this Presentation are referred to without the ® and TM symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Today's Agenda

AGENDA TOPIC	SPEAKER
CABA-201 Overview	Steven Nichtberger, MD *Chief Executive Officer*
Lessons from Oncology: Expanding CAR T Cell Therapies into Autoimmunity	Carl H. June, MD *Director of the Center for Cellular Immunotherapies, Penn Medicine*
CABA-201 Clinical and Translational Data from the RESET™ Clinical Program	David Chang, MD, MPH, FACR *Chief Medical Officer*
Conclusions	Steven Nichtberger, MD *Chief Executive Officer*
Q&A	

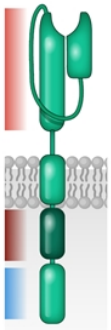
CABA-201: CD19-CAR T specifically designed for autoimmunity

Cabaletta's CD19 binder with similar *in vitro* & *in vivo* activity to construct used in academic studies[1,3]

Fully human anti-CD19 binder
Similar binding affinity & biologic activity to FMC63, with binding to the same epitopes[1,2]

4-1BB costimulatory domain
Same co-stim. domain as used in academic studies

CD3-ζ signaling domain



CABA-201[5]

Clinical data reported by IASO using licensed CD19 binder in oncology[4]

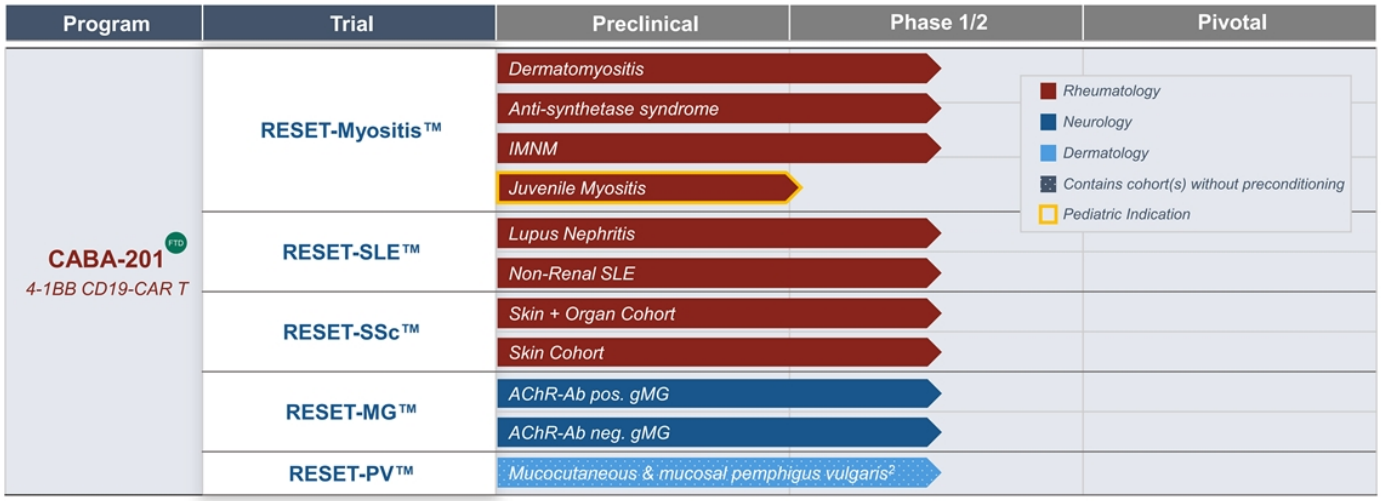
- **Fully human binder**
  Evaluated as dual-CAR combined with CD22 binder with standard Flu/Cy preconditioning
- **Data reported in ~20 patients to date**
  B cell leukemia and lymphoma in IIT in China
- **Safety data supports autoimmune development**

IIT – Investigator-initiated trial; Flu/Cy – Fludarabine/Cyclophosphamide

1. Peng, Binghao J, et al. "Preclinical specificity and activity of CABA-201, a fully human 4-1BB containing CD19 CAR T therapy for treatment-resistant autoimmune disease." Poster presented at: American Society Gene and Cell Therapy 26th Annual Meeting; 2023 May 19; Los Angeles, CA.
2. Dai, Zhenyu, et al. "Development and functional characterization of novel fully human anti-CD19 chimeric antigen receptors for T-cell therapy." Journal of Cellular Physiology 236.8 (2021): 5832-5847.
3. Müller, Fabian, et al. "CD19 CAR T-Cell Therapy in Autoimmune Disease—A Case Series with Follow-up." New England Journal of Medicine 390.8 (2024): 687-700.
4. Evaluated as part of CT120, a dual-CD19xCD22 CAR T product candidate under development by Nanjing IASO Biotherapeutics, Co., Ltd. (IASO Bio).
5. Transmembrane domain in CABA-201 is CD8α vs. TNFRSF19 (Troy) utilized in the academic construct. The two transmembrane domains have not been shown to have a significant difference in function or IFN-γ production in preclinical studies. The CD8α transmembrane domain is employed in tisagenlecleucel.

RESET™ clinical program for CABA-201, a CD19-directed CAR T

Multiple autoimmune diseases evaluated in distinct disease cohorts across five clinical trials



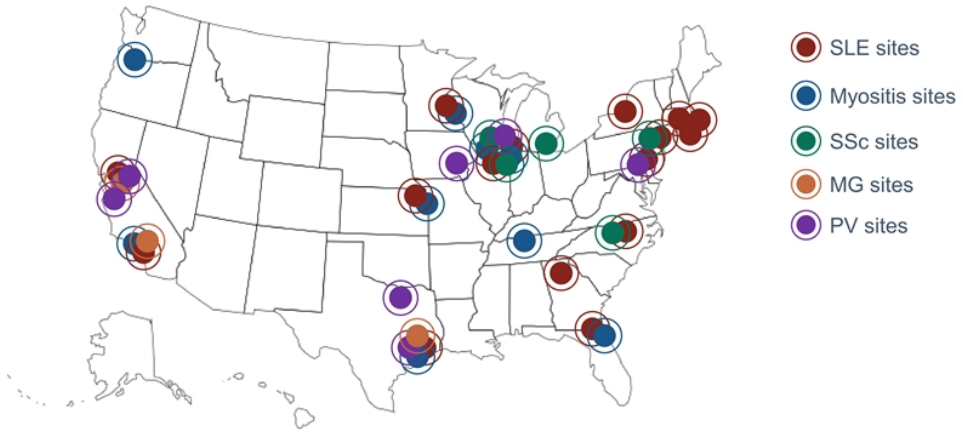
RESET™ – **RE**storing **SE**lf-**T**olerance; IMNM – Immune-mediated necrotizing myopathy; SLE – Systemic lupus erythematosus; Ab – Antibody; AChR – Acetylcholine receptor; gMG – Generalized myasthenia gravis

● FDA Fast Track Designation received in dermatomyositis, SLE and lupus nephritis, systemic sclerosis, mucosal pemphigus vulgaris, and MuSK-Ab positive MG.

Expanding clinical site footprint across RESET™ program[1]

16 patients enrolled and 10 patients dosed across RESET™ studies, with 40 actively recruiting U.S. sites

- Clinical development expanding to Europe in 2025 with EMA CTA authorization for CABA-201 received for RESET-SLE™
- Gerwin Winter appointed as SVP and Head of International at Cabaletta Bio



RESET™ Program Upcoming Milestone:

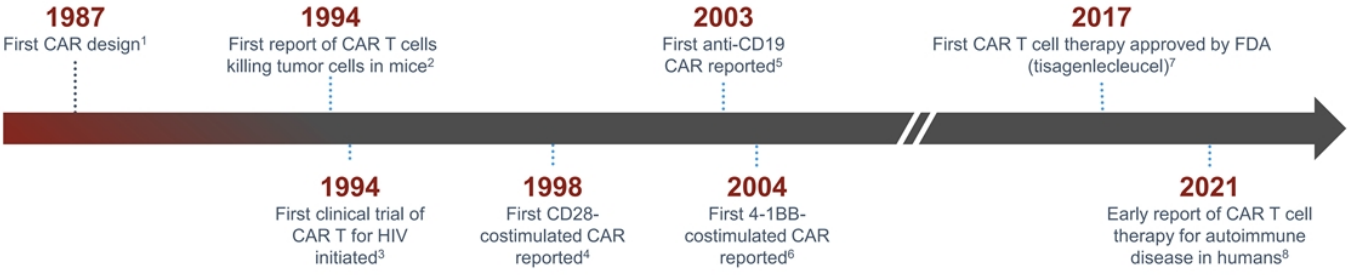
- ❑ **2025:** Data permitting, anticipate meeting with FDA regarding potential registrational trial designs for CABA-201

1. Data per clinicaltrials.gov as of November 12, 2024, as compared to companies with actively recruiting U.S. clinical sites for autoimmune cell therapy trials under company-sponsored INDs.

Cabaletta Bio®

Success of CAR T in oncology established over decades

B cell cancer experience with CAR T informs use in autoimmune patients



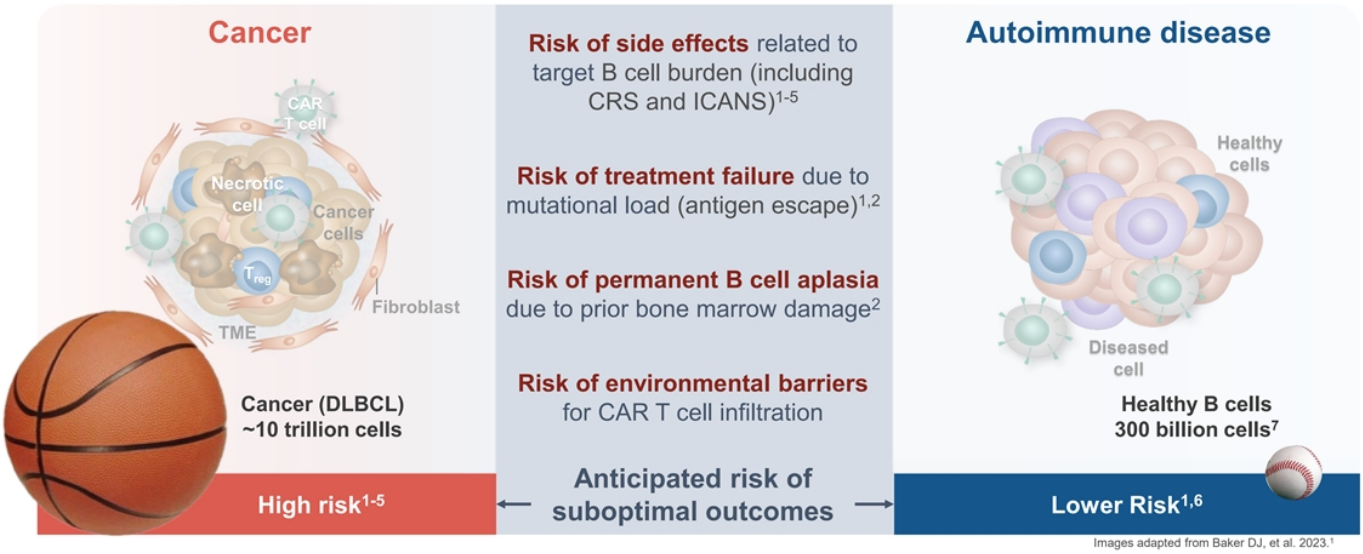
- Multiple types of cell therapies are in Phase 1/2 studies, with the majority being autologous CAR T cell therapy[9]
- ~800 ongoing CAR T trials, with the majority in the US and China[10]

Experience in oncology has established foundation for application in autoimmune disease

1. Kuwana Y, et al. Biochem Biophys Res Commun. 1987;149(3):960-968. 2. Moritz D, et al. Proc Natl Acad Sci USA. 1994;91:4318-4322. 3. Roberts MR, et al. Blood. 1994;84(9):2878-2889. 4. Krause A, et al. J Exp Med. 1998;188:619-626. 5. Brentjens RJ, et al. Nat Med. 2003;101(4):1637-1644. 6. Imai C, et al. Leukemia. 2004;18:676-684. 7. O'Leary MC, et al. Clin Cancer Res. 2019;25(4):1142-146. 8. Mougiakakos D, et al. N Engl J Med. 2021;385(6):567-569. 9. Krishnamurthy A, et al. Wells Fargo, November 2017. 10. Clinicaltrials.gov. Accessed November 14, 2024. https://clinicaltrials.gov/search?intr=chimeric%20antigen%20receptor.

Considerations for CAR T therapy in cancer and autoimmunity

Factors that predict adverse events and relapse differ in patients with autoimmune diseases[1]



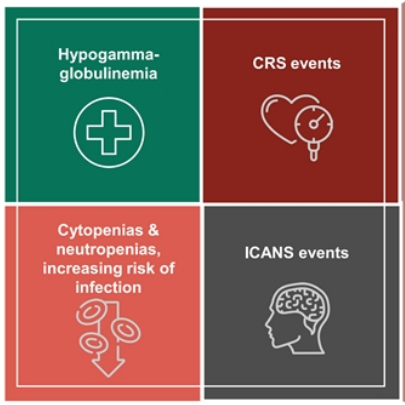
Images adapted from Baker DJ, et al. 2023.[1]

TME, tumor microenvironment.

1. Baker DJ, et al. *Nature*. 2023;619(7971):707-715. 2. Sterner RC, Sterner RM. *Blood Cancer J*. 2021;11(4):69. 3. Breyanzi. Prescribing information; 2024. 4. Yescarta. Prescribing information; 2024. 5. Kymriah. Prescribing information; 2022. 6. Müller F, et al. *N Engl J Med*. 2024;390(8):687-700. 7. Sender, R et al. *PNAS* 2023 e2308511120.

