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

June 14, 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 June 14, 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, June 14, 2024, at 8:00 a.m. ET to review the initial clinical data presented at the EULAR 2024 Congress 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 June 14, 2024, the Company issued a Press Release reporting positive initial clinical data from each of the first two patients dosed with CABA-201 in the Phase 1/2 RESET-Myositis™ and RESET-SLE™ trials (the "Press Release"). A copy of the Press Release is furnished herewith as Exhibit 99.2 to this Current Report on Form 8-K.

On June 14, 2024, the Company also presented a clinical update at the EULAR European Congress of Rheumatology 2024 Industry Symposia. A copy of the slides, which has been published to the "News & Media" section of the Company's website, is furnished herewith as Exhibit 99.3 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, 99.2 and 99.3 attached hereto, is being furnished and shall not be deemed to be "filed" for the purposes of Section 18 of 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 or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

Item 8.01 Other Events.

On June 14, 2024, the Company issued the Press Release reporting positive initial clinical data from each of the first two patients dosed with CABA-201 in the Phase 1/2 RESET-Myositis and RESET-SLE trials. These data were presented today at 8:15 a.m. CEST (2:15 a.m. ET) at a EULAR European Congress of Rheumatology 2024 Industry Symposia session titled "Immune Reset: The Potential of CAR T Cell Therapy to Transform the Treatment of Patients with Autoimmune Disease" in Vienna, Austria.

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

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

Initial Clinical Data Summary

Safety and Tolerability

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

Clinical and Translational Profile

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

About the RESET-Myositis™ Trial

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

About the RESET-SLE™ Trial

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

Forward-Looking Statements

The information under this Item 8.01 contains “forward-looking statements” of the Company within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including without limitation, express or implied statements regarding: Cabaletta’s ability to grow its autoimmune pipeline; Cabaletta’s future plans and strategies for its CAAR T and CARTA technologies and the company’s business plans and objectives as a whole; Cabaletta’s expectations around the potential safety and therapeutic benefits of CABA-201, including its belief that CABA-201 may enable an “immune system reset” with the potential for durable remission without chronic therapy in patients with autoimmune diseases; the Company’s advancement of separate Phase 1/2 clinical trials of CABA-201 in patients with SLE, myositis, SSc and gMG and advancement of aRESET-PV sub-study within the

ongoing DesCAARTes trial in PV, including the Company's expectations for the efficiency of the trial designs and updates related to status, safety data, or otherwise and the expected timing of the related data read-outs; Cabaletta's ability to accelerate its pipeline, develop meaningful therapies for patients and leverage its research and translational insights; the clinical significance of the initial clinical data read-out at the EULAR 2024 Congress in June 2024 for patients with myositis and SLE treated with CABA-201; Cabaletta's additional planned initial clinical data read-outs for patients with SSc and gMG treated with CABA-201 or otherwise; Cabaletta's advancement of the process to activate clinical trial sites and pursue patient enrollment; and Cabaletta's planned assessment of its DesCAARTes™ and MusCAARTes™ trials.

Any forward-looking statements in this 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 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 June 14, 2024, furnished herewith.
99.2	Press Release issued by the registrant on June 14, 2024, furnished herewith.
99.3	Slides from Cabaletta Bio, Inc.'s EULAR European Congress of Rheumatology 2024 Industry Symposia Presentation, dated June 14, 2024, furnished herewith.
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: June 14, 2024

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

Exhibit 99.1

Cabaletta Bio®

CABA-201 Initial Clinical Data from the RESET-Myositis™ & RESET-SLE™ Phase 1/2 Trials

JUNE 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; the Company's business plans and objectives; our expectations around the potential success and therapeutic benefits of CABA-201, including our belief that CABA-201 may enable an "immune system reset"; Cabaletta's belief of the potential for CAR T to enable a paradigm shift in autoimmunity, including its potential achieve durable remissions without chronic therapy;; our plans for Phase 1/2 clinical trials of CABA-201 in patients with systemic lupus erythematosus (SLE), myositis, SSc, and generalized myasthenia gravis (gMG), and for advancement of a RESET-PV sub-study within the ongoing DesCAARTes trial in PV, 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; our initial clinical data read-out in the first half of 2024 at the EULAR 2024 symposium for patients with myositis and SLE treated with CABA-201; our planned initial clinical data read-out in the second half of 2024 for patients with SSc and gMG treated with CABA-201 and additional data; our ability to enroll the requisite number of patients, dose each dosing cohort in the intended manner, and advance the trial as planned in our Phase 1/2 clinical trials of CABA-201; the timing any planned regulatory filings for our development programs, including IND applications; the progress and results of our DesCAARTes™ Phase 1 trial, including the significance and impact around reported safety and clinical and translational data of cohorts from our DesCAARTes™ and MusCAARTes™ Phase 1 trials; Cabaletta's potential to eliminate the need for apheresis by using a simpler collection process to obtain the starting material for the CABA-201 manufacturing process the therapeutic potential and clinical benefits of our product candidates; the expectation that Cabaletta may improve outcomes for patients suffering from SLE, SSc, myositis, gMG, mucosal pemphigus vulgaris, MuSK myasthenia gravis, 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; 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; our ability to contract with third-party suppliers and manufacturers and retain such manufacturers, whether due to legislative action or otherwise; to implement an enhanced manufacturing process and further develop our internal manufacturing strategy, capabilities and facilities; our potential commercial opportunities, including value and addressable market, for our product candidates; 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, our plans to evaluate additional cohorts in the DesCAARTes™ trial, including a cohort implementing a pre-treatment regimen, the risk that signs of biologic activity or persistence may not inform long-term results, the risk that persistence 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*
Current & Investigational Treatments for Patients with Autoimmune Disease	Iain McInnes, MD, FRCP, PhD, FRSE, FMedSci *Vice Principal and Head of the College of Medical, Veterinary and Life Sciences, Muirhead Chair of Medicine and Versus Arthritis Professor of Rheumatology at the University of Glasgow*
Initial CABA-201 Data in Myositis & Lupus	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

Designed to replicate and expand on the academic clinical data that generated interest in the field

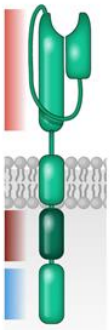
CABA-201 designed to optimize the potential safety and efficacy of CD19-CAR T for patients with autoimmune disease

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

Safety data in ~20 oncology patients evaluated and reported by IASO as part of a dual-CAR[3]

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

CD3-zeta signaling domain



CABA-201

Key Questions for RESET™ Phase 1/2 Studies

Safety of CABA-201
- CABA-201 AE profile
- *CRS, ICANS, SAEs*

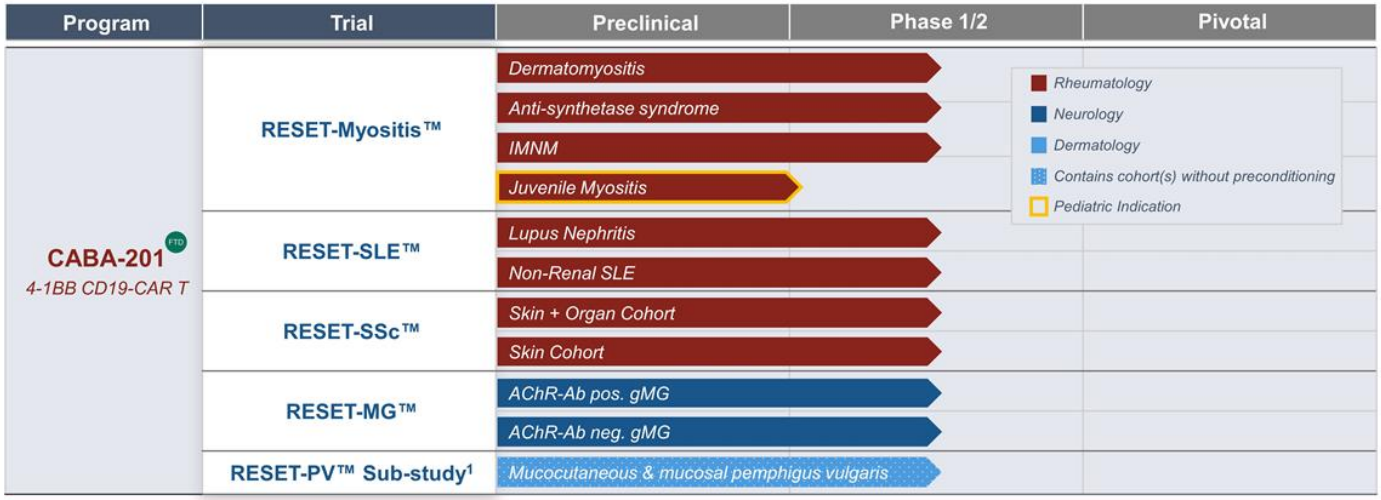
Dose selection
1 x 10^6 cells/kg
- PK – CAR T persistence
- PD – B cell depletion
- Autoantibody reduction
- Clinical outcomes