Potential adverse events after CAR T cell therapy in cancer

Physician experience in oncology has established algorithms for routine management of common AEs



CRS/ICANS assessment parameters[1]

CRS

Graded 1–4 depending on severity & manifestations

Fever

with

Hypotension

and/or

Hypoxia

ICANS

Graded 1–4 depending on severity & manifestations

- ICE score — *Measures alterations in speech, orientation, handwriting, attention, & receptive aphasia[2]*
- Consciousness
- Seizure
- Motor findings
- ICP/cerebral edema

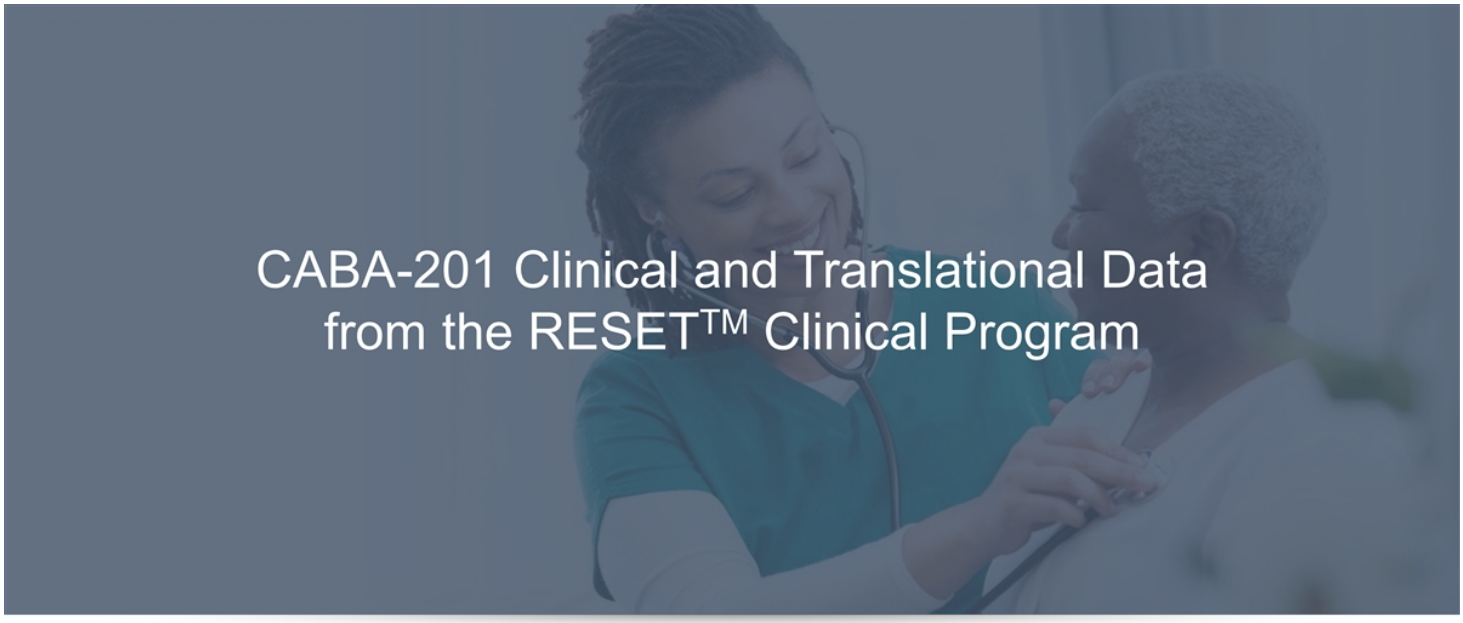
Managing CRS & ICANS events

- CRS: Tocilizumab +/- steroids & supportive care[3]
- ICANS: Steroids, supportive care and anti-seizure medications when appropriate[4]
- Seizure prophylaxis is a routine part of some CAR T therapy administration protocols [5-8]

Image adapted from Bonifant CL, et al. 2016,[9] Verdun N and Marks P. 2024,[10] Adkins S, et al. 2019.[11]

AE, adverse event; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; ICE, immune effector cell encephalopathy; ICP, intracranial pressure

1. Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25(4):625–638. 2. Herr MM, et al. *Biol Blood Marrow Transplant*. 2020;26(11):e271–e2744. 3. Zhang Y, et al. *J Clin Med*. 2023;12(19):6124. 4. Jain MD, et al. *Blood*. 2023;141(20):2430–2442. 5. The EBMT/EHA CAR-T Cell Handbook. Available at: www.ebmt.org/sites/default/files/2022-02/2022_Book_TheEBMTEHACAR-TCellHandbook.pdf (accessed October 2022). 6. Pensato U, et al. *J Neurol*. 2023;270(5):2659–2673. 7. Pensato U, et al. *Neurol Sci*. 2024;45(8):4007–4014. 8. Mackensen A, et al. *Nat Med*. 2022;28(10):2124–2132. 9. Bonifant CL, et al. *Mol Ther Oncolytics*. 2016;3:16011. 10. Verdun N, Marks P. *N Eng J Med*. 2024;390(7):584-586. 11. Adkins S. *J Adv Pract Oncol*. 2019;10(suppl 3):21-28.



CABA-201 Clinical and Translational Data from the RESET™ Clinical Program

Cabaletta Bio®

Autoimmune disease patients face substantial unmet medical needs

Despite therapies with chronic broad immunosuppression, mortality is increased, and quality of life is reduced*[1-4]

Myositis

- Chronic inflammation often leads to permanent tissue damage[1]
- Progressive weakness, pain, dysphagia, and extramuscular manifestations are also common[5]

Systemic lupus erythematosus

- Progressive, multi-organ damage[6]
- ~40% develop lupus nephritis with 25% risk of death or ESKD within 10 years[7,8]

Systemic sclerosis

- Progressive skin and organ fibrosis, which often leads to irreversible lung, cardiac and kidney damage[2]
- Average survival from diagnosis is ~12 years[9]

Patients are seeking a drug-free, symptom-free life; physicians also prioritize prevention of end-organ damage[10]

*Compared with the general population
ESKD, end-stage kidney disease

1. Lundberg IE, et al. Nat Rev Dis Primers. 2021;7(1):86. 2. Allanore Y, et al. Nat Rev Dis Primers. 2015;1:15002. 3. Zen M, et al. Eur J Intern Med. 2023;112:45–51. 4. Refai RH, et al. Sci Rep. 2024;14(1):5234. 5. Suh J, Amato AA. Muscle Nerve. 2024;70(2):166–172. 6. Murimi-Worstell IB, et al. BMJ Open. 2020;10(5):e031850. 7. Anders HJ, et al. Nat Rev Dis Primers. 2020;6(1):7. 8. Hoover PJ, Costenbader KH. Kidney Int. 2016;90(3):487–492. 9. Mayes MD. Rheum Dis Clin North Am. 2003;29(2):239-254. 10. Golder, et al. Lupus. 2018;27(3): 501-506

Key inclusion and exclusion criteria in RESET™ clinical program

Designed to evaluate the safety and tolerability of CABA-201 in subjects with active, refractory disease

Key inclusion criteria[1–3]

Evidence of active disease despite prior or current treatment with standard of care

RESET-Myositis™

- Age ≥18 and ≤75 with a diagnosis of IIM (ASyS, DM, or IMNM)
- Presence of at least one MSA
- **JIIM**: Age ≥6 and ≤17 with presence of at least one MSA or MAA

RESET-SLE™

- Age ≥18 and ≤65 with an SLE diagnosis
- Positive ANA or anti-dsDNA at screening
- **SLE (non-renal)**: active, moderate to severe SLE, SLEDAI-2K ≥8; pure class V LN patients eligible for this cohort
- **LN**: active, biopsy-proven LN class III or IV (± class V)

RESET-SSc™

- Age ≥18 and ≤70 with a limited or diffuse SSc diagnosis
- Evidence of significant skin, pulmonary, renal, or cardiac involvement

Key exclusion criteria[1–3]

B cell-depleting agent within prior 3-6 months; Previous CAR T therapy and/or HSCT

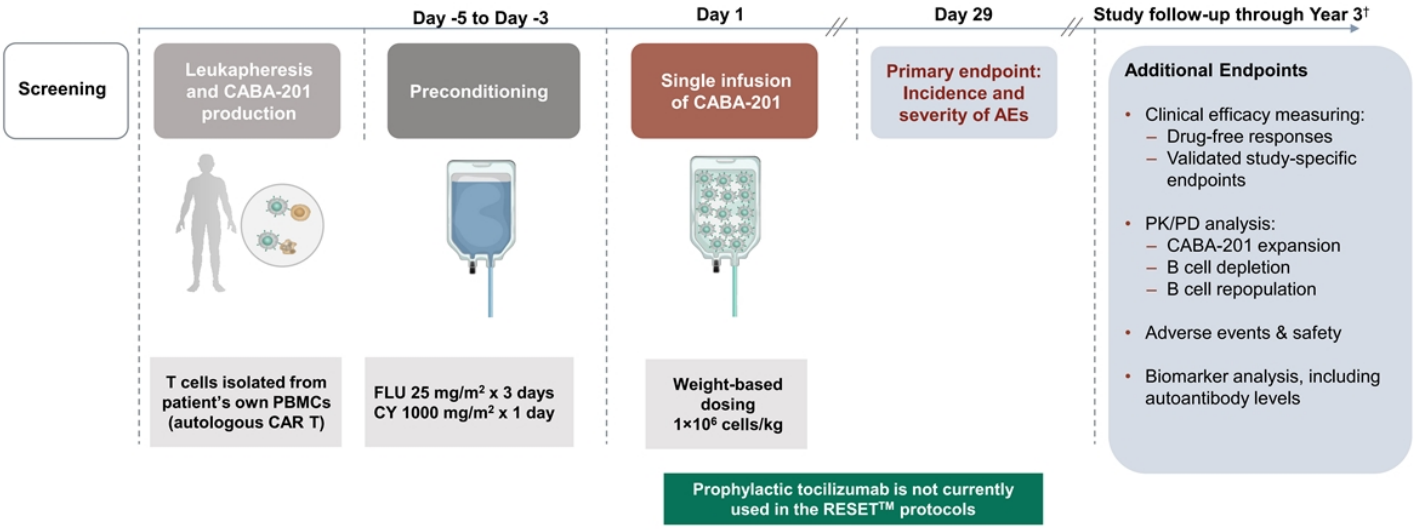
- Cancer-associated myositis
- Significant lung or cardiac impairment
- Presence of kidney disease other than LN
- Current symptoms of severe, progressive, or uncontrolled pulmonary or cardiac disease
- Severe lung or cardiac impairment

ASyS, antisynthetase syndrome; CAR, chimeric antigen receptor; DM, dermatomyositis; HSCT, hematopoietic stem cell transplantation; IIM, idiopathic inflammatory myopathy; JIIM, juvenile idiopathic inflammatory myopathy; LN, lupus nephritis; MAA, myositis-associated antibody; MSA, myositis-specific antibodies; SLEDAI-2k, SLE disease activity index 2000; SSc, systemic sclerosis.

1. ClinicalTrials.gov. Available at: www.clinicaltrials.gov/study/NCT06121297 (accessed October 2024).
2. ClinicalTrials.gov. Available at: www.clinicaltrials.gov/study/NCT06328777 (accessed October 2024).
3. ClinicalTrials.gov. Available at: www.clinicaltrials.gov/study/NCT06154252 (accessed October 2024).

RESET™ clinical trials have consistent design principles[1]

Individual trials in myositis, SLE, and SSc share common elements of preconditioning, dose, and study design



†Follow up period encompasses 15 years in total, aligned to regulatory guidance for CAR T cell therapies

AE, adverse event; CABA, Cabaletta Approach to B cell Ablation; FLU, fludarabine; CY, cyclophosphamide; PBMC, peripheral blood mononuclear cell; PD, pharmacodynamics; PK, pharmacokinetics

Cabaletta Bio: Data on file; 1. Peng BJ, et al. Mol Ther Methods Clin Dev. 2024;32(2):101267.

Baseline characteristics of first 8 patients in the RESET™ program

All patients had active, refractory disease and most had failed B cell-targeting therapies

	RESET-Myositis™			RESET-SLE™				RESET-SSc™
Patient / Cohort	**IMNM-1**	**IMNM-2**	**DM-1**	**SLE-1**† Class V LN	**SLE-2**	**SLE-3**	**LN-1**	**SSc-Skin-1** (severe skin cohort)
Age, sex	33 M	60 M	57 M	26 M	36 F	44 F	24 F	66 F
Disease duration	~2 years	~4 years	~4 years	~6 years	~17 years	~9 years	~2 years	~2 years
Autoantibodies	SRP	HMGCR	SAE	dsDNA	dsDNA	dsDNA	dsDNA	RNA P III
Baseline Disease activity*	**MMT-8**			**SLEDAI-2K**				**mRSS**
	130	126	131	26	10	8	22	42
	CK (U/L)			**UPCR (mg/mg)**				
	617	4725	94	1.08†	n/a	n/a	7.22	
Therapies at Screening	GC, MTX	GC, IVIG	GC, MMF, HCQ	GC, MMF, HCQ	GC, AZA, HCQ	HCQ, MMF, BEL	GC, ANI, VOC, MMF, HCQ	MMF
Other prior therapies	RTX, IVIG	RTX, MMF, MTX	IVIG	CYC, BEL, VOC, TAC	MSC, RTX, ANI, BEL, ADA, MTX	GC, MTX	BEL, LEF	HCQ
GC dose at Screening (mg/day)	5	5	20	10	7	n/a	20	n/a

*Baseline disease activity = activity before pre-conditioning. † SLE-1 had class V LN; inclusion criteria for LN cohort requires class III/IV LN.

ADA, adalimumab; ANI, anifrolumab; AZA, azathioprine; BEL, belimumab; CK, creatinine kinase; dsDNA, double-stranded DNA; GC, glucocorticoid; HCQ, hydroxychloroquine; HMGCR, 3-hydroxy-3-methylglutaryl-coenzyme A reductase; IVIG, intravenous immunoglobulin; LEF, leflunomide; MMF, mycophenolate mofetil; MMT-8, manual muscle testing 8; mRSS, modified Rodnan skin score; MSC, mesenchymal stem cell; MTX, methotrexate; RNA P III, RNA polymerase III; RTX, rituximab; SAE, small ubiquitin-like modifier activating enzyme; SRP, signal recognition particle; TAC, tacrolimus; U/L, units per liter; UPCR, urinary protein-to-creatinine ratio; VOC, voclosporin.

Cabaletta Bio: Data on file.

Incidence and severity of adverse events in the first 8 patients*

	RESET-Myositis™			RESET-SLE™				RESET-SSc™
Cohort	**IMNM**		**DM**	**Non-renal SLE**			**LN**	**SSc – Severe Skin**
Patient	**IMNM-1**	**IMNM-2**	**DM-1**	**SLE-1**	**SLE-2**	**SLE-3**	**LN-1**	**SSc-Skin-1**
CRS†	None	None	None	None	Grade 1	None	Grade 1	Grade 2
ICANS†	None	None	None	None	None	None	Grade 4	None
Serious infections‡	None	None	None	None	None	None	None	None
Hypogammaglobulinemia	None	None	None	None	None	None	Grade 2	None
Related SAEs (Grade)§ (excluding CRS and ICANS)	None	None	None	None	None	None	Fever (1) Pancytopenia¶ (4)	None
Unrelated SAEs (Grade)§	None	Back Pain (3) PE# (4)	None	None	None	None	None	Neutropenia (4) (FLU/CY related)

*As of Nov 1, 2024; Primary endpoint is incidence and severity of Adverse Events through Day 29. †Graded per ASTCT Consensus Grading Criteria. Of these patients, only DM-1, SLE-2, SLE-3, and SSc-Skin-1 **received** medication for seizure prophylaxis. Tocilizumab was **not** administered for any cases of CRS. ‡Coded in System Organ Class of Infections and Infestations and meets seriousness criteria. §As assessed per FDA guidelines.

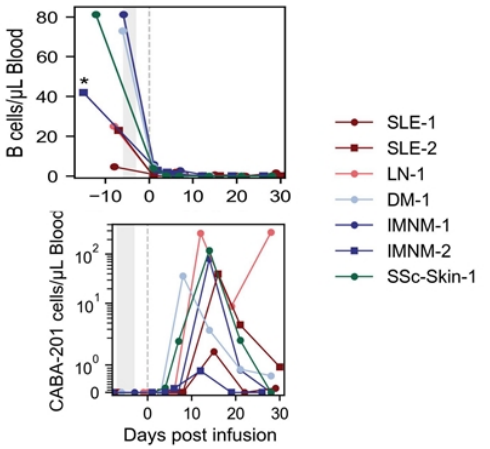
#Patient with Factor V Leiden heterozygosity (increased risk for thrombosis), recent intravenous immunoglobulin treatment, history of myocardial infarction, recent hospitalization for back pain & fatigue with decreased mobility. Undetectable CABA-201 levels since Day 22. Event occurred at Day 38 and was reported as PE leading to cardiac arrest, followed by successful pulmonary artery thrombectomy.
¶Consistent with "Prolonged Cytopenias," which is a labeled warning and precaution for approved oncology CAR T products.

CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; PE, pulmonary embolism; SAE, serious adverse event
Cabaletta Bio: Data on file.

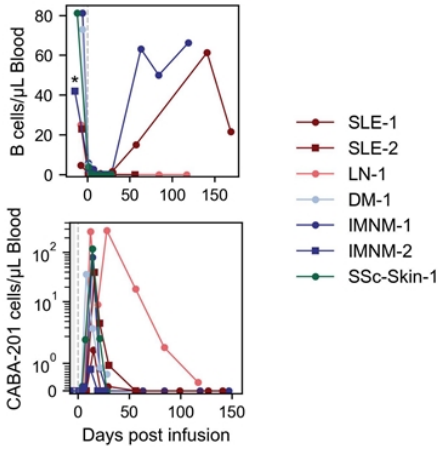
Consistent and complete B cell depletion by Day 22[1]

In patients with >3-month follow-up, B cell repopulation with naïve cells started as early as 8 weeks

B cell depletion & CABA-201 expansion through Day 30



B cell depletion/repopulation & CABA-201 expansion through Day 150



CABA-201 exhibited a PK/PD profile with peak expansion between Day 8 and 15 as expected, with a later 2nd peak for the first LN patient

PK, pharmacokinetic; PD, pharmacodynamic

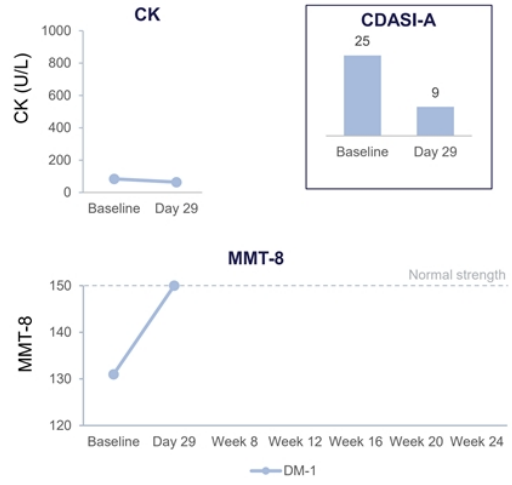
* Pre-infusion B-cell levels were measured at pre-preconditioning for all subjects other than IMNM-2 where apheresis was used

1. Nunez et al. Correlative Studies of CABA-201 from the RESET-Myositis™ and RESET-SLE™ Clinical Trials. Presented at ACR Convergence 2024. Abstract 0324

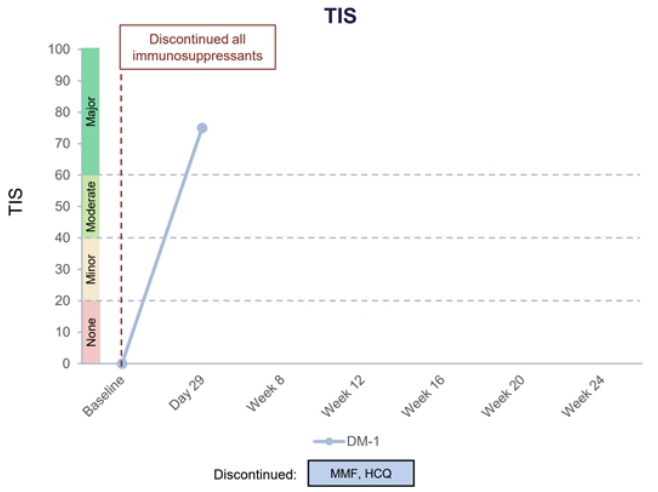
RESET-Myositis™: Early efficacy data following CABA-201 infusion

1st known adult DM patient dosed with CAR T demonstrated compelling early response off immunosuppressants‡

Disease activity & improvement measures



DM patient demonstrated a major TIS response at Day 29

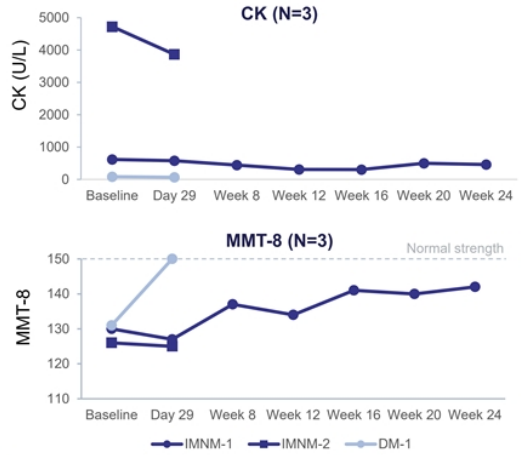


‡ As of Nov 1, 2024
CDASI-A, Cutaneous Dermatomyositis Disease Area and Severity Index – Activity; TIS, total improvement score; U/L, units per liter.
Cabaletta Bio: Data on file.

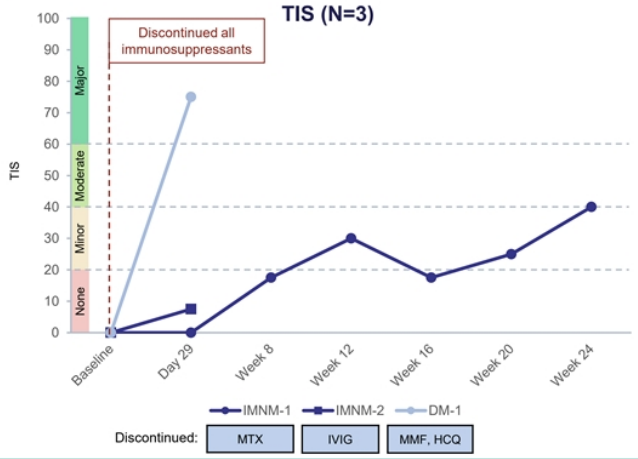
RESET-Myositis™: Efficacy data following CABA-201 infusion

1st IMNM patient with longer follow up demonstrated continuing response off immunosuppressants without flares‡

Disease activity & improvement measures



1st IMNM patient showed a moderate TIS response at Week 24



Initial clinical responses in IMNM are consistent with published data[1]; response kinetics may differ among myositis subtypes

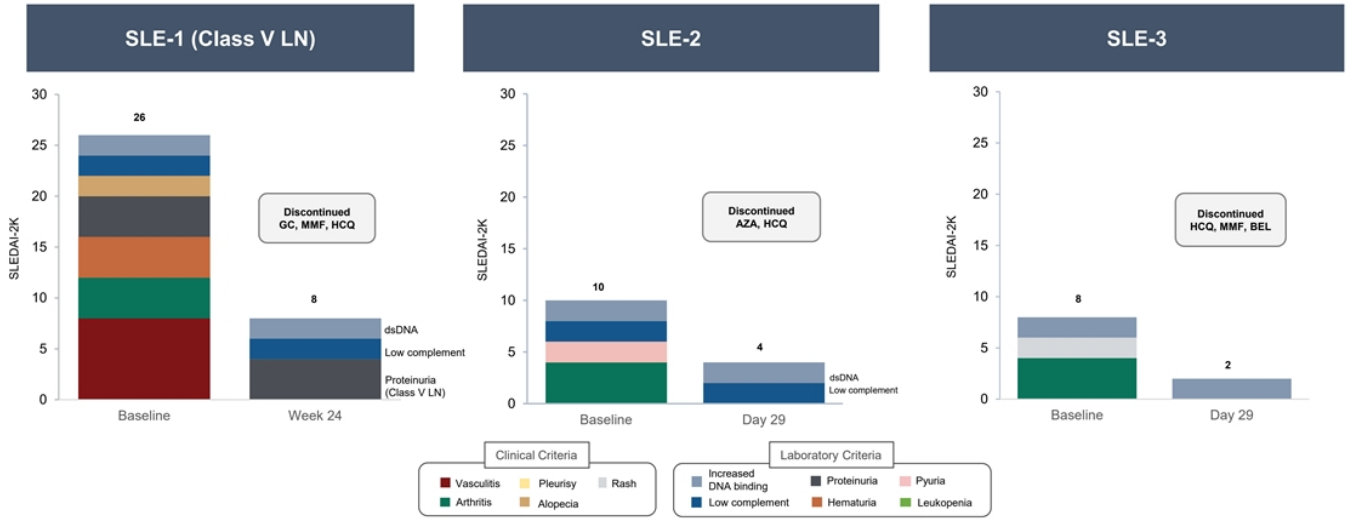
‡ As of Nov 1, 2024

Cabaletta Bio: Data on file. 1. Schett, G. 'CAR-T Cell Therapy: "The Future is Now."' 5th Global Conference on Myositis. iMyoS. Pittsburgh, PA.

Cabaletta Bio®

RESET-SLE™: Efficacy data in SLE following CABA-201 infusion

All 3 SLE patients demonstrated clinical responses off immunosuppressants; first patient completed steroid taper‡



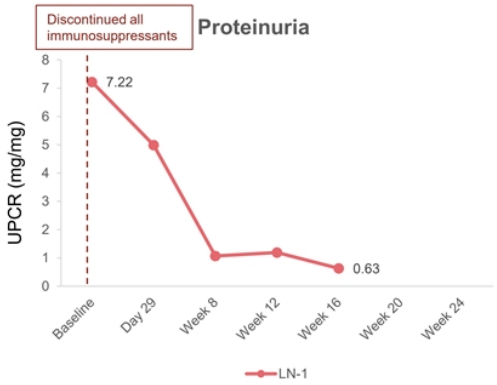
No clinical symptoms on SLEDAI-2K through latest follow up, including SLE-1 with isolated Class V LN (non-renal cohort) with persistent proteinuria as expected

‡ As of Nov 1, 2024
SLEDAI-2k, SLE disease activity index 2000.
Cabaletta Bio: Data on file.

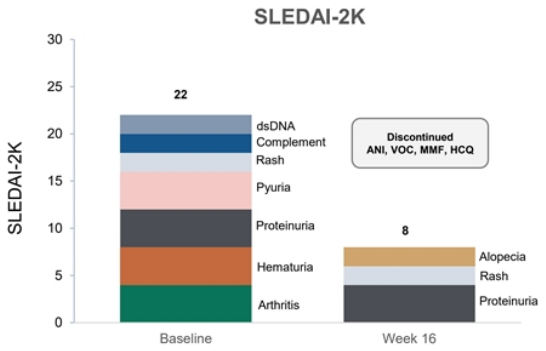
RESET-SLE™: Efficacy data in LN following CABA-201 infusion

LN-1 demonstrated marked improvement of proteinuria off all immunosuppressants, continuing steroid taper‡

UPCR decreased from 7.22 to 0.63 mg/mg at Week 16



1st LN patient SLEDAI reduced by 14 points at Week 16



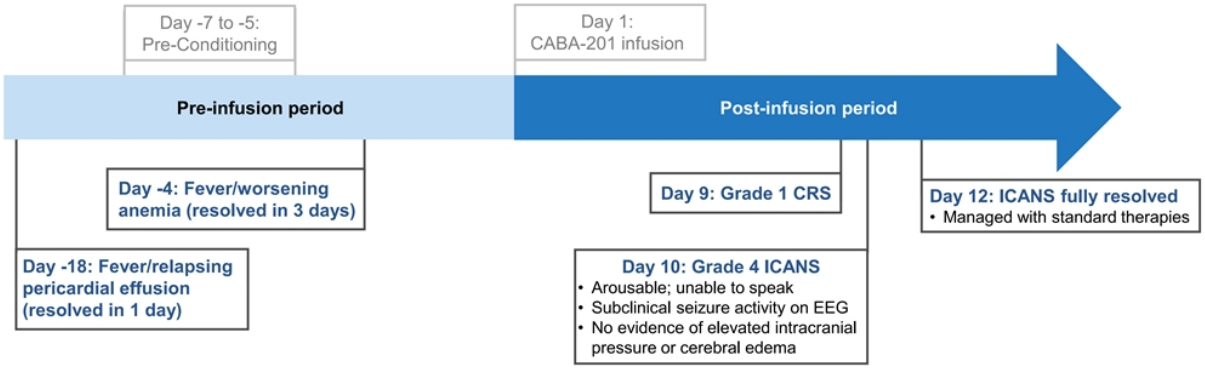
LN-1 proteinuria markedly improved by Week 8 with alopecia/rash as the remaining clinical manifestations at Week 16 after discontinuing all immunosuppressants & continuing prednisone taper

‡ As of Nov 1, 2024
SLEDAI-2k, SLE disease activity index 2000; UPCR, urinary protein-to-creatinine ratio.
Cabaletta Bio: Data on file.

ICANS event timeline in first LN patient

Patient with recent fever in setting of acute and severe inflammation

- 24-year-old female with SLE for ~2 years and with active class III LN
- Active, severe (SLEDAI-2K = 22; UPCR = 7.22 mg/mg) refractory disease despite 5 systemic treatments* for SLE at screening



Patient had acute, febrile inflammatory events & highly elevated pro-inflammatory cytokines‡ pre-infusion that continued after treatment, suggesting a possible occult infection; supportive data from TCR clonal sequencing[1]

*Therapies at Screening: glucocorticoids, anifrolumab, voclosporin, mycophenolate mofetil, hydroxychloroquine
‡MIP-1β, IL-27
Cabaletta Bio: Data on file. 1. Nunez et al. Correlative Studies of CABA-201 from the RESET-Myositis™ and RESET-SLE™ Clinical Trials. Presented at ACR Convergence 2024. Abstract 0324

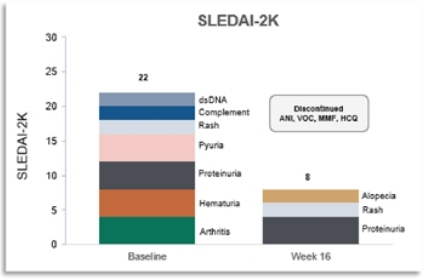
Cabaletta Bio®

Outcomes in first LN patient 4 months post-treatment

Compelling clinical response since discontinuation of all immunosuppressants, continuing steroid taper

Patient Month 4 Follow-up*

- Off all immunosuppressants‡
- Prednisone 8mg/day; taper ongoing
- SLEDAI-2K: 22 → 8
- UPCR (mg/mg): 7.22 → 0.63



"Overall, I feel much better than I felt before CABA-201 therapy. I have much more energy, I have significantly less joint pain and inflammation, my proteinuria has improved, I no longer have any mouth sores, and I am getting back to my normal self!

At 25 years old, my kidneys were not functioning properly and continued to get worse despite all of the strong medications I was on. I had multiple occurrences of fluid around my heart. CABA-201 has put a stop to that and has allowed my body to heal. Although I faced complications afterwards, I believe the improvement that I have seen in both my numbers and how I feel, was far worth it.

If I had the choice, I would choose to receive CABA-201 again…. "

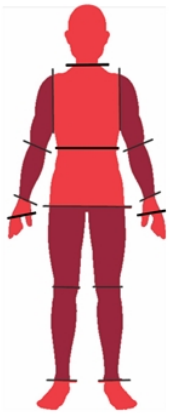
- LN-1 patient at 4 months post-therapy

*As of Nov 1, 2024
‡Therapies at Screening: glucocorticoids, anifrolumab, voclosporin, mycophenolate mofetil, hydroxychloroquine
Cabaletta Bio: Data on file.