PK, pharmacokinetics; PD, pharmacodynamics, SAEs: serious adverse events

1. Peng, BinghaoJ, et al. Presented at: American Society Gene and Cell Therapy 26th Annual Meeting; 2023 May 19; Los Angeles, CA.
2. Dai, Zhenyu, et al. Journal of Cellular Physiology. 2021;236(8): 5832-5847.
3. Evaluated as part of CT120, a dual-CD19xCD22 CAR T product candidate under development by Nanjing IASO Biotherapeutics, Co., Ltd. (IASO Bio).

CABA-201 pipeline targeting a broad range of autoimmune diseases

Innovative and scalable clinical strategy with potential for accelerated development path



Clinical & translational data[2] support the selected single dose of CABA-201 at 1 x 10^6 cells/kg

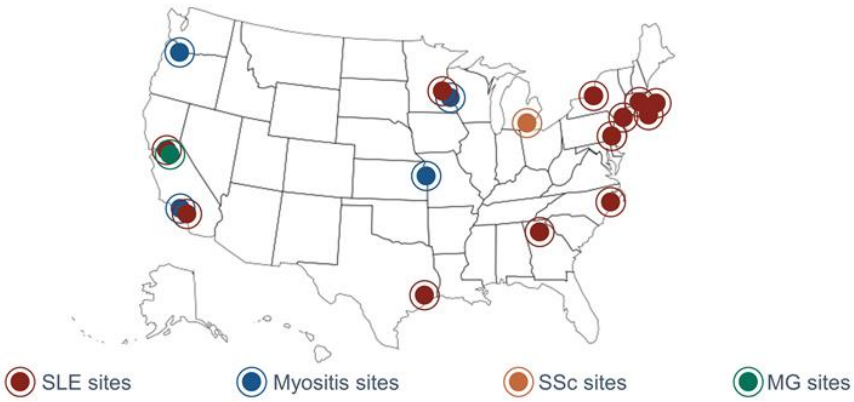
RESET™ – **RE**storing **SE**lf-**T**olerance; IMNM – Immune-mediated necrotizing myopathy; SLE – Systemic lupus erythematosus; Ab – Antibody; AChR – Acetylcholine receptor; gMG – Generalized myasthenia gravis, PV – Pemphigus vulgaris

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

1. Sub-study incorporated into DesCAARTes™ study.
2. Data cut-off as of 28 May 2024.

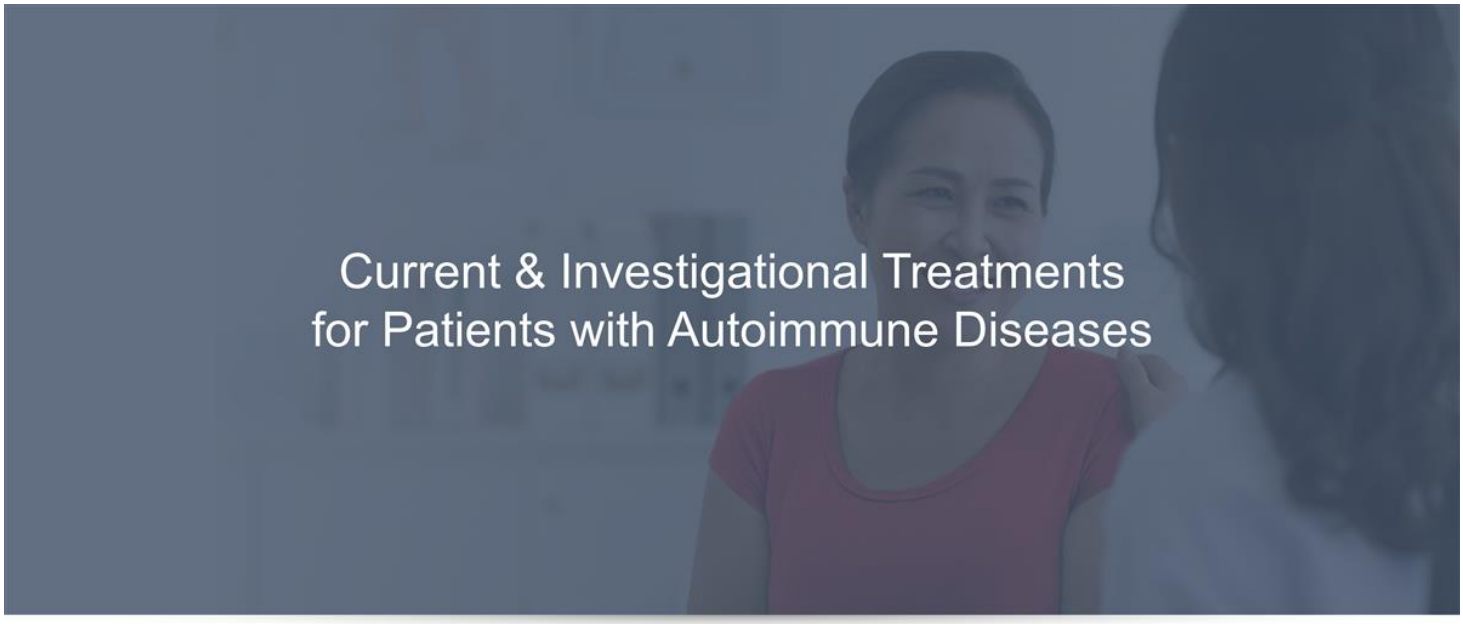
Sites actively recruiting patients in the RESET™ clinical program[1]

Acceleration in enrollment anticipated in 2H24 with initial CABA-201 data & engaged clinical investigators



- 5 patients enrolled across RESET-SLE™ & RESET-Myositis™, with 3 patients enrolled over the last 2 months
- 18 actively recruiting clinical sites in the U.S. across the RESET™ studies
- RESET-SSc™ and RESET-MG™ trials now open for enrollment

1. As of June 12, 2024.



Cabaletta Bio®

Current therapies for autoimmunity do not achieve drug-free remission

Broad immunosuppression and chronic administration often required to achieve partial, transient responses

High Unmet Clinical Need in SLE & Myositis

Myositis

- High mortality due to lung & cardiac involvement[1]
- Only FDA & EMA-approved therapy is IVIg in DM[2]
- Many patients remain refractory to standard of care therapies – particularly high unmet need in IMNM[1]

Lupus

- Potential for life-threatening complications
- ~40% of patients with SLE develop LN[3,4]
  - ~25% risk of death or ESRD within 10y
- Incomplete responses despite chronic therapy

Current Therapies in Autoimmunity

- Broad immunosuppression
- Modest & inconsistent clinical responses
- Chronic therapy requirements

There is a need for durable, effective and safe therapies that reestablish immune tolerance to eliminate the need for long-term therapy[5,6]

(Hematopoietic stem cell transplant has been shown to be curative in systemic sclerosis but has increased mortality in the first year[6])

1. Khoo T, et al. *Nat Rev Rheumatol*. 2023;19(11):695-712.
2. Octapharma. Accessed June 10, 2024.
3. Hoover PJ, Costenbader KH. *Kidney Int*. 2016;90(3):487-92.
4. Hahn BH, et al. *Arthritis Care Res (Hoboken)*. 2012; 64(6): 797–808.
5. Rosenblum MD, et al. Sci Transl Med. 2012;4(125):125sr1.
6. Swart J, et al. Nat Rev Rheumatol. 2017;13:244-256.