Emerging efficacy data 42 days post infusion in first SSc patient

Early disease improvements in face and hands after discontinuation of disease-specific medication

Baseline mRSS score by body area[1]



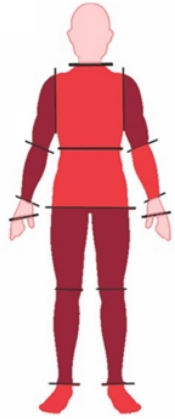
0 None
1 Mild
2 Moderate
3 Severe

Overall mRSS score[1]

	Baseline	Day 22	Day 42
mRSS	42	38	36

- Modified Rodnan Skin Score (mRSS): a measure of skin thickness in SSc across 17 body areas, with a maximum score of 51[1]
- Used as an outcome measure in SSc clinical trials as a surrogate for disease activity, severity and mortality[1]

Day 42 mRSS score by body area[1]

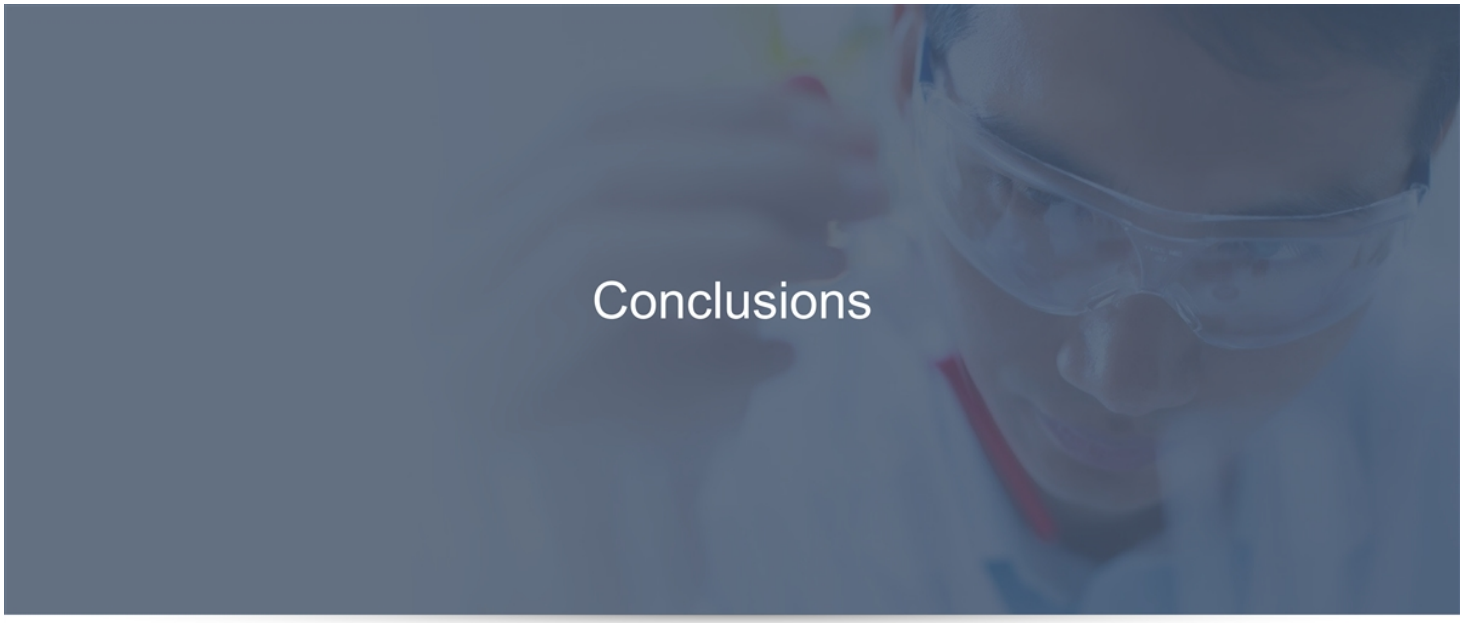


0 None
1 Mild
2 Moderate
3 Severe

Early clinical data in SSc-Skin-1 indicate potential emergence of a drug-free clinical response‡

‡ As of Nov 1, 2024 patient is not taking immunosuppressants or steroids

Cabaletta Bio: Data on file. 1. Khanna D, et al. J Scleroderma Relat Disord. 2017;2(1):11–18.



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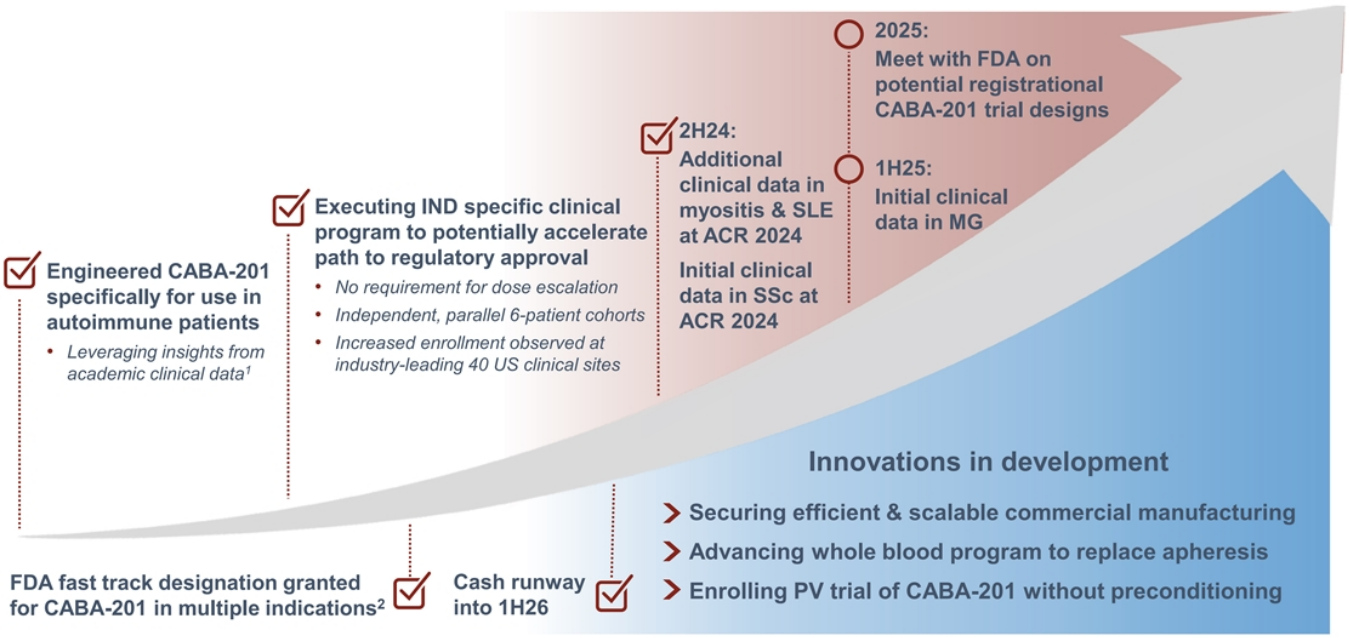
Summary from clinical & translational data on the first 8 patients

- CABA-201 appears to have a favorable risk-benefit profile
  - In patients with recent fever or infections, delaying CAR T infusion should be considered
- CABA-201 provided compelling efficacy in highly active and refractory autoimmune patients through the follow-up period
- Initial data support the potential for drug-free clinical responses
  - All patients discontinued all immunosuppressants
  - SLE patients with longer follow-up: steroid taper completed or ongoing (prednisone 8mg/day)
- The PK/PD data support the current dose of CABA-201[1]

1. Nunez et al. Correlative Studies of CABA-201 from the RESET-Myositis™ and RESET-SLE™ Clinical Trials. Presented at ACR Convergence 2024. Abstract 0324

Realizing the vision to transform autoimmune disease treatment



SLE – Systemic lupus erythematosus; SSc – Systemic sclerosis; PV – Pemphigus vulgaris; ACR 2024 – American College of Rheumatology 2024 annual meeting from November 14-19, 2024.

1. Müller, Fabian, et al. "CD19 CAR T-Cell Therapy in Autoimmune Disease—A Case Series with Follow-up." New England Journal of Medicine 390.8 (2024): 687-700. The construct utilized in these studies has a similar design to CABA-201, sharing the 4-1BB costimulatory domain, but is a different construct.
2. FDA Fast Track Designation received in dermatomyositis, SLE, lupus nephritis and systemic sclerosis.

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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 off 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 – 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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Exhibit 99.3

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Presented at the
ACR Convergence 2024
Nov 14-19, 2024
Washington, D.C.

Correlative Studies of CABA-201, a Fully Human, Autologous 4-1BB Anti-CD19 CAR T Cell Therapy in Patients with Immune-Mediated Necrotizing Myopathy and Systemic Lupus Erythematosus from the RESET-Myositis™ and RESET-SLE™ Clinical Trials

Daniel Nunez[1], Jenell Volkov[1], Jason Stadanlick[1], Zach Vorndran[1], Alexandra Ellis[1], Mallorie Werner[1], Justin Cicarelli[1], Jazmean Williams[1], Fatemeh Hadi-Nezhad[1], Thomas Furmanak[1], Quynh Lam[1], Rebecca Estremera[1], Yvonne White[1], Jonathan Hogan[1], Claire Miller[1], Courtney Little[1], Tahseen Mozaffar[2], Saira Sheikh[3], David J Chang[1], Samik Basu[1]

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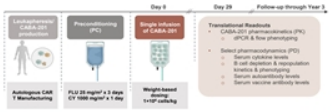
www.cabalettabio.com/technology/posters-publications

Background

CD19 targeting chimeric antigen receptor (CAR) T cells have demonstrated durable clinical responses in patients with idiopathic inflammatory myopathies (IIM), systemic sclerosis (SSc), and systemic lupus erythematosus (SLE) in an academic case series. The safety and tolerability of CABA-201, an autologous, fully human, 4-1BB anti-CD19-CAR T cell therapy is being evaluated in multiple phase I/II clinical trials for B-cell-mediated autoimmune diseases. The primary endpoint of these trials is safety and tolerability. Here we report on initial pharmacokinetic (PK), pharmacodynamic (PD), and other correlative data from the first 7 patients dosed across the RESET-Myositis (NCT06154252), RESET-SLE (NCT06121297), and RESET-SSc (NCT06328777) clinical trials. For IIM, we report initial exploratory data from two immune-mediated necrotizing myopathy (IMNM) patients and one dermatomyositis (DM) patient. For lupus, we report data from two SLE patients (one of which includes a Class V lupus nephritis (LN) patient ineligible for the LN cohort) and one LN patient. For SSc, we report data from one patient in the severe skin cohort (SSc-Skin).



Methods

CABA-201 cell PK profiles were assessed by dPCR for the vector in pre- and post-infusion PBMC samples. CABA-201 cells / µL blood reported values were determined with the patient's total PBMC count and the average CABA-201 vector copy number (VCN) for each patient's manufactured product. CABA-201 cells per µL blood was calculated using the following equation:

$$\frac{CAR\ T\ cells}{\mu L\ blood} = \frac{CAR\ copies}{\mu g\ DNA} * \frac{\mu g\ DNA}{1e5\ cells} * \frac{PBMC}{\mu L\ blood} * \frac{1}{VCN}$$

where an estimation of 1 µg DNA per 1x10⁵ cells was used[1] and patient's PBMC count was determined using lymphocytes + monocytes counts[2]. Serum cytokines were measured via a multiplexed V-plex or U-plex mesoscale discovery (MSD) immunoassay. Flow cytometric analyses were performed on cell samples from apheresis, manufactured product (MP), and post-infusion time points to assess CAR expression in T cells and CD4/CD8 expression in CAR⁺ T cells. Flow cytometry was also used to quantify B-cell numbers (via CD19 and CD20) and phenotypically determine maturity (via CD24 and CD38). All flow cytometry was performed using custom multi-color antibody panels; samples and controls were labelled and read on the Novocyte Quanteon flow cytometer (Agilent), and data were analyzed using FlowJo Software. Serum antibody panels were used to measure selected IIM-, SLE-, SSc-, and vaccine/infectious pathogen-associated antibodies in patient sera pre and post CABA-201 infusion utilizing the Luminex FlexMap. Serum antibody levels were reported as net median fluorescence intensity (MFI). T cell receptor (TCR) sequencing was performed on peripheral blood mononuclear cell (PBMC) samples isolated from LN-1 at various timepoints before and throughout the first month post-infusion. CAR⁺ (CD8⁺, CD8⁻CD4⁻ and CD4⁺, where possible) and CAR⁻ T cell populations were sorted via the MACSQuant Tyto prior to sequencing. Short-read sequencing (Illumina) of these populations was performed on libraries prepared using primer pools that amplify the beta chains of each TCR (Adaptive Biotech). A unique TCR clone was defined as a unique complementarity-determining region 3 nucleotide sequence. Data cut for this poster was 01-Nov-2024.

[1] Baumer et al. 2018 Scientific Reports
[2] Boris et al. 2020 Molecular Therapy Methods & Clinical Development

Results

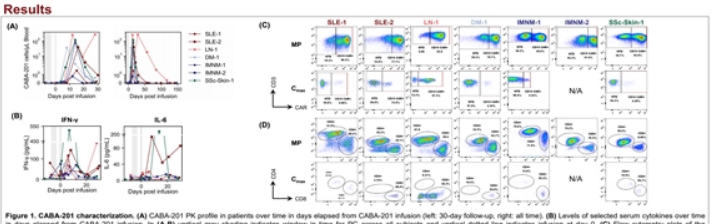


Figure 1. CABA-201 characterization. (A) CABA-201 PK profile in patients over time in days elapsed from CABA-201 infusion (left: 30-day follow-up, right: all time). **(B)** Levels of selected serum cytokines over time in days elapsed from CABA-201 infusion. In **(A-B)** vertical gray shading indicates window in time for PC across all subjects and vertical dotted line indicates infusion at day 0. **(C)** Flow cytometry plots of the manufactured product (MP) and PBMCs at the time of maximum CABA-201 exposure post-infusion (C_{max}: Day 15 for SLE-1, SLE-2, IMNM-1 and SSc-Skin-1, Day 29 for LN-1, Day 8 for DM-1, and no CAR T cell detected post-infusion for IMNM-2). Percentage of T cells that are CAR⁺ in the MP and at post-infusion C_{max} **(D)** Flow cytometry plots showing the percentage of CAR⁺ T cells expressing CD4 and CD8 in the MP and post-infusion C_{max}.

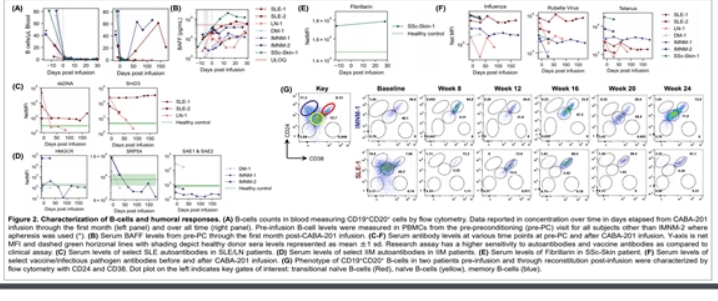


Figure 2. Characterization of B-cells and humoral responses. (A) B-cells counts in blood measuring CD19⁺CD20⁺ cells by flow cytometry. Data reported in concentration over time in days elapsed from CABA-201 infusion through the first month (left panel) and over all time (right panel). Pre-infusion B-cell levels were measured in PBMCs from the pre-preconditioning (pre-PC) visit for all subjects other than IMNM-2 where apheresis was used (*). **(B)** Serum BAFF levels from pre-PC through the first month post-CABA-201 infusion. **(C-F)** Serum antibody levels at various time points at pre-PC and after CABA-201 infusion. Y-axis is net MFI and dashed green horizonal lines with shading depict healthy donor sera levels represented as mean ±1 sd. Research assay has a higher sensitivity to autoantibodies and vaccine antibodies as compared to clinical assay. **(C)** Serum levels of select SLE autoantibodies in SLE/LN patients. **(D)** Serum levels of select IIM autoantibodies in IIM patients. **(E)** Serum levels of Fibrillarin in SSc-Skin patient. **(F)** Serum levels of select vaccine/infectious pathogen antibodies before and after CABA-201 infusion. **(G)** Phenotype of CD19⁺CD20⁺ B-cells in two patients pre-infusion and through reconstitution post-infusion were characterized by flow cytometry with CD24 and CD38. Dot plot on the left indicates key gates of interest: transitional naive B-cells (Red), naive B-cells (yellow), memory B-cells (blue).