Potential for treatment paradigm to evolve in autoimmunity

CAR T therapy has the potential to provide drug-free, durable & reliable responses

What are the clinical outcomes with autologous 4-1BB CD19-CAR T cell therapy?

Promising clinical responses reported in 15 patients with an academic 4-1BB CD19-CAR T[1-3]

100%
Clinical responses in SLE, myositis, SSc off immunosuppressive therapies

<7%
Rate of CRS more severe than fever (1/15)
Rate of ICANS (1/15)

Within 7 months
Repopulation of naïve B cells post-infusion

2+ years
SLE drug-free remission with single infusion of CD19-CAR T[3]

How is CAR T cell therapy designed to reset the immune system?

A 'living drug' potentially enabling complete B cell depletion in the blood, tissues, lymph nodes & secondary lymphoid organs

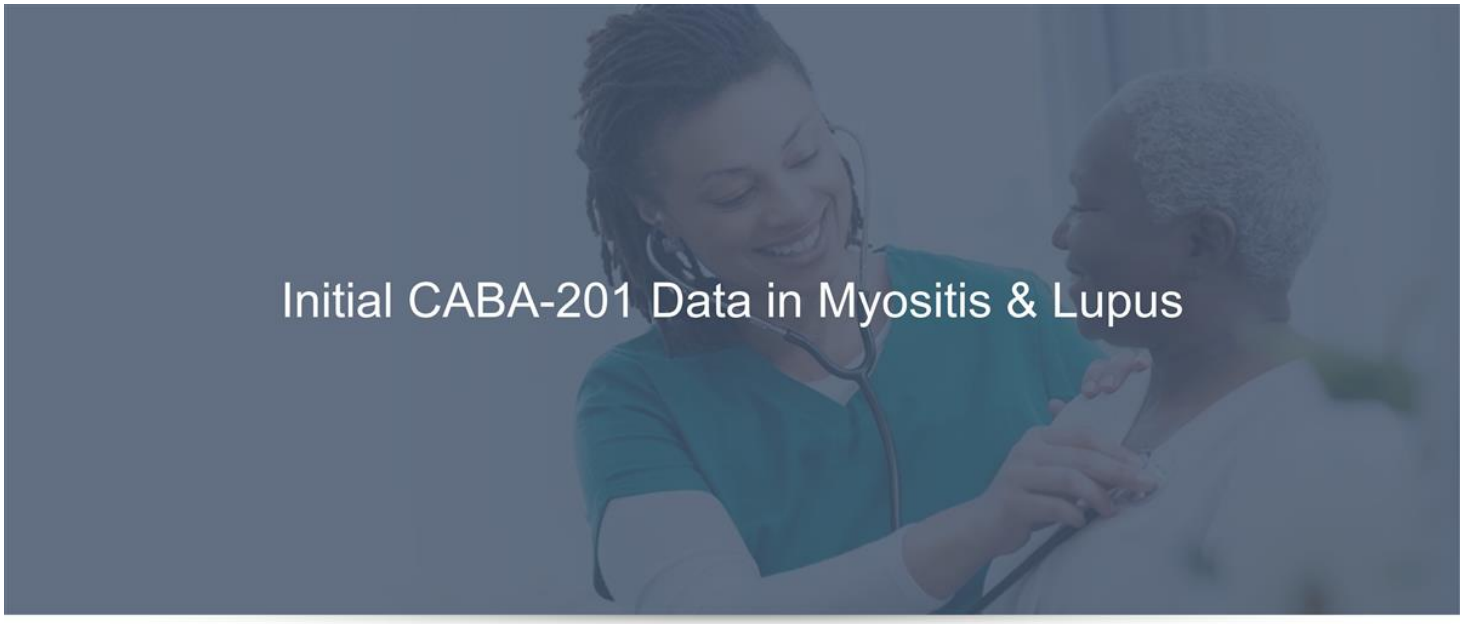
While autologous CD19-CAR T has potential to deliver drug-free, durable & reliable responses, multiple other therapeutic modalities may find a role within the future treatment paradigm

CRS – Cytokine release syndrome; ICANS – Immune effector cell-associated neurotoxicity syndrome

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.

2. The construct utilized in these studies has a similar design to CABA-201, sharing the 4-1BB costimulatory domain, but is a different construct.

3. It has been publicly reported that one idiopathic inflammatory myopathy subject in this academic study had a reoccurrence of disease following ~18 months of clinical remission.



Cabaletta Bio®

Phase 1/2 Myositis Study for CABA-201

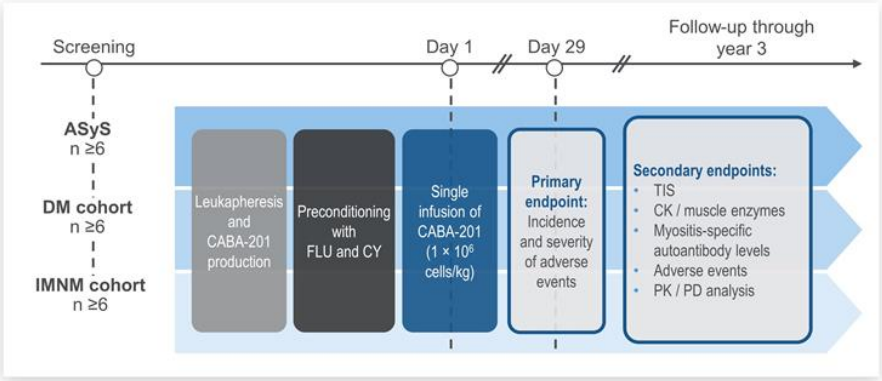
RESET Myositis

Key inclusion criteria

- Age ≥18 and ≤75 with a definite or probable clinical diagnosis of IIM (2017 EULAR/ACR classification criteria)
- Diagnosis of antisynthetase syndrome (ASyS), dermatomyositis (DM), or immune-mediated necrotizing myopathy (IMNM) based on presence of serum myositis-specific antibodies
- Evidence of active disease despite prior or current treatment with standard of care

Key exclusion criteria

- Cancer-associated myositis
- Significant lung or cardiac impairment
- B cell-depleting agent within prior ~6 months
- Previous CAR T cell therapy and/or HSCT



Juvenile idiopathic inflammatory myopathy (JIIM, juvenile myositis) cohort recently incorporated into trial

CY, cyclophosphamide; EULAR/ACR, European Alliance of Associations for Rheumatology/America College of Rheumatology; FLU, fludarabine; HSCT, hematopoietic stem cell transplantation. TIS, Total Improvement Score.

Phase 1/2 Lupus Study for CABA-201

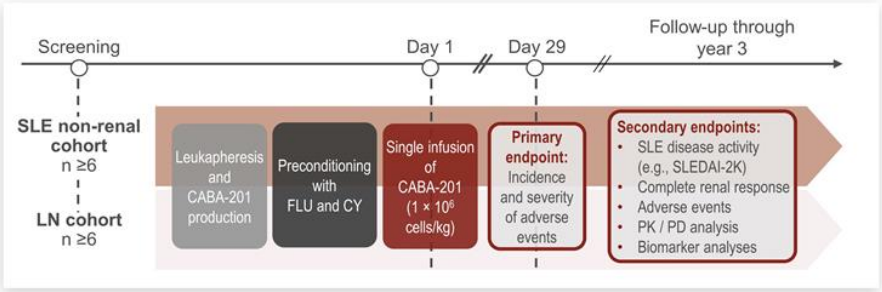
RESET SLE

Key inclusion criteria

- Age ≥18 to ≤65 with an SLE diagnosis (2019 EULAR/ACR classification criteria)
- ANA+ or anti-dsDNA+ at screening
- For SLE (non-renal) cohort: active, moderate to severe SLE, SLEDAI 2K ≥8 despite standard therapy
- For Lupus Nephritis cohort: active, biopsy-proven LN class III or IV, ± class V

Key exclusion criteria

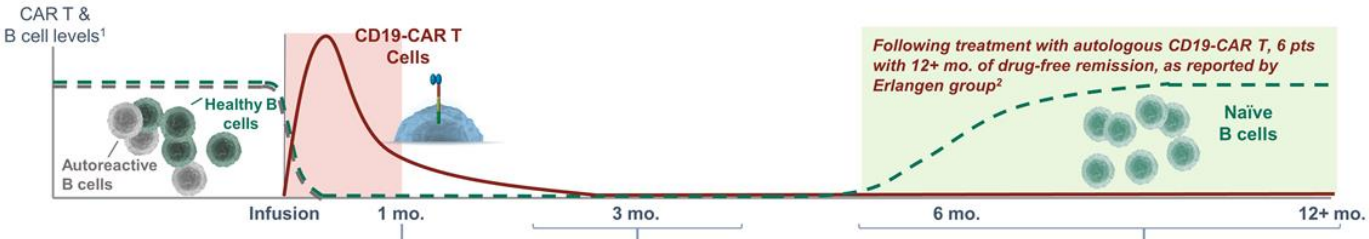
- B cell-depleting agent within prior ~6 months
- Previous CAR T cell therapy and/or HSCT
- Presence of kidney disease other than LN



ANA, antinuclear antibody; SLEDAI-2K, Safety of Estrogens in Lupus Erythematosus National Assessment Systemic Lupus Erythematosus Disease Activity Index-2K.

Metrics to assess outcomes of B cell depletion in autoimmunity

Translational & clinical parameters inform framework to evaluate advanced modalities in autoimmunity



Metrics of evaluation	Within 1 month	~3 months	Up to 12+ months
Translational measures	✓ B cell depletion: Timing & depth ✓ CAR T expansion: Magnitude & timing	✓ Autoantibody changes ✓ Vaccine titer changes ✓ Inflammatory marker changes	✓ Time to B cell repopulation ✓ B cell phenotype[3] ❑ Autoantibody changes
Clinical data	✓ Rate of CRS more severe than fever ✓ Rate & grade of ICANS ✓ Rate & severity of infection	✓ Early efficacy signals ✓ Rate & severity of infection	❑ Durability of clinical activity ❑ Rate & severity of infection
Patient experience	✓ Hospitalization requirements ✓ Apheresis & preconditioning ✓ Single vs. multiple infusions	✓ Chronic maintenance therapy / concomitant medications, if any	❑ Chronic maintenance / concomitant medications, if any

✓ Indicates data being presented for either or both of the first two patients in the RESET clinical program.

1. Illustrative graphic, adapted from Taubmann, J., et al. "OP0141 Long Term Safety and Efficacy Of CAR-T Cell Treatment in Refractory SLE-Data from the First Seven Patients." (2023): 93-94.
2. 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.
3. Flow phenotyping data; confirmatory analyses ongoing.

IMNM #1 SLE #1

Baseline characteristics of first two patients in RESET™ trials

Both patients with refractory disease, including to B cell-targeting antibodies & other agents

	RESET-Myositis Patient #1	RESET-SLE Patient #1
Age (years), sex	33, male	26, male
Cohort	IMNM	Non-renal SLE
Disease duration	~2 years	~6 years
Prior disease-specific therapy	IVIG, rituximab, MTX, glucocorticoids	Cyclophosphamide, voclosporin, belimumab, tacrolimus
Disease-specific therapy at screening	MTX, glucocorticoids	MMF, hydroxychloroquine, glucocorticoids
Autoantibodies	SRP, Ro-52	ANA, dsDNA
Disease activity[1]	MMT-8: 130, CK: 617	SLEDAI-2K: 26
Disease manifestations[1,2]	Muscle weakness, dysphagia	Vasculitis, arthritis, alopecia, hematuria, proteinuria (isolated class V LN), low complement

Expanding CD19-CAR T experience in IMNM & SLE

dsDNA, double-stranded DNA; IMNM, immune-mediated necrotizing myopathy; MMF, mycophenolate mofetil; MMT-8, manual muscle testing of 8 muscles; MTX, methotrexate; Ro-52, ribonucleoprotein 52; SRP, signal recognition particle.
1. Baseline=pre-preconditioning visit.
2. Disease manifestations were assessed according to Myositis Disease Activity Assessment Tool (MDAAT) and SLEDAI-2K for myositis and SLE, respectively.

IMNM #1 SLE #1

CABA-201 was well-tolerated in initial patients

No CRS, ICANS or infections of any grade reported through follow-up period[1]

		RESET-Myositis Patient #1	RESET-SLE Patient #1
Dose of CABA-201		83 million (1 x 10^6/kg) CAR^+ cells	63 million (1 x 10^6/kg) CAR^+ cells
Duration of inpatient monitoring[2]		4 days	4 days
Adverse events[4]	CRS	None	None
	ICANS	None	None
	Infections	None	None
	Hypogammaglobulinemia	None	None
	Serious adverse events	None	None
Concomitant disease-specific therapy		Discontinued MTX prior to infusion; Prednisone discontinued day 3 post-infusion	Discontinued MMF and HCQ prior to infusion; Ongoing taper from prednisone 10mg daily by 8 weeks[3]
Duration of follow-up[1]		84 days	28 days

Vaccination titers preserved post-infusion, with no reported infections in the duration of follow-up period[1]

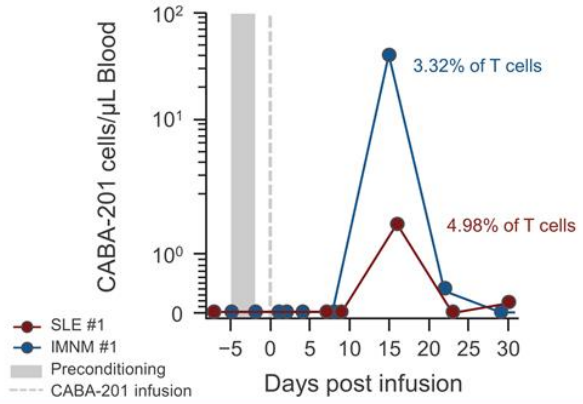
Both patients discharged after 4 days of monitoring post-infusion & neither received tocilizumab

1. Data cut-off as of 28 May 2024.
2. Protocol requires a minimum of 4-day hospitalization for monitoring.
3. PI-directed taper from 10mg daily prednisone.
4. Grade 4 leukopenia, neutropenia and lymphopenia reported for SLE Patient #1, the Grade 4 cytopenias resolved and were attributed to the preconditioning regimen (fludarabine and cyclophosphamide).