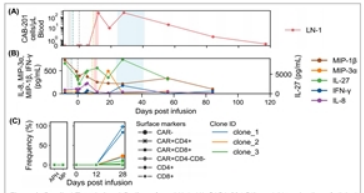


Figure 3. Detailed Translational findings from LN-1. (A) CABA-201 PK overlaid on timeline of clinical events reported in LN-1. Vertical dashed lines represent hospitalization with a fever of indeterminate etiology (blue), CABA-201 infusion (grey), and CRS (orange). Shaded areas represent timing of lymphodepletion (grey), grade 4 ICANS (day 10-12; red) and fever with pancytopenia (day 24-41; blue). **(B)** Serum cytokine levels over the first 8-12 weeks post-CABA-201 infusion. MIP-1β, MIP-3α, IL-27, and IL-8 were either not elevated or detected in other subjects. **(C)** TCR sequencing depicting the top 3 clones in the apheresis, MP, and PBMCs collected at days 12 and 28 post-infusion in LN-1. Apheresis samples were sorted into CD4+ and CD8+ populations. Other samples were sorted into CAR⁻, CAR⁺CD4⁺, CAR⁺CD8⁺, and CAR⁺CD4⁻CD8⁻ where possible. Day 28 T cells comprised of three dominant clones (clones 1-3), regardless of the CAR, CD4, or CD8 expression.

Conclusions

- We report on early translational data on 7 patients with various autoimmune diseases (1 DM, 2 IMNM, 2 SLE, 1 LN, and 1 SSc) treated with CABA-201 across three clinical trials.
- Peak expansion (C_{max}) was observed between Day 8 and Day 15, with the exception of LN-1, which had a biomodal expansion profile (C_{max} observed at Day 29).
- CABA-201 manufactured product CAR T cells were CD4 dominant and exhibited an inversion to CD8 dominance at C_{max} for most patients.
- Peripheral B-cells were rapidly depleted following CABA-201 infusion and began to reconstitute as early as 8 weeks post-infusion.
  - Reconstituted B-cells primarily exhibited a transitional naïve phenotype.
  - Despite clinical improvement in all three subjects, as of the most recent follow up, disease-associated antibodies were reduced in 2 of the 3 subjects with extended follow up after CABA-201 infusion (IMNM-1, SLE-1, LN-1).
  - Vaccine and infectious pathogen antibodies remained stable for most patients.
- LN-1 had multiple inflammatory events that started before preconditioning (PC) and had highly elevated pro-inflammatory cytokines (MIP-1β and IL-27) which continued after infusion, and some findings suggest occult infection (supported by TCR clonal sequencing).
  - Prior to PC, an inflammatory process possibly consistent with infection or disease flare was present (elevated IL-27 and MIP-1β).
  - Shortly after CABA-201 infusion, patient had elevated IL-8 consistent with ICANS.
  - Starting at day 18, an inflammatory event occurred (elevated MIP-3α, IFN-γ, and IL-27) correlated with endogenous TCR (non-CAR-T) expansion.
- These data further support the potential for CABA-201 to provide an immune system reset that could lead to durable disease response without the need for chronic immunosuppression.

Exhibit 99.4

Safety and efficacy of CABA-201, a fully human, autologous 4-1BB anti-CD19 CAR T cell therapy in patients with immune-mediated necrotizing myopathy and systemic lupus erythematosus from the RESET-Myositis™ and RESET-SLE™ clinical trials

Saira Sheikh[1]; Tahseen Mozaffar[2]; Vimal Derebail[1]; Natalie Grover[1]; Jonathan Hogan[3]; Courtney Little[3]; Yvonne White[3]; Claire Miller[3]; Rebecca Estremera[3]; Jenell Volkov[3]; Daniel Nunez[3]; Jason Stadanlick[3]; Mallorie Werner[3]; Zachary Vorndran[3]; Alexandra Ellis[3]; Jazmean Williams[3]; Justin Cicarelli[3]; Quynh Lam[3]; Thomas Furmanak[3]; Chris Schmitt[3]; Fatemeh Nezhad[3]; Dan Thompson[3]; Samik Basu[3]

Presenting author: David J. Chang[3]

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NOVEMBER 2024

Disclosures

Author		Disclosures
David J. Chang		**Employee**: Cabaletta Bio
Saira Sheikh		**Consultant:** AstraZeneca; Biogen; Cabaletta Bio; GSK
Tahseen Mozaffar		**Advisor or Review Panel Member, Grant/Research Support:** Amicus; AnnJi; Argenx; Astellas Gene Therapy; AstraZeneca; Janssen; Sanofi; Spark Therapeutics; UCB **Advisor or Review Panel Member:** Arvinas; AskBio; Horizon Therapeutics; Maze Therapeutics; Sarepta **Grant/Research Support:** Bristol-Myers Squibb (BMS); Cartesian Therapeutics; Grifols; ML-Bio; Valerion
Vimal Derebail		**Consultant:** Amgen; Forma Therapeutics (NovoNordisk); iCell Gene; Novartis
Natalie Grover		**Consultant**: BMS
Jonathan Hogan Courtney Little Yvonne White Claire Miller Rebecca Estremera Jenell Volkov Quynh Lam Thomas Furmanak Fatemeh Nezhad	Dan Thompson Daniel Nunez Jason Stadanlick Mallorie Werner Zachary Vorndran Alexandra Ellis Jazmean Williams Justin Cicarelli Chris Schmitt Samik Basu	**Employees:** Cabaletta Bio

Autoimmune Disease Patients Face Substantial Unmet Medical Needs

Despite therapies with chronic broad immunosuppression, mortality is increased, and quality of life is reduced*[1-4]

Myositis

- Chronic inflammation often leads to permanent tissue damage[1]
- Progressive weakness, pain, dysphagia, and extramuscular manifestations are also common[5]

Systemic lupus erythematosus

- Progressive, multi-organ damage[6]
- ~40% develop lupus nephritis with 25% risk of death or ESKD within 10 years[7,8]

Systemic sclerosis

- Progressive skin and organ fibrosis, which often leads to irreversible lung, cardiac and kidney damage[2]
- Average survival from diagnosis is ~12 years[9]

Patients are seeking a drug-free, symptom-free life; physicians also prioritize prevention of end-organ damage[10]

*Compared with the general population; ESKD, end-stage kidney disease

1. Lundberg IE, et al. *Nat Rev Dis Primers*. 2021;7(1):86. 2. Allanore Y, et al. *Nat Rev Dis Primers*. 2015;1:15002. 3. Zen M, et al. *Eur J Intern Med*. 2023;112:45–51. 4. Refai RH, et al. *Sci Rep*. 2024;14(1):5234. 5. Suh J, Amato AA. *Muscle Nerve*. 2024;70(2):166–172. 6. Murimi-Worstell IB, et al. *BMJ Open*. 2020;10(5):e031850. 7. Anders HJ, et al. *Nat Rev Dis Primers*. 2020;6(1):7. 8. Hoover PJ, Costenbader KH. *Kidney Int*. 2016;90(3):487–492. 9. Mayes MD. *Rheum Dis Clin North Am*. 2003;29(2):239-254. 10. Golder V, et al. *Lupus*. 2018;27(3): 501-506

What are Chimeric Antigen Receptor (CAR) T Cells?

Engineered T cells that combine the targeting ability of antibodies with the cell-killing machinery of T cells[1]

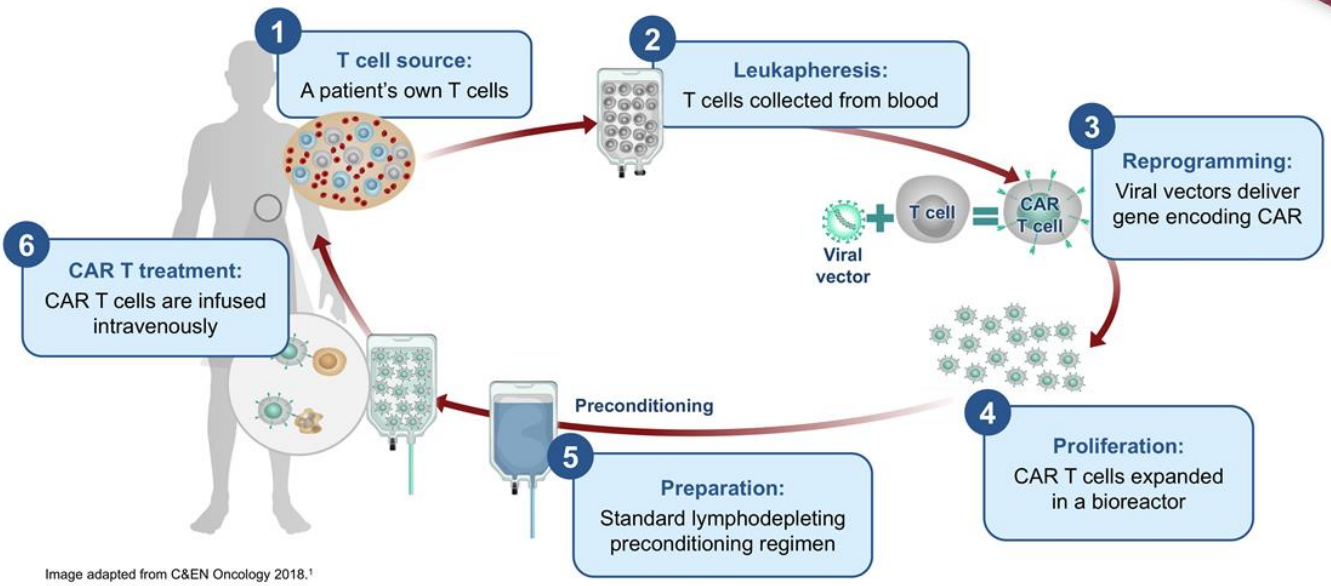


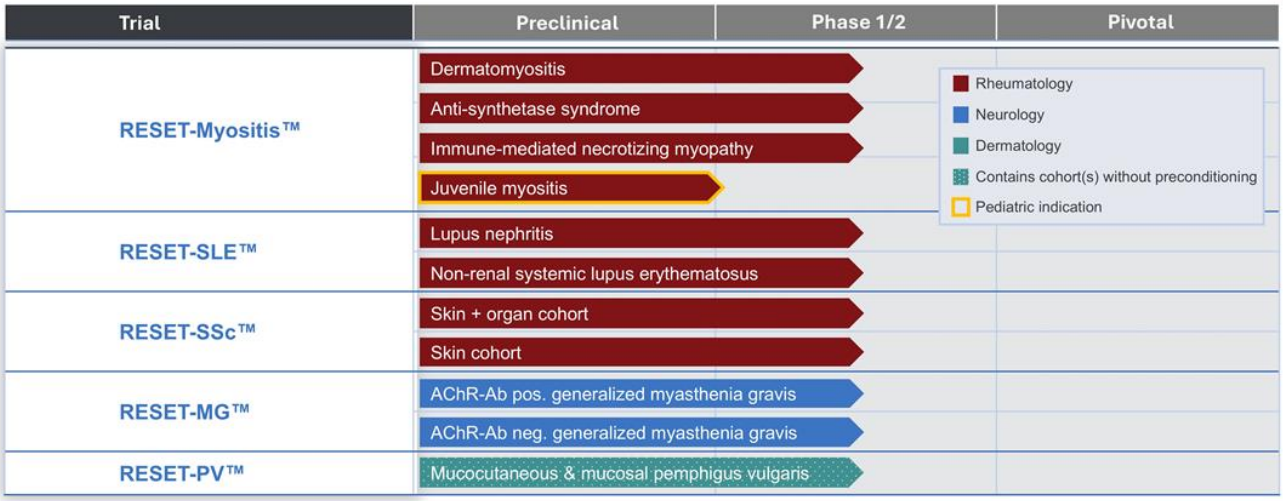
Image adapted from C&EN Oncology 2018.[1]

CAR, chimeric antigen receptor.

1. C&EN Oncology. 2024. Available at: https://cen.acs.org/pharmaceuticals/oncology/Controlling-CAR-T-scientists-plan/96/i19 (accessed October 2024).

RESET™ Clinical Program for CABA-201, a CD19-directed CAR T

Multiple autoimmune diseases evaluated in distinct disease cohorts enrolling at 40 US sites



AChR-Ab, acetylcholine receptor antibody; CABA, Cabaletta Approach to B cell Ablation; CAR, chimeric antigen receptor; RESET, REstoring SElf-Tolerance.
Cabaletta Bio: CABA-201. Available at: www.cabalettabio.com/pipeline/caba-201 (accessed October 2024).

RESET™ Program: Key Inclusion and Exclusion Criteria

Designed to evaluate the safety and tolerability of CABA-201 in subjects with active, refractory disease

Key inclusion criteria[1–3]

Evidence of active disease despite prior or current treatment with standard of care

RESET-Myositis™	RESET-SLE™	RESET-SSc™
• Age ≥18 and ≤75 with a diagnosis of IIM (ASyS, DM, or IMNM) • Presence of at least one MSA • **JIIM**: Age ≥6 and ≤17 with presence of at least one MSA or MAA	• Age ≥18 and ≤65 with an SLE diagnosis • Positive ANA or anti-dsDNA at screening • **SLE (non-renal)**: active, moderate to severe SLE, SLEDAI-2K ≥8; pure class V LN patients eligible for this cohort • **LN**: active, biopsy-proven LN class III or IV (± class V)	• Age ≥18 and ≤70 with a limited or diffuse SSc diagnosis • Evidence of significant skin, pulmonary, renal, or cardiac involvement

Key exclusion criteria[1–3]

B cell-depleting agent within prior 3-6 months; Previous CAR T therapy and/or HSCT

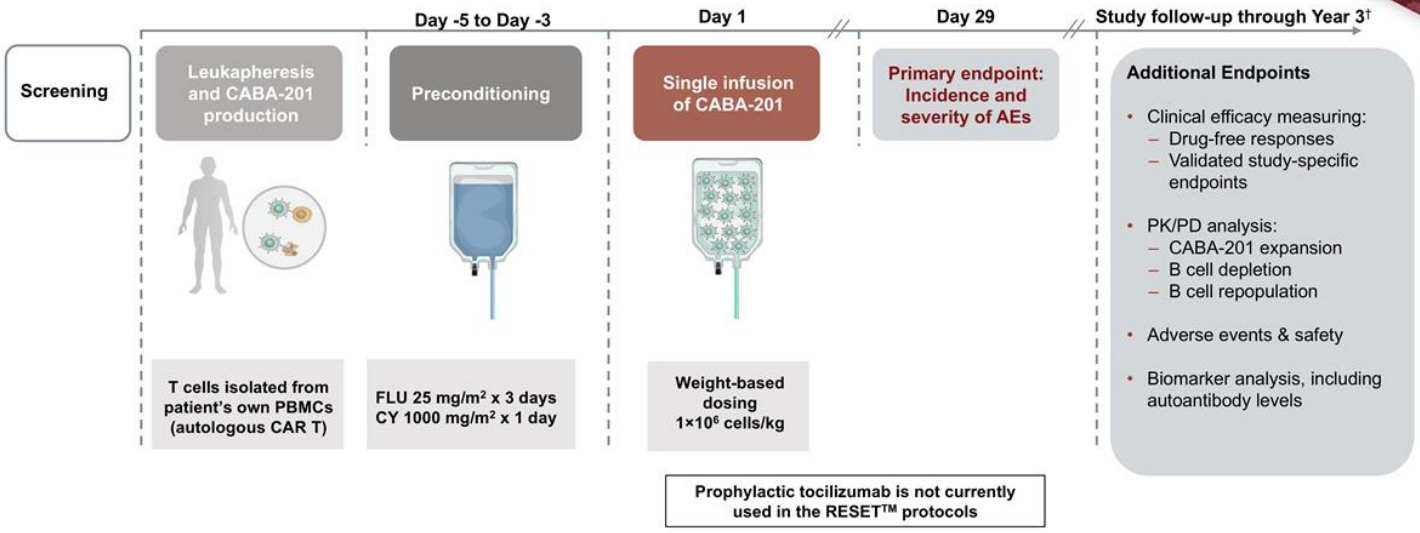
• Cancer-associated myositis • Significant lung or cardiac impairment	• Presence of kidney disease other than LN • Current symptoms of severe, progressive, or uncontrolled pulmonary or cardiac disease	• Severe lung or cardiac impairment

ANA, antinuclear antibody; anti-dsDNA, anti-double strand DNA antibodies; ASyS, antisynthetase syndrome; CAR, chimeric antigen receptor; DM, dermatomyositis; HSCT, hematopoietic stem cell transplantation; IIM, idiopathic inflammatory myopathy; IMNM, immune mediated necrotising myopathy; JIIM, juvenile idiopathic inflammatory myopathy; LN, lupus nephritis; MAA, myositis-associated antibody; MSA, myositis-specific antibodies; SLEDAI-2k, SLE disease activity index 2000; SLE, systemic lupus erythematosus; SSc, systemic sclerosis.