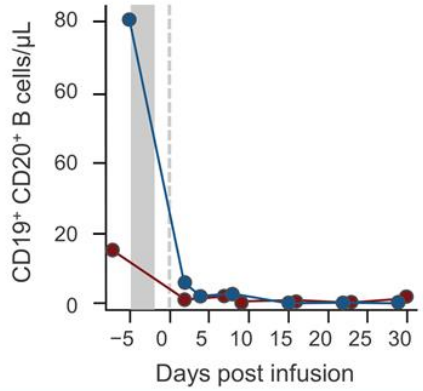
CABA-201 demonstrated expansion & targeted B cell depletion

CABA-201 exhibited anticipated profile of expansion and contraction[1]

Expansion of CAR T cells to anticipated range suggests target engagement



Complete B cell depletion achieved by day 15 on flow cytometry



Peripheral peak CAR T expansion occurred at approximately 2 weeks & rapid contraction suggests systemic B cell aplasia was achieved

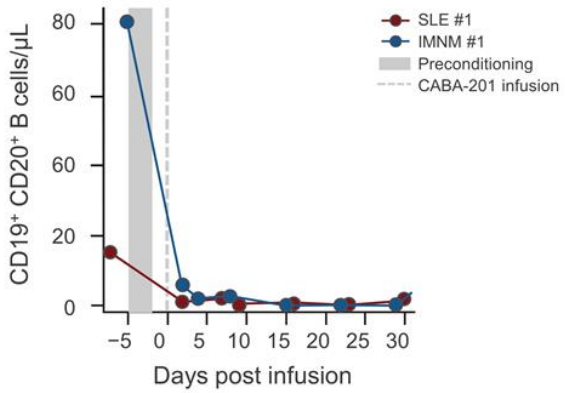
1. Response appears to be consistent with published data of cryopreserved CAR T products as well as the expansion profile of BCMA-CAR T products in patients with multiple myeloma, in which the number of target cells is more similar to autoimmune disease than to B cell leukemias and lymphomas.[2-6]
2. Shah BD, et al. *Lancet*. 2021;398(10299):491-502.
3. Awasthi R, et al. *Blood Adv*. 2020;4(3):560-572.
4. Munshi NC, et al. *N Engl J Med*. 2021;384(8):705-716.
5. Cohen AD, et al. *Blood Cancer J*. 2022;12(2):32.
6. Müller F, et al. *N Engl J Med*. 2024;390(8):687-700.

IMNM #1 SLE #1

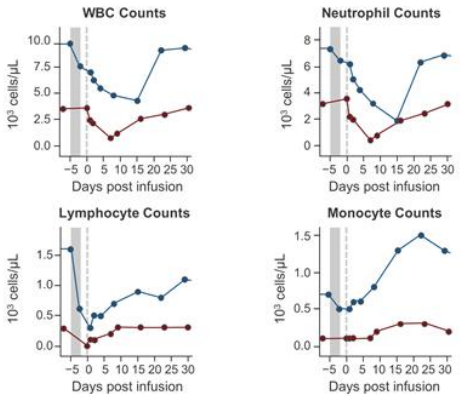
Systemic B cell depletion with CABA-201

Complete B cell depletion achieved by day 15 on flow cytometry & maintained in context of WBC recovery

$CD19^+$ $CD20^+$ B cell count



Leukocyte counts



B cell depletion was achieved & maintained in follow up or until naïve B cell recovery; early, transient leukopenia observed in both patients, as expected with preconditioning[1]

WBC, white blood cell.

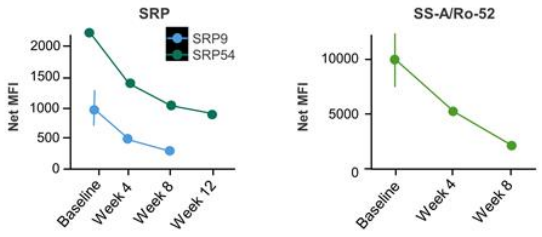
1. Nadir of lymphocyte count following fludarabine and cyclophosphamide administration estimated based on respective product labels.[2,3]
2. Fludarabine phosphate injection. Prescribing information. 2010. https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/022137s003lbl.pdf.
3. Cyclophosphamide. Prescribing information. 2013. https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/012141s090,012142s112lbl.pdf.

CK reduction & clinical improvement observed in SRP IMNM

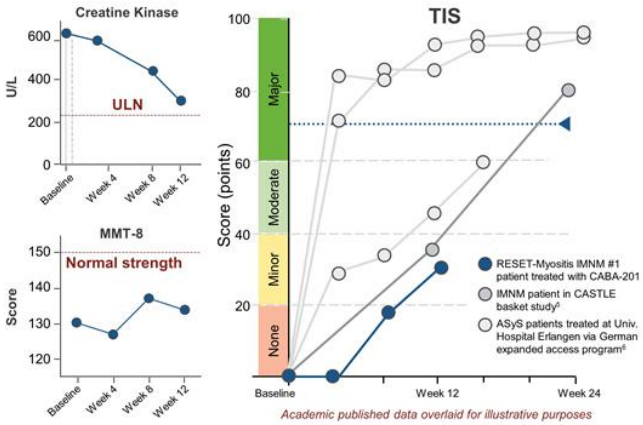
Antibody reduction & clinical improvement in disease activity as anticipated with follow-up of 12 weeks[1]

- Discontinued all disease-specific therapies
- Disease markers continuing to trend positively
- Patient reported symptoms as much improved

Quantitative translational assay shows ongoing reduction in SRP & Ro-52 antibodies[2,3]



Disease activity & improvement measures



Academic published data overlaid for illustrative purposes

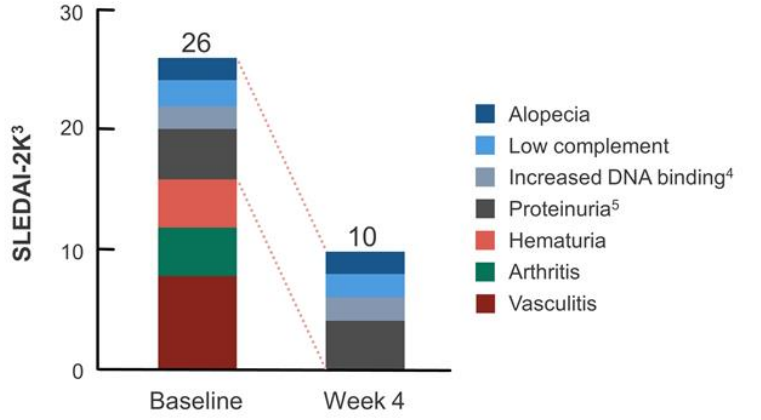
12-week TIS consistent with IMNM case report[5]

1. Data cut-off as of May 28, 2024.
2. Luminex assay developed and performed by Cabaletta Labs.
3. Qualitative commercial assay (Myositis Antigen Panel, performed at National Jewish Health Advanced Diagnostic Laboratories) suggests SRP54 antibody remains strongly positive at Week 12; Ro-52 normalizes by week 8.
4. Based on patient's moderate level of muscle disease at baseline, mild-moderate disability and limited extramuscular manifestations, the maximum achievable score is 70 points on the 100-point TIS scale.
5. Patient treated in third-party CASTLE Phase I/II basket study, TIS data at Week 12 and 24 provided via personal communication with and as presented by Dr. Georg Schett at the EULAR 2024 symposium.
6. Müller F, et al. *N Engl J Med*. 2024;390(8):687-700.

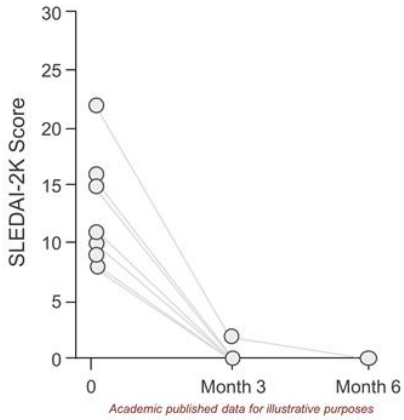
Early efficacy signals in first patient in non-renal SLE cohort[1]

Trend toward improvement in disease manifestations with follow up of 4 weeks[2]

SLE patient #1



Academic SLE data[6]



Academic published data for illustrative purposes

Vasculitis, arthritis and hematuria resolved within 4 weeks despite discontinuation of all therapies at infusion other than ongoing taper from prednisone 10mg per day

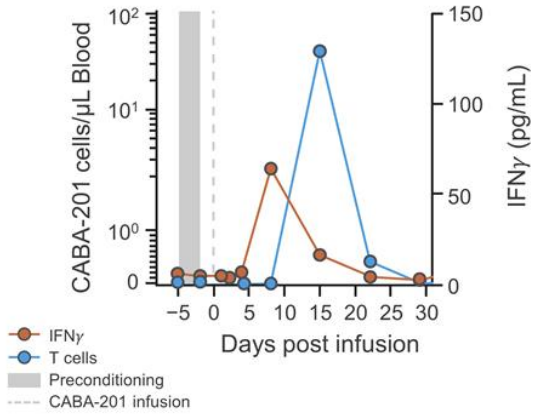
1. Patient in non-renal SLE cohort due to isolated Class V LN.
2. Data cut-off as of 28 May 2024.
3. Baseline and Day 29 SLEDAI-2K score are reflective of disease activity at study visit day.
4. Anti-dsDNA antibody titer decreased from 1:40 to 1:10 from Baseline to Week 4.
5. Urine Protein Creatinine Ratio decreased from 1.08 to 0.80 from Baseline to Week 4.
6. SLE patients treated at Univ. Hospital Erlangen via German expanded access program; Müller F, et al. *N Engl J Med.* 2024;390(8):687-700.