1. ClinicalTrials.gov. Available at: www.clinicaltrials.gov/study/NCT06121297 (accessed October 2024). 2. ClinicalTrials.gov. Available at: www.clinicaltrials.gov/study/NCT06328777 (accessed October 2024). 3. ClinicalTrials.gov. Available at: www.clinicaltrials.gov/study/NCT06154252 (accessed October 2024).

RESET™ Clinical Trials Have Consistent Design Principles[1]

Individual trials in myositis, SLE, and SSc share common elements of preconditioning, dose, and study design



†Follow up period encompasses 15 years in total, aligned to regulatory guidance for CAR T cell therapies

AE, adverse event; CABA, Cabaletta Approach to B cell Ablation; FLU, fludarabine; CY, cyclophosphamide; PBMC, peripheral blood mononuclear cell; PD, pharmacodynamics; PK, pharmacokinetics; RESET, REstoring SElf-Tolerance; SLE, systemic lupus erythematosus; SSc, systemic sclerosis.

Cabaletta Bio: Data on file; 1. Peng BJ, et al. *Mol Ther Methods Clin Dev*. 2024;32(2):101267.

Baseline Characteristics: First 8 Patients in the RESET™ Program

All patients had active, refractory disease and most had failed B cell-targeting therapies

	RESET-Myositis™		
Patient / Cohort	**IMNM-1**	**IMNM-2**	**DM-1**
Age, sex	33 M	60 M	57 M
Disease duration	~2 years	~4 years	~4 years
Autoantibodies	SRP	HMGCR	SAE
Baseline Disease activity*	**MMT-8**		
	130	126	131
	CK (U/L)		
	617	4725	94
Therapies at Screening	GC, MTX	GC, IVIG	GC, MMF, HCQ
Other prior therapies	RTX, IVIG	RTX, MMF, MTX	IVIG
GC dose at Screening (mg/day)	5	5	20

*Baseline disease activity = activity before preconditioning. † SLE-1 had class V LN; inclusion criteria for LN cohort requires class III/IV LN.
ADA, adalimumab; ANI, anifrolumab; AZA, azathioprine; BEL, belimumab; CK, creatinine kinase; CYC, cyclophosphamide; DM, dermatomyositis; dsDNA, double-stranded DNA; GC, glucocorticoid; HCQ, hydroxychloroquine; HMGCR, 3-hydroxy-3-methylglutaryl-coenzyme A reductase; IMNM, immune-mediated necrotizing myopathy; IVIG, intravenous immunoglobulin; LEF, leflunomide; LN, lupus nephritis; MMF, mycophenolate mofetil; MMT-8, manual muscle testing 8; mRSS, modified Rodnan skin score; MSC, mesenchymal stem cell; MTX, methotrexate; RESET, REstoring SElf-Tolerance; RNA P III, RNA polymerase III; RTX, rituximab; SAE, small ubiquitin-like modifier activating enzyme; SLE, systemic lupus erythematosus; SLEDAI-2K, SLE disease activity index 2000; SRP, signal recognition particle; SSc, systemic sclerosis; TAC, tacrolimus; U/L, units per liter; UPCR, urinary protein-to-creatinine ratio; VOC, voclosporin.
Cabaletta Bio: Data on file.

Baseline Characteristics: First 8 Patients in the RESET™ Program

All patients had active, refractory disease and most had failed B cell-targeting therapies

	RESET-Myositis™			RESET-SLE™		
Patient / Cohort	**IMNM-1**	**IMNM-2**	**DM-1**	**SLE-1**† Class V LN	**SLE-2**	**SLE-3**
Age, sex	33 M	60 M	57 M	26 M	36 F	44 F
Disease duration	~2 years	~4 years	~4 years	~6 years	~17 years	~9 years
Autoantibodies	SRP	HMGCR	SAE	dsDNA	dsDNA	dsDNA
Baseline Disease activity*	**MMT-8**			**SLEDAI-2K**		
	130	126	131	26	10	8
	CK (U/L)			**UPCR (mg/mg)**		
	617	4725	94	1.08†	n/a	n/a
Therapies at Screening	GC, MTX	GC, IVIG	GC, MMF, HCQ	GC, MMF, HCQ	GC, AZA, HCQ	HCQ, MMF, BEL
Other prior therapies	RTX, IVIG	RTX, MMF, MTX	IVIG	CYC, BEL, VOC, TAC	MSC, RTX, ANI, BEL, ADA, MTX	GC, MTX
GC dose at Screening (mg/day)	5	5	20	10	7	n/a

*Baseline disease activity = activity before preconditioning. † SLE-1 had class V LN; inclusion criteria for LN cohort requires class III/IV LN.

ADA, adalimumab; ANI, anifrolumab; AZA, azathioprine; BEL, belimumab; CK, creatinine kinase; CYC, cyclophosphamide; DM, dermatomyositis; dsDNA, double-stranded DNA; GC, glucocorticoid; HCQ, hydroxychloroquine; HMGCR, 3-hydroxy-3-methylglutaryl-coenzyme A reductase; IMNM, immune-mediated necrotizing myopathy; IVIG, intravenous immunoglobulin; LEF, leflunomide; LN, lupus nephritis; MMF, mycophenolate mofetil; MMT-8, manual muscle testing 8; mRSS, modified Rodnan skin score; MSC, mesenchymal stem cell; MTX, methotrexate; RESET, REstoring SElf-Tolerance; RNA P III, RNA polymerase III; RTX, rituximab; SAE, small ubiquitin-like modifier activating enzyme; SLE, systemic lupus erythematosus; SLEDAI-2K, SLE disease activity index 2000; SRP, signal recognition particle; SSc, systemic sclerosis; TAC, tacrolimus; U/L, units per liter; UPCR, urinary protein-to-creatinine ratio; VOC, voclosporin.

Cabaletta Bio: Data on file.

Baseline Characteristics: First 8 Patients in the RESET™ Program

All patients had active, refractory disease and most had failed B cell-targeting therapies

	RESET-Myositis™			RESET-SLE™			
Patient / Cohort	**IMNM-1**	**IMNM-2**	**DM-1**	**SLE-1**† Class V LN	**SLE-2**	**SLE-3**	**LN-1**
Age, sex	33 M	60 M	57 M	26 M	36 F	44 F	24 F
Disease duration	~2 years	~4 years	~4 years	~6 years	~17 years	~9 years	~2 years
Autoantibodies	SRP	HMGCR	SAE	dsDNA	dsDNA	dsDNA	dsDNA
Baseline Disease activity*	**MMT-8**			**SLEDAI-2K**			
	130	126	131	26	10	8	22
	CK (U/L)			**UPCR (mg/mg)**			
	617	4725	94	1.08†	n/a	n/a	7.22
Therapies at Screening	GC, MTX	GC, IVIG	GC, MMF, HCQ	GC, MMF, HCQ	GC, AZA, HCQ	HCQ, MMF, BEL	GC, ANI, VOC, MMF, HCQ
Other prior therapies	RTX, IVIG	RTX, MMF, MTX	IVIG	CYC, BEL, VOC, TAC	MSC, RTX, ANI, BEL, ADA, MTX	GC, MTX	BEL, LEF
GC dose at Screening (mg/day)	5	5	20	10	7	n/a	20

*Baseline disease activity = activity before preconditioning. † SLE-1 had class V LN; inclusion criteria for LN cohort requires class III/IV LN.

ADA, adalimumab; ANI, anifrolumab; AZA, azathioprine; BEL, belimumab; CK, creatinine kinase; CYC, cyclophosphamide; DM, dermatomyositis; dsDNA, double-stranded DNA; GC, glucocorticoid; HCQ, hydroxychloroquine; HMGCR, 3-hydroxy-3-methylglutaryl-coenzyme A reductase; IMNM, immune-mediated necrotizing myopathy; IVIG, intravenous immunoglobulin; LEF, leflunomide; LN, lupus nephritis; MMF, mycophenolate mofetil; MMT-8, manual muscle testing 8; mRSS, modified Rodnan skin score; MSC, mesenchymal stem cell; MTX, methotrexate; RESET, REstoring SElf-Tolerance; RNA P III, RNA polymerase III; RTX, rituximab; SAE, small ubiquitin-like modifier activating enzyme; SLE, systemic lupus erythematosus; SLEDAI-2K, SLE disease activity index 2000; SRP, signal recognition particle; SSc, systemic sclerosis; TAC, tacrolimus; U/L, units per liter; UPCR, urinary protein-to-creatinine ratio; VOC, voclosporin.

Cabaletta Bio: Data on file.

Baseline Characteristics: First 8 Patients in the RESET™ Program

All patients had active, refractory disease and most had failed B cell-targeting therapies

	RESET-Myositis™			RESET-SLE™				RESET-SSc™
Patient / Cohort	**IMNM-1**	**IMNM-2**	**DM-1**	**SLE-1**† Class V LN	**SLE-2**	**SLE-3**	**LN-1**	**SSc-Skin-1** (severe skin cohort)
Age, sex	33 M	60 M	57 M	26 M	36 F	44 F	24 F	66 F
Disease duration	~2 years	~4 years	~4 years	~6 years	~17 years	~9 years	~2 years	~2 years
Autoantibodies	SRP	HMGCR	SAE	dsDNA	dsDNA	dsDNA	dsDNA	RNA P III
Baseline Disease activity*	**MMT-8**			**SLEDAI-2K**				**mRSS**
	130	126	131	26	10	8	22	42
	CK (U/L)			**UPCR (mg/mg)**				
	617	4725	94	1.08†	n/a	n/a	7.22	
Therapies at Screening	GC, MTX	GC, IVIG	GC, MMF, HCQ	GC, MMF, HCQ	GC, AZA, HCQ	HCQ, MMF, BEL	GC, ANI, VOC, MMF, HCQ	MMF
Other prior therapies	RTX, IVIG	RTX, MMF, MTX	IVIG	CYC, BEL, VOC, TAC	MSC, RTX, ANI, BEL, ADA, MTX	GC, MTX	BEL, LEF	HCQ
GC dose at Screening (mg/day)	5	5	20	10	7	n/a	20	n/a

*Baseline disease activity = activity before preconditioning. † SLE-1 had class V LN; inclusion criteria for LN cohort requires class III/IV LN.

ADA, adalimumab; ANI, anifrolumab; AZA, azathioprine; BEL, belimumab; CK, creatinine kinase; CYC, cyclophosphamide; DM, dermatomyositis; dsDNA, double-stranded DNA; GC, glucocorticoid; HCQ, hydroxychloroquine; HMGCR, 3-hydroxy-3-methylglutaryl-coenzyme A reductase; IMNM, immune-mediated necrotizing myopathy; IVIG, intravenous immunoglobulin; LEF, leflunomide; LN, lupus nephritis; MMF, mycophenolate mofetil; MMT-8, manual muscle testing 8; mRSS, modified Rodnan skin score; MSC, mesenchymal stem cell; MTX, methotrexate; RESET, REstoring SElf-Tolerance; RNA P III, RNA polymerase III; RTX, rituximab; SAE, small ubiquitin-like modifier activating enzyme; SLE, systemic lupus erythematosus; SLEDAI-2K, SLE disease activity index 2000; SRP, signal recognition particle; SSc, systemic sclerosis; TAC, tacrolimus; U/L, units per liter; UPCR, urinary protein-to-creatinine ratio; VOC, voclosporin.

Cabaletta Bio: Data on file.

Baseline Characteristics: First 8 Patients in the RESET™ Program

All patients had active, refractory disease and most had failed B cell-targeting therapies

	RESET-Myositis™			RESET-SLE™				RESET-SSc™
Patient / Cohort	**IMNM-1**	**IMNM-2**	**DM-1**	**SLE-1**† Class V LN	**SLE-2**	**SLE-3**	**LN-1**	**SSc-Skin-1** (severe skin cohort)
Age, sex	33 M	60 M	57 M	26 M	36 F	44 F	24 F	66 F
Disease duration	~2 years	~4 years	~4 years	~6 years	~17 years	~9 years	~2 years	~2 years
Autoantibodies	SRP	HMGCR	SAE	dsDNA	dsDNA	dsDNA	dsDNA	RNA P III
Baseline Disease activity*	**MMT-8**			**SLEDAI-2K**				**mRSS**
	130	126	131	26	10	8	22	42
	CK (U/L)			**UPCR (mg/mg)**				
	617	4725	94	1.08†	n/a	n/a	7.22	
Therapies at Screening	GC, MTX	GC, IVIG	GC, MMF, HCQ	GC, MMF, HCQ	GC, AZA, HCQ	HCQ, MMF, BEL	GC, ANI, VOC, MMF, HCQ	MMF
Other prior therapies	RTX, IVIG	RTX, MMF, MTX	IVIG	CYC, BEL, VOC, TAC	MSC, RTX, ANI, BEL, ADA, MTX	GC, MTX	BEL, LEF	HCQ
GC dose at Screening (mg/day)	5	5	20	10	7	n/a	20	n/a

*Baseline disease activity = activity before preconditioning. † SLE-1 had class V LN; inclusion criteria for LN cohort requires class III/IV LN.

ADA, adalimumab; ANI, anifrolumab; AZA, azathioprine; BEL, belimumab; CK, creatinine kinase; CYC, cyclophosphamide; DM, dermatomyositis; dsDNA, double-stranded DNA; GC, glucocorticoid; HCQ, hydroxychloroquine; HMGCR, 3-hydroxy-3-methylglutaryl-coenzyme A reductase; IMNM, immune-mediated necrotizing myopathy; IVIG, intravenous immunoglobulin; LEF, leflunomide; LN, lupus nephritis; MMF, mycophenolate mofetil; MMT-8, manual muscle testing 8; mRSS, modified Rodnan skin score; MSC, mesenchymal stem cell; MTX, methotrexate; RESET, REstoring SElf-Tolerance; RNA P III, RNA polymerase III; RTX, rituximab; SAE, small ubiquitin-like modifier activating enzyme; SLE, systemic lupus erythematosus; SLEDAI-2K, SLE disease activity index 2000; SRP, signal recognition particle; SSc, systemic sclerosis; TAC, tacrolimus; U/L, units per liter; UPCR, urinary protein-to-creatinine ratio; VOC, voclosporin.

Cabaletta Bio: Data on file.

Incidence and Severity of Adverse Events*

	RESET-Myositis™		
Cohort	**IMNM**		**DM**
Patient	**IMNM-1**	**IMNM-2**	**DM-1**
CRS†	None	None	None
ICANS†	None	None	None
Serious infections‡	None	None	None
Hypogammaglobulinemia	None	None	None
Related SAEs (Grade)§ (excluding CRS and ICANS)	None	None	None

*As of Nov 1, 2024; Primary endpoint is incidence and severity of Adverse Events through Day 29. †Graded per ASTCT Consensus Grading Criteria. Tocilizumab was **not** administered for any cases of CRS.
‡Coded in System Organ Class of Infections and Infestations and meets seriousness criteria. §As assessed per FDA guidelines.