IMNM #1

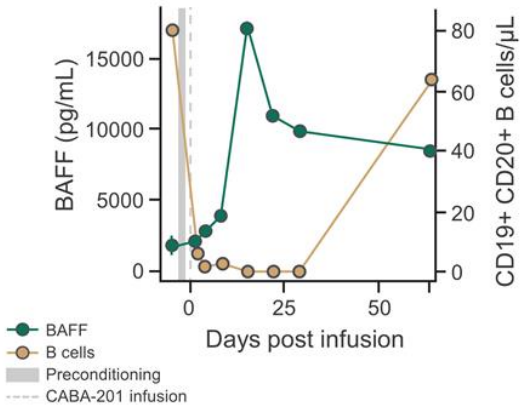
B cell repopulation occurred at 2 months in first IMNM patient

IMNM patient data provides insights supporting tissue-level effects of CAR T

IFNγ peak prior to peripheral CABA-201 peak suggests tissue-resident B cell cytotoxicity



Systemic B cell depletion triggers BAFF to encourage bone marrow B cell repopulation



1. Data cut-off as of May 28, 2024.

B cell repopulation with naïve B cells

Initial patient phenotyping data consistent with potential immune system reset; confirmatory analyses ongoing

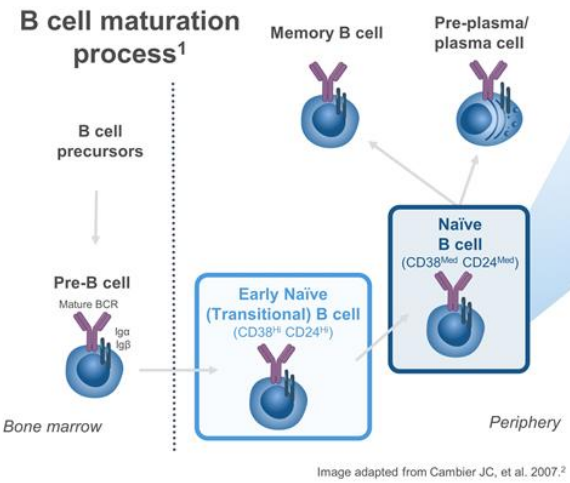
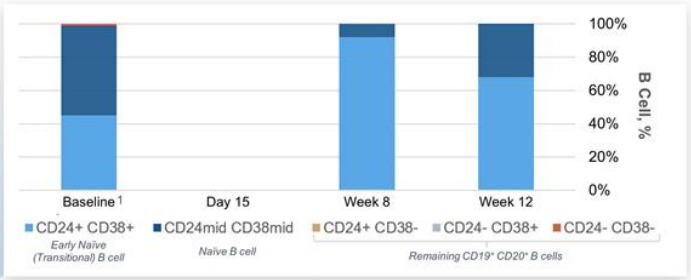
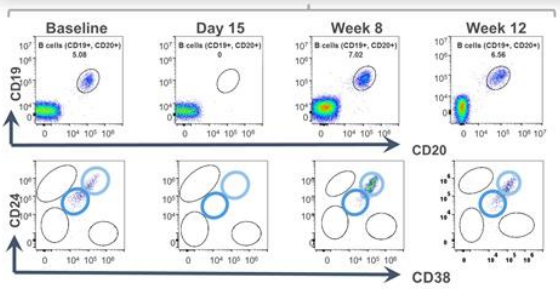


Image adapted from Cambier JC, et al. 2007.[2]





B cell phenotyping data

BCR, B cell receptor; Note: Flow plot gating reflects CD19+ CD20+ live lymphocytes.
1. Patient received multiple courses of rituximab, with most recent dose approximately 9 months prior to CABA-201 infusion.
2. Cambier JC, et al. *Nat Rev Immunol.* 2007;7(8):633-643.

Cabaletta Bio®

Key takeaways from initial CABA-201 data in first two patients[1]

CABA-201: Engineered specifically for autoimmune patients at the selected dose based on a construct design and function that is similar to the academic CD19-CAR T construct[2]

Safety of CABA-201

- In the first 2 patients (IMNM & SLE), CABA-201 was well-tolerated
  - No CRS, ICANS or infections reported through follow-up period

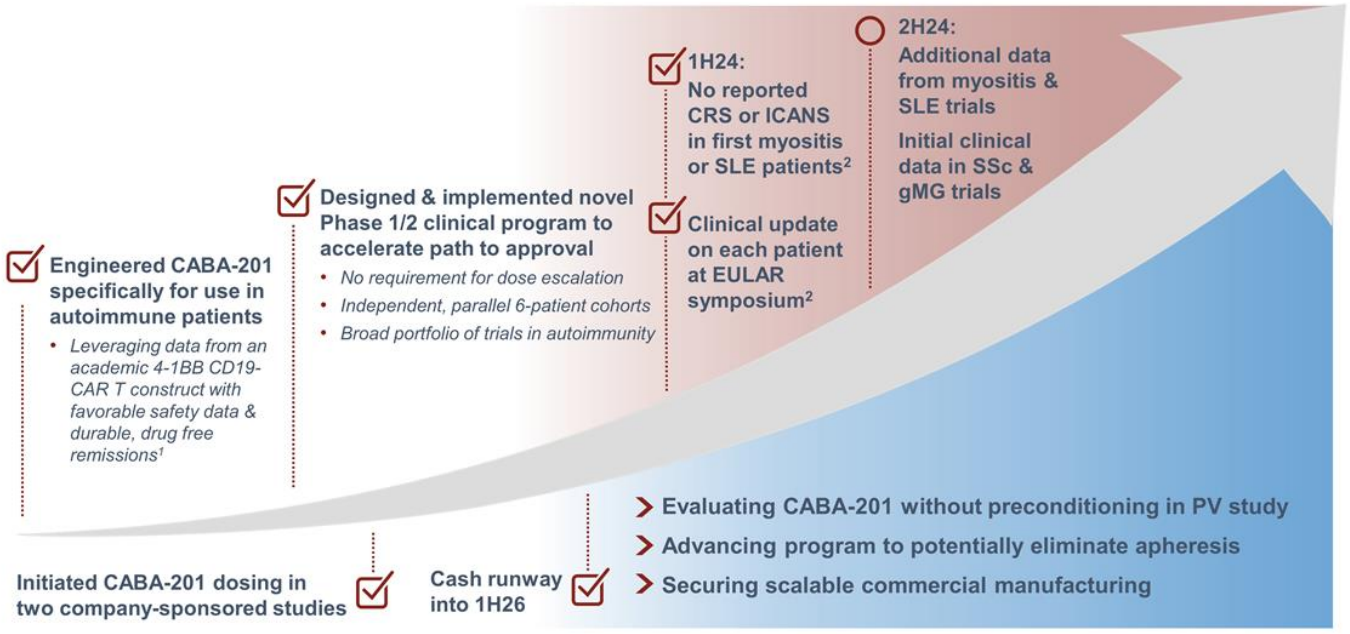
Dose selection
1 x 10^6 cells/kg

- Clinical & translational data support the selected dose of CABA-201
  - PK: IFNγ peak prior to peak of CABA-201 suggests tissue-level B cell cytotoxicity
  - PD: Systemic B cell depletion followed by repopulation with naïve B cells
  - Autoantibody levels: Decline generally consistent with Univ. Hospital Erlangen data[2]
  - Clinical & translational data: Improvement consistent with reported CD19-CAR T data[2,3]

18 clinical sites now enrolling patients in the CABA-201 RESET™ program across four trials – myositis, SLE/LN, systemic sclerosis and myasthenia gravis[4]

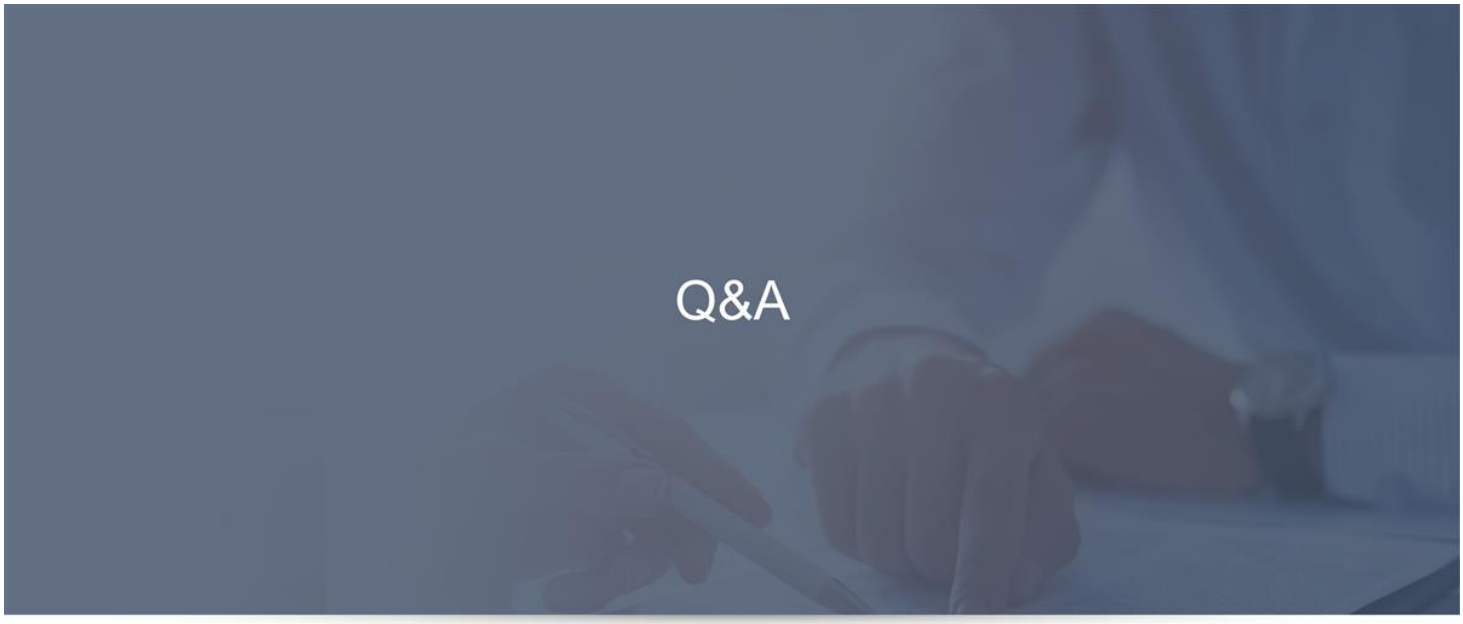
1. Data cut-off as of 28 May 2024.
2. Müller F, et al. N Engl J Med. 2024;390(8):687-700.
3. Third-party CASTLE Phase I/II basket study.
4. As of June 12, 2024.

Realizing the vision to transform autoimmune disease treatment



SLE – Systemic lupus erythematosus; SSc – Systemic sclerosis; gMG – Generalized myasthenia gravis; PV – Pemphigus vulgaris

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. Data cut-off as of 28 May 2024.



Cabaletta Bio®

Cabaletta Bio®

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

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

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

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

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

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

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

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

"We are encouraged by the initial safety, clinical and translational data from the RESET-Myositis and RESET-SLE trials which we believe provide important early validation regarding the potential of the selected clinical dose of CABA-201 to enable an immune system reset for patients with autoimmune diseases. By demonstrating a potentially well-tolerated safety profile along with initial clinical and translational data consistent with the academic experience of a similar 4-1BB CD19-CAR T construct, we believe CABA-201 may be uniquely positioned to fulfill unmet patient needs across a broad range of autoimmune diseases," said David J. Chang, M.D., Chief Medical Officer of Cabaletta. "With the RESET-SSc™ and RESET-MG™ trials recently opening for enrollment, an additional cohort evaluating patients with juvenile myositis incorporated into the RESET-Myositis trial and the momentum provided by the promising early clinical data, we are looking forward to accelerating clinical trial enrollment in the RESET clinical program. We continue to expect to report initial clinical data from the Phase 1/2 RESET-SSc and RESET-MG trials as well as additional data from the RESET-Myositis and RESET-SLE trials in the second half of this year."

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

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

Initial Clinical Data Summary

Safety and Tolerability

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

Clinical and Translational Profile

- Complete B cell depletion was observed within 15 days post-infusion with CABA-201 in both patients. Both patients had early, transient leukopenia, as expected with the preconditioning regimen.
- CAR T cell expansion associated with CABA-201 reached its peak magnitude at day 15 post-infusion in both patients and the magnitude of expansion was consistent with the academic experience with a similar 4-1BB CD19-CAR T construct.

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

Investor Conference Call and Webcast Information

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

About the RESET-Myositis™ Trial

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

About the RESET-SLE™ Trial

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

About CABA-201

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

About Cabaletta Bio

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

Forward-Looking Statements

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

Any forward-looking statements in this press release are based on management's current expectations and beliefs of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to: risks related to regulatory filings and potential clearance; the risk that signs of biologic activity or persistence may not inform long-term results; Cabaletta's ability to demonstrate sufficient evidence of safety, efficacy and tolerability in its preclinical studies and clinical trials of CABA-201; the risk that the results observed with the similarly-designed construct employed in academic publications, including due to the dosing regimen, are not indicative of the results we seek to achieve with CABA-201; risks related to clinical trial site activation, delays in enrollment

generally or enrollment rates that are lower than expected; delays related to assessment of clinical trial results; risks related to unexpected safety or efficacy data observed during clinical studies; risks related to volatile market and economic conditions and public health crises; Cabaletta's ability to retain and recognize the intended incentives conferred by Orphan Drug Designation and Fast Track Designation or other designations for its product candidates, as applicable; risks related to Cabaletta's ability to protect and maintain its intellectual property position; risks related to fostering and maintaining successful relationships with Cabaletta's collaboration and manufacturing partners, including in light of recent legislation; uncertainties related to the initiation and conduct of studies and other development requirements for its product candidates; the risk that any one or more of Cabaletta's product candidates will not be successfully developed and/or commercialized; and the risk that the initial or interim results of preclinical studies or clinical studies will not be predictive of future results in connection with future studies. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause Cabaletta's actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in Cabaletta's most recent annual report on Form 10-K as well as discussions of potential risks, uncertainties, and other important factors in Cabaletta's other filings with the Securities and Exchange Commission. All information in this press release is as of the date of the release, and Cabaletta undertakes no duty to update this information unless required by law.