CRS, cytokine release syndrome; CY, cyclophosphamide; DM, dermatomyositis; FLU, fludarabine; ICANS, immune effector cell-associated neurotoxicity syndrome; IMNM, immune-mediated necrotizing myopathy; LN, lupus nephritis; PE, pulmonary embolism; SAE, serious adverse event; RESET, REstoring SElf-Tolerance; SLE, systemic lupus erythematosus; SSc, systemic sclerosis.
Cabaletta Bio: Data on file.

Incidence and Severity of Adverse Events*

	RESET-Myositis™			RESET-SLE™		
Cohort	**IMNM**		**DM**	**Non-renal SLE**		
Patient	**IMNM-1**	**IMNM-2**	**DM-1**	**SLE-1**	**SLE-2**	**SLE-3**
CRS†	None	None	None	None	Grade 1	None
ICANS†	None	None	None	None	None	None
Serious infections‡	None	None	None	None	None	None
Hypogammaglobulinemia	None	None	None	None	None	None
Related SAEs (Grade)§ (excluding CRS and ICANS)	None	None	None	None	None	None

*As of Nov 1, 2024; Primary endpoint is incidence and severity of Adverse Events through Day 29. †Graded per ASTCT Consensus Grading Criteria. Of these patients, only DM-1, SLE-2, SLE-3, and SSc-Skin-1 **received** medication for seizure prophylaxis. Tocilizumab was **not** administered for any cases of CRS. ‡Coded in System Organ Class of Infections and Infestations and meets seriousness criteria. §As assessed per FDA guidelines.

CRS, cytokine release syndrome; CY, cyclophosphamide; DM, dermatomyositis; FLU, fludarabine; ICANS, immune effector cell-associated neurotoxicity syndrome; IMNM, immune-mediated necrotizing myopathy; LN, lupus nephritis; PE, pulmonary embolism; SAE, serious adverse event; RESET, REstoring SElf-Tolerance; SLE, systemic lupus erythematosus; SSc, systemic sclerosis.
Cabaletta Bio: Data on file.

Incidence and Severity of Adverse Events*

	RESET-Myositis™			RESET-SLE™			RESET-SSc™
Cohort	**IMNM**		**DM**	**Non-renal SLE**			**SSc – Severe Skin**
Patient	**IMNM-1**	**IMNM-2**	**DM-1**	**SLE-1**	**SLE-2**	**SLE-3**	**SSc-Skin-1**
CRS†	None	None	None	None	Grade 1	None	Grade 2
ICANS†	None	None	None	None	None	None	None
Serious infections‡	None	None	None	None	None	None	None
Hypogammaglobulinemia	None	None	None	None	None	None	None
Related SAEs (Grade)§ (excluding CRS and ICANS)	None	None	None	None	None	None	None

*As of Nov 1, 2024; Primary endpoint is incidence and severity of Adverse Events through Day 29. †Graded per ASTCT Consensus Grading Criteria. Of these patients, only DM-1, SLE-2, SLE-3, and SSc-Skin-1 **received** medication for seizure prophylaxis. Tocilizumab was **not** administered for any cases of CRS. ‡Coded in System Organ Class of Infections and Infestations and meets seriousness criteria. §As assessed per FDA guidelines.

CRS, cytokine release syndrome; CY, cyclophosphamide; DM, dermatomyositis; FLU, fludarabine; ICANS, immune effector cell-associated neurotoxicity syndrome; IMNM, immune-mediated necrotizing myopathy; LN, lupus nephritis; PE, pulmonary embolism; SAE, serious adverse event; RESET, REstoring SElf-Tolerance; SLE, systemic lupus erythematosus; SSc, systemic sclerosis.
Cabaletta Bio: Data on file.

Incidence and Severity of Adverse Events*

	RESET-Myositis™			RESET-SLE™				RESET-SSc™
Cohort	**IMNM**		**DM**	**Non-renal SLE**			**LN**	**SSc – Severe Skin**
Patient	**IMNM-1**	**IMNM-2**	**DM-1**	**SLE-1**	**SLE-2**	**SLE-3**	**LN-1**	**SSc-Skin-1**
CRS†	None	None	None	None	Grade 1	None	Grade 1	Grade 2
ICANS†	None	None	None	None	None	None	Grade 4	None
Serious infections‡	None	None	None	None	None	None	None	None
Hypogammaglobulinemia	None	None	None	None	None	None	Grade 2	None
Related SAEs (Grade)§ (excluding CRS and ICANS)	None	None	None	None	None	None	Fever (1) Pancytopenia¶ (4)	None

*As of Nov 1, 2024; Primary endpoint is incidence and severity of Adverse Events through Day 29. †Graded per ASTCT Consensus Grading Criteria. Of these patients, only DM-1, SLE-2, SLE-3, and SSc-Skin-1 **received** medication for seizure prophylaxis. Tocilizumab was **not** administered for any cases of CRS. ‡Coded in System Organ Class of Infections and Infestations and meets seriousness criteria. §As assessed per FDA guidelines.

¶Consistent with "Prolonged Cytopenias," which is a labeled warning and precaution for approved oncology CAR T products.

CRS, cytokine release syndrome; CY, cyclophosphamide; DM, dermatomyositis; FLU, fludarabine; ICANS, immune effector cell-associated neurotoxicity syndrome; IMNM, immune-mediated necrotizing myopathy; LN, lupus nephritis; PE, pulmonary embolism; SAE, serious adverse event; RESET, REstoring SElf-Tolerance; SLE, systemic lupus erythematosus; SSc, systemic sclerosis.
Cabaletta Bio: Data on file.

Incidence and Severity of Adverse Events*

	RESET-Myositis™			RESET-SLE™				RESET-SSc™
Cohort	**IMNM**		**DM**	**Non-renal SLE**			**LN**	**SSc – Severe Skin**
Patient	**IMNM-1**	**IMNM-2**	**DM-1**	**SLE-1**	**SLE-2**	**SLE-3**	**LN-1**	**SSc-Skin-1**
CRS†	None	None	None	None	Grade 1	None	Grade 1	Grade 2
ICANS†	None	None	None	None	None	None	Grade 4	None
Serious infections‡	None	None	None	None	None	None	None	None
Hypogammaglobulinemia	None	None	None	None	None	None	Grade 2	None
Related SAEs (Grade)§ (excluding CRS and ICANS)	None	None	None	None	None	None	Fever (1) Pancytopenia¶ (4)	None
Unrelated SAEs (Grade)§	None	Back Pain (3) PE# (4)	None	None	None	None	None	Neutropenia (4) (FLU/CY related)

*As of Nov 1, 2024; Primary endpoint is incidence and severity of Adverse Events through Day 29. †Graded per ASTCT Consensus Grading Criteria. Of these patients, only DM-1, SLE-2, SLE-3, and SSc-Skin-1 **received** medication for seizure prophylaxis. Tocilizumab was **not** administered for any cases of CRS. ‡Coded in System Organ Class of Infections and Infestations and meets seriousness criteria. §As assessed per FDA guidelines.

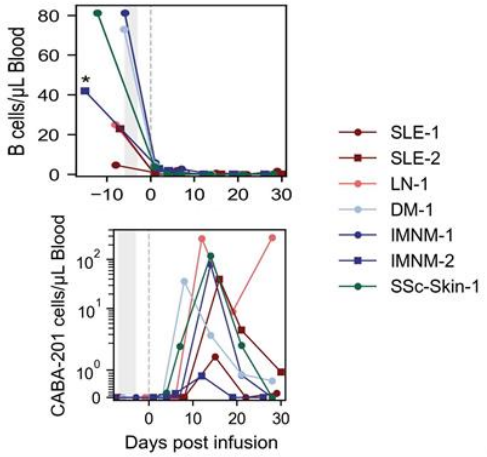
#Patient with Factor V Leiden heterozygosity (increased risk for thrombosis), recent intravenous immunoglobulin treatment, history of myocardial infarction, recent hospitalization for back pain & fatigue with decreased mobility. Undetectable CABA-201 levels since Day 22. Event occurred at Day 38 and was reported as PE leading to cardiac arrest, followed by successful pulmonary artery thrombectomy.
¶Consistent with "Prolonged Cytopenias," which is a labeled warning and precaution for approved oncology CAR T products.

CRS, cytokine release syndrome; CY, cyclophosphamide; DM, dermatomyositis; FLU, fludarabine; ICANS, immune effector cell-associated neurotoxicity syndrome; IMNM, immune-mediated necrotizing myopathy; LN, lupus nephritis; PE, pulmonary embolism; SAE, serious adverse event; RESET, REstoring SElf-Tolerance; SLE, systemic lupus erythematosus; SSc, systemic sclerosis.
Cabaletta Bio: Data on file.

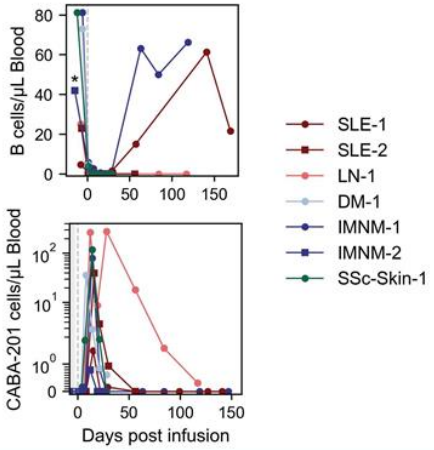
Consistent and Complete B cell Depletion by Day 22[1]

In patients with >3-month follow-up, B cell repopulation with naïve cells started as early as 8 weeks

B cell depletion & CABA-201 expansion through Day 30



B cell depletion/repopulation & CABA-201 expansion through Day 150



CABA-201 exhibited a PK/PD profile with peak expansion between Day 8 and 15 as expected, with a later 2nd peak for LN-1

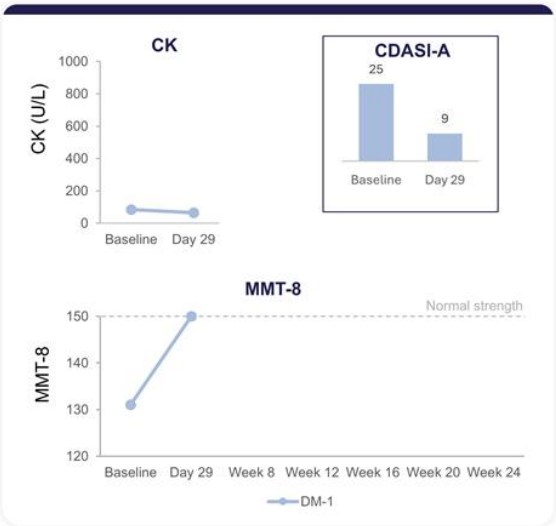
PK, pharmacokinetic; PD, pharmacodynamic

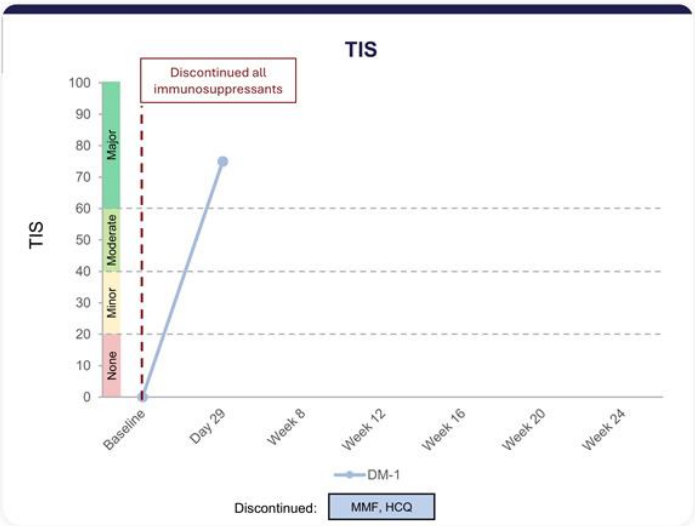
* Pre-infusion B-cell levels were measured at pre-preconditioning for all subjects other than IMNM-2 where apheresis was used

1. Nunez et al. Correlative Studies of CABA-201 from the RESET-Myositis™ and RESET-SLE™ Clinical Trials. Presented at ACR Convergence 2024. Abstract 0324

RESET- Myositis™: Early Efficacy Data Following CABA-201 Infusion

1st known adult DM patient dosed with CAR T demonstrated compelling early clinical response off immunosuppressants‡





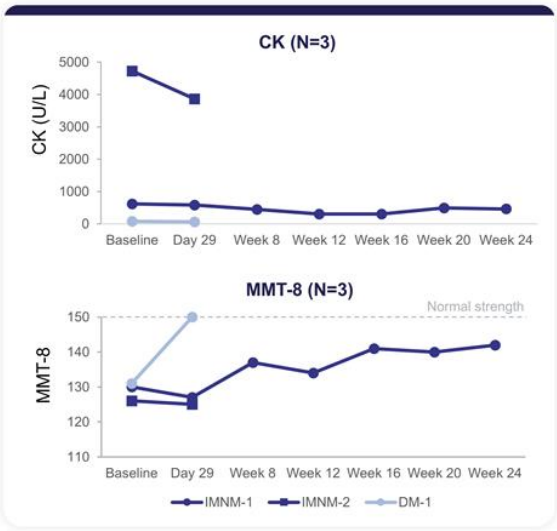
‡ As of Nov 1, 2024

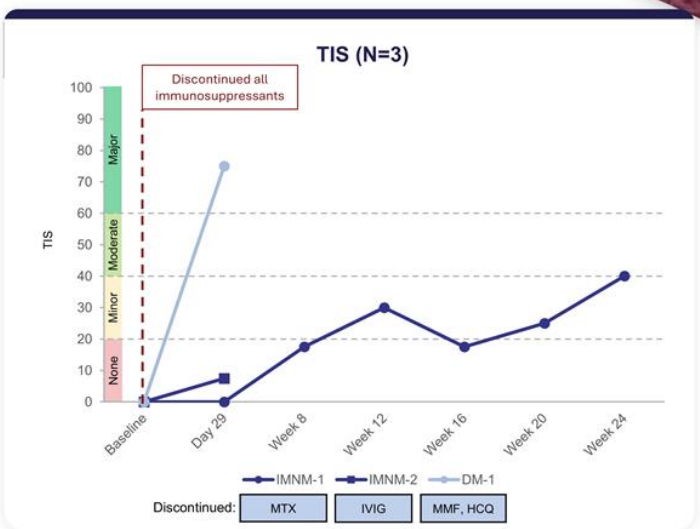
CAR; chimeric antigen receptor; CDASI-A, Cutaneous Dermatomyositis Disease Area and Severity Index – Activity; CK, creatinine kinase; DM, dermatomyositis; GC, glucocorticoid; HCQ, hydroxychloroquine; IMNM, immune-mediated necrotizing myopathy; IVIG, intravenous immunoglobulin; MMF, mycophenolate mofetil; MMT-8, manual muscle testing 8; RESET, REstoring SElf-Tolerance; TIS, total improvement score; U/L, units per liter.

Cabaletta Bio: Data on file.

RESET-Myositis™: Efficacy Data Following CABA-201 Infusion

1st IMNM patient with longer follow up demonstrated continuing clinical response off immunosuppressants‡





Initial clinical responses in IMNM are consistent with published data[1]; response kinetics may differ among myositis subtypes

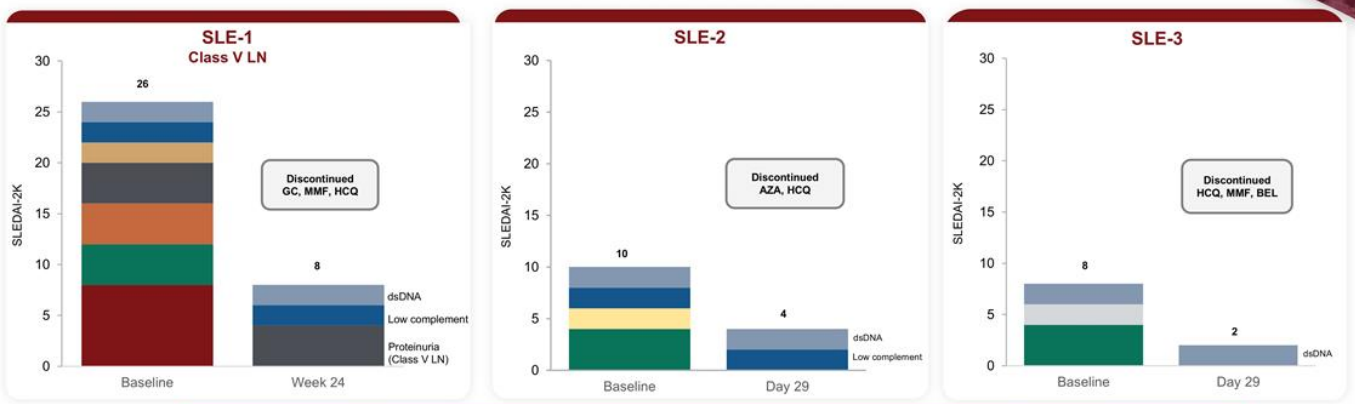
‡ As of Nov 1, 2024

CDASI-A, Cutaneous Dermatomyositis Disease Area and Severity Index – Activity; CK, creatinine kinase; DM, dermatomyositis; GC, glucocorticoid; HCQ, hydroxychloroquine; IMNM, immune-mediated necrotizing myopathy; IVIG, intravenous immunoglobulin; MTX, Methotrexate; MMF, mycophenolate mofetil; MMT-8, manual muscle testing 8; RESET, REstoring SElf-Tolerance; TIS, total improvement score; U/L, units per liter.

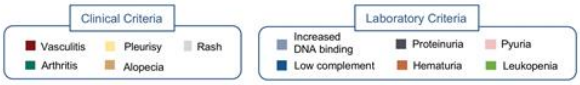
Cabaletta Bio: Data on file. 1. Schett, G. "CAR-T Cell Therapy: "The Future is Now."' 5th Global Conference on Myositis. iMyoS. Pittsburgh, PA.

RESET-SLE™: Efficacy Data in SLE Following CABA-201 Infusion

All 3 SLE patients demonstrated clinical responses off immunosuppressants; longer follow up patient SLE-1 completed steroid taper‡



No clinical symptoms on SLEDAI-2K through latest follow up, including SLE-1 with isolated Class V LN (non-renal cohort) with persistent proteinuria as expected



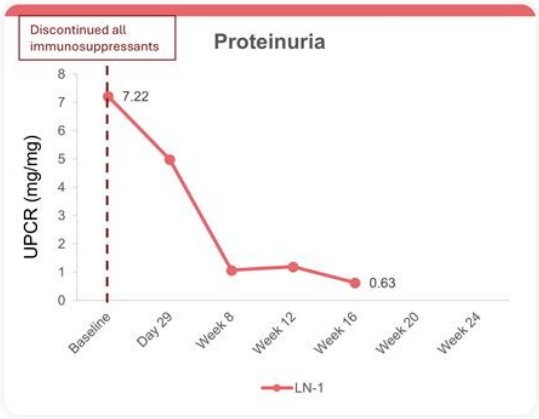
‡ As of Nov 1, 2024

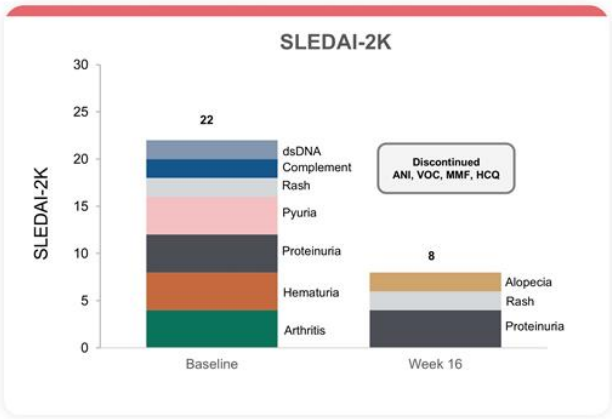
AZA, azathioprine; BEL, belimumab; GC, glucocorticoid; dsDNA, double-stranded DNA; HCQ, hydroxychloroquine; LN, lupus nephritis; MMF, mycophenolate mofetil; RESET, REstoring SElf-Tolerance; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000.

Cabaletta Bio: Data on file.

RESET-SLE™: Efficacy Data in LN Following CABA-201 infusion

LN-1 demonstrated marked improvement of proteinuria off all immunosuppressants, continuing steroid taper ‡





LN-1 proteinuria markedly improved by Week 8 with alopecia/rash as the remaining clinical manifestations at Week 16 after discontinuation of all immunosuppressants and continuing prednisone taper

‡ As of Nov 1, 2024

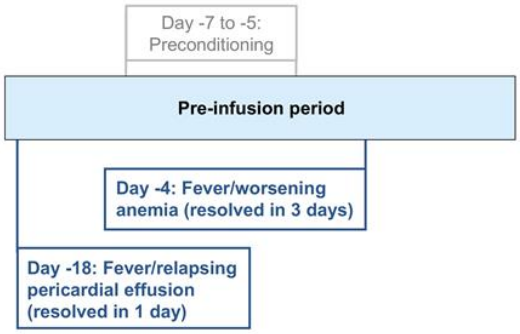
ANI, anifrolumab; dsDNA, double-stranded DNA; HCQ, hydroxychloroquine; LN, lupus nephritis; MMF, mycophenolate mofetil; RESET, REstoring SElf-Tolerance; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; UPCR, urinary protein-to-creatinine ratio; VOC, voclosporin

Cabaletta Bio: Data on file.

LN-1 Patient : ICANS Event Timeline

Patient with recent fever in setting of acute and severe inflammation

- 24-year-old female with SLE for ~2 years and with active class III LN
- Active, severe (SLEDAI-2K = 22; UPCR = 7.22 mg/mg) refractory disease despite 5 systemic treatments* for SLE at screening



*Therapies at Screening: glucocorticoids, anifrolumab, voclosporin, mycophenolate mofetil, hydroxychloroquine

CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; LN, lupus nephritis; RESET, REstoring SElf-Tolerance; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; UPCR, urinary protein-to-creatinine ratio

Cabaletta Bio: Data on file. 1. Nunez et al. Correlative Studies of CABA-201 from the RESET-Myositis™ and RESET-SLE™ Clinical Trials. Presented at ACR Convergence 2024. Abstract 0324

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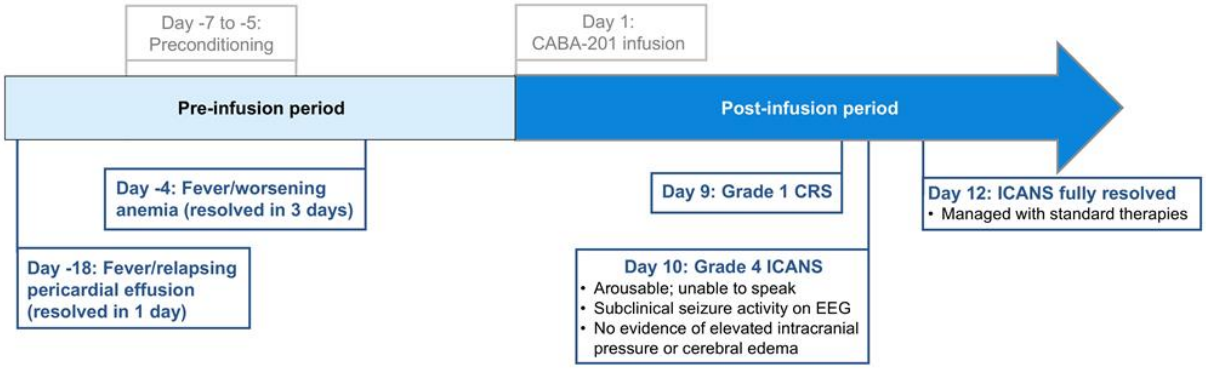

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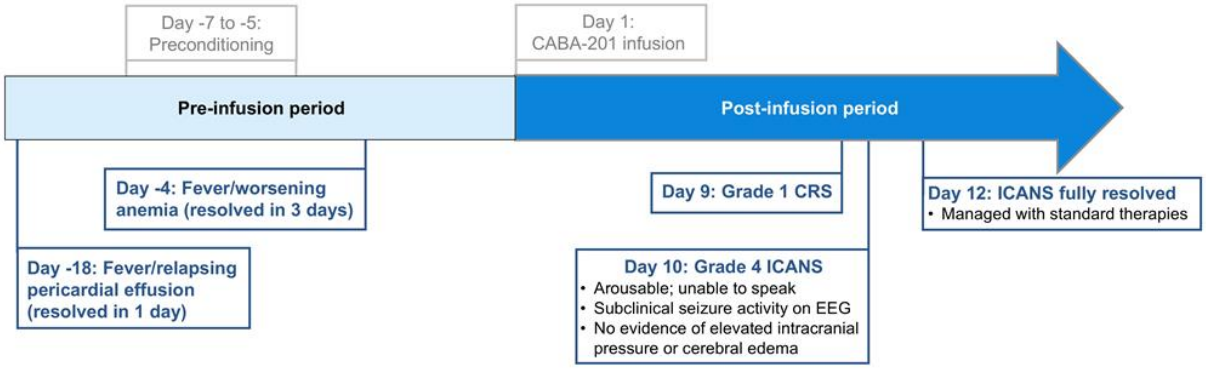


Patient had acute, febrile inflammatory events and highly elevated pro-inflammatory cytokines (MIP-1β, IL-27) prior to infusion that continued after treatment, suggesting a possible occult infection; supportive data from TCR clonal sequencing[1]

*Therapies at Screening: glucocorticoids, anifrolumab, voclosporin, mycophenolate mofetil, hydroxychloroquine

CRS, cytokine release syndrome; EEG, electroencephalogram; ICANS, immune effector cell-associated neurotoxicity syndrome; LN, lupus nephritis; RESET, REstoring SElf-Tolerance; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; TCR, T Cell Receptor; UPCR, urinary protein-to-creatinine ratio

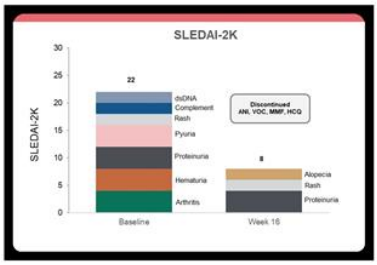
Cabaletta Bio: Data on file. 1. Nunez et al. Correlative Studies of CABA-201 from the RESET-Myositis™ and RESET-SLE™ Clinical Trials. Presented at ACR Convergence 2024. Abstract 0324

LN-1 Patient Outcome: 4 Months Post-Treatment

Compelling clinical response since discontinuation of all immunosuppressants, continuing steroid taper

Patient 4 Months Follow-up*

- Off all immunosuppressants‡
- Prednisone 8mg/day; taper ongoing
- SLEDAI-2K: 22 → 8
- UPCR (mg/mg): 7.22 → 0.63



*As of Nov 1, 2024
‡Therapies at Screening: glucocorticoids, anifrolumab, voclosporin, mycophenolate mofetil, hydroxychloroquine
ANI, anifrolumab; dsDNA, double-stranded DNA; HCQ, hydroxychloroquine; LN, lupus nephritis; MMF, mycophenolate mofetil; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; UPCR, urinary protein-to-creatinine ratio; VOC, voclosporin
Cabaletta Bio: Data on file.

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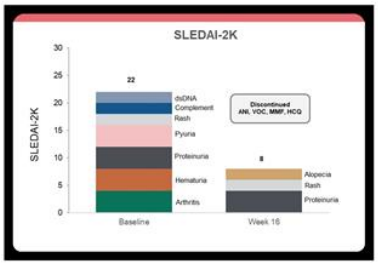


"Overall, I feel much better than I felt before CABA-201 therapy. I have much more energy, I have significantly less joint pain and inflammation, my proteinuria has improved, I no longer have any mouth sores, and I am getting back to my normal self!

At 25 years old, my kidneys were not functioning properly and continued to get worse despite all of the strong medications I was on. I had multiple occurrences of fluid around my heart. CABA-201 has put a stop to that and has allowed my body to heal. Although I faced complications afterwards, I believe the improvement that I have seen in both my numbers and how I feel, was far worth it.

If I had the choice, I would choose to receive CABA-201 again…. "

- LN-1 patient at 4 months post-therapy

*As of Nov 1, 2024

‡Therapies at Screening: glucocorticoids, anifrolumab, voclosporin, mycophenolate mofetil, hydroxychloroquine

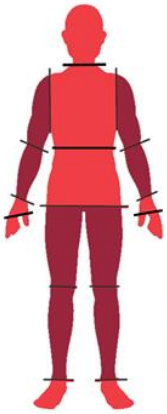
ANI, anifrolumab; dsDNA, double-stranded DNA; HCQ, hydroxychloroquine; LN, lupus nephritis; MMF, mycophenolate mofetil; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; UPCR, urinary protein-to-creatinine ratio; VOC, voclosporin

Cabaletta Bio: Data on file.

RESET-SSc™: Emerging Efficacy Data - 42 days post infusion

Early disease improvements in face and hands after discontinuation of disease-specific medication

Baseline mRSS score by body area
SSc-Skin-1



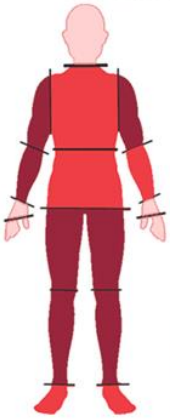
0 None
1 Mild
2 Moderate
3 Severe

Overall mRSS score
SSc-Skin-1

	Baseline	Day 22	Day 42
mRSS	42	38	36

- Modified Rodnan Skin Score (mRSS): a measure of skin thickness in SSc across 17 body areas, with a maximum score of 51[1]
- Used as an outcome measure in SSc clinical trials as a surrogate for disease activity, severity and mortality[1]

Day 42 mRSS score by body area
SSc-Skin-1



0 None
1 Mild
2 Moderate
3 Severe

Early clinical data indicate potential emergence of a drug-free clinical response‡

‡ As of Nov 1, 2024 patient is not taking immunosuppressants or steroids
mRSS, modified Rodnan Skin Score; RESET, REstoring SElf-Tolerance; SSc, systemic sclerosis
Cabaletta Bio: Data on file. 1. Khanna D, et al. *J Scleroderma Relat Disord*. 2017;2(1):11–18.

Summary from Clinical and Translational Data on the First 8 Patients

- CABA-201 appears to have a favorable risk-benefit profile
  - In patients with recent fever or infections, delaying CAR T infusion should be considered
- CABA-201 provided compelling efficacy in highly active and refractory autoimmune patients through the follow-up period
- Initial data support the potential for drug-free clinical responses
  - All patients discontinued all immunosuppressants
  - SLE patients with longer follow-up: steroid taper completed or ongoing (prednisone 8mg/day)
- The PK/PD data support the current dose of CABA-201[1]

CAR, chimeric antigen receptor; PK, pharmacokinetic; PD, pharmacodynamic; SLE, systemic lupus erythematosus

1. Nunez et al. Correlative Studies of CABA-201 from the RESET-Myositis™ and RESET-SLE™ Clinical Trials. Presented at ACR Convergence 2024. Abstract 0324

Acknowledgements

Patients and caregivers involved in the RESET™ clinical program

Site investigators and staff involved with these patients from the RESET™ clinical program
- Mayo Clinic, Rochester
- University of California, Davis
- University of California, Irvine
- University of Michigan
- University of North Carolina

Cabaletta Bio team
- Biostatistics
- Clinical Development
- Clinical Operations
- Computational Biology
- Manufacturing
- Medical Affairs
- Translational Medicine