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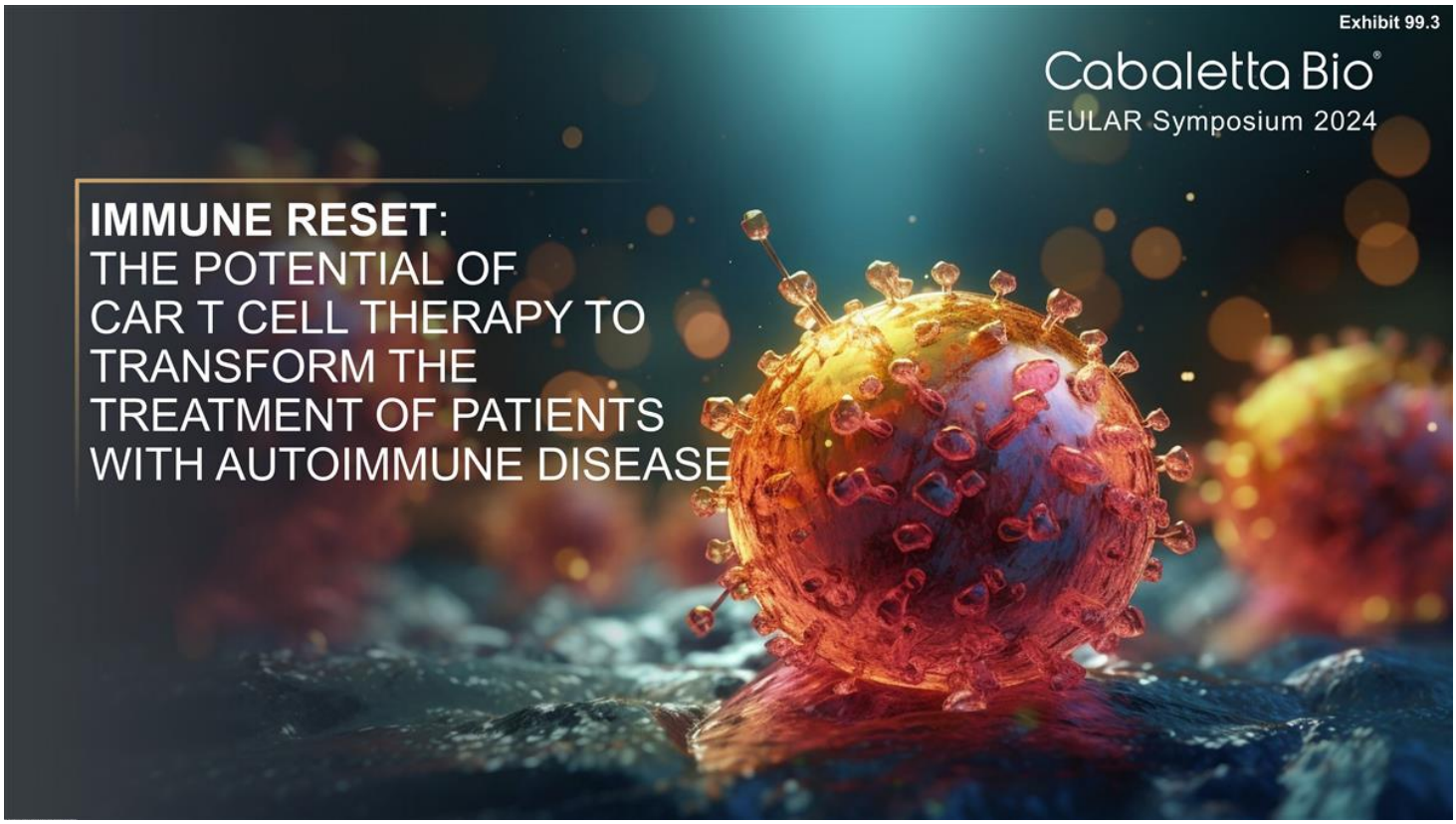
Exhibit 99.3

Cabaletta Bio®

EULAR Symposium 2024

IMMUNE RESET: THE POTENTIAL OF CAR T CELL THERAPY TO TRANSFORM THE TREATMENT OF PATIENTS WITH AUTOIMMUNE DISEASE



Symposium Speakers

Carl H. June, MD
Director of the Center for Cellular Immunotherapies
Penn Medicine
Philadelphia, PA

Penn Medicine
Center for Cellular Immunotherapies

Georg Schett, MD
Vice President Research
Friedrich-Alexander Universität [FAU]
Erlangen-Nürnberg
Erlangen, Germany

FAU FRIEDRICH-ALEXANDER UNIVERSITÄT ERLANGEN-NÜRNBERG

David J. Chang, MD, MPH, FACR
Chief Medical Officer
Cabaletta Bio
Philadelphia, PA

Cabaletta Bio

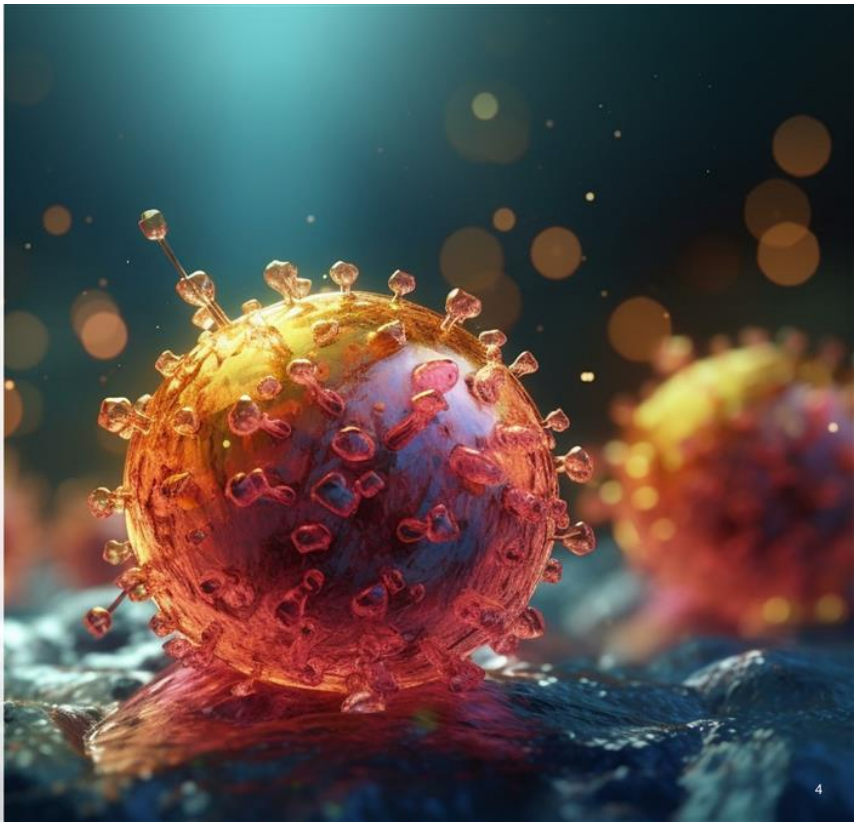
Drs Georg Schett and Carl June are members of Cabaletta Bio's Scientific Advisory Board.

Agenda

8:15 AM-8:20 AM	8:20 AM-8:35 AM	8:35 AM-8:50 AM	8:50 AM-9:15 AM	9:15 AM-9:30 AM
Welcome and introductions *David J. Chang, MD, MPH, FACR*	**Evolving the potential of chimeric antigen receptor (CAR) T cell therapies to autoimmunity** *Carl H. June, MD*	**Resetting the immune system of patients with autoimmune disease** *Georg Schett, MD*	**Unlocking the potential of CD19-CAR T cell therapy in myositis and lupus** *David J. Chang, MD, MPH, FACR*	**Questions and answers**

Learning Objectives

- Learn about the history of CAR T cell therapies in oncology and their potential in autoimmunity
- Review the role of B cells in autoimmune disease and the potential for CD19-CAR T cell therapy to transform treatment
- Understand the potential of CD19-CAR T cell therapy to reset the immune system in myositis and lupus




Evolving the Potential of Chimeric Antigen Receptor (CAR) T Cell Therapies to Autoimmunity
5

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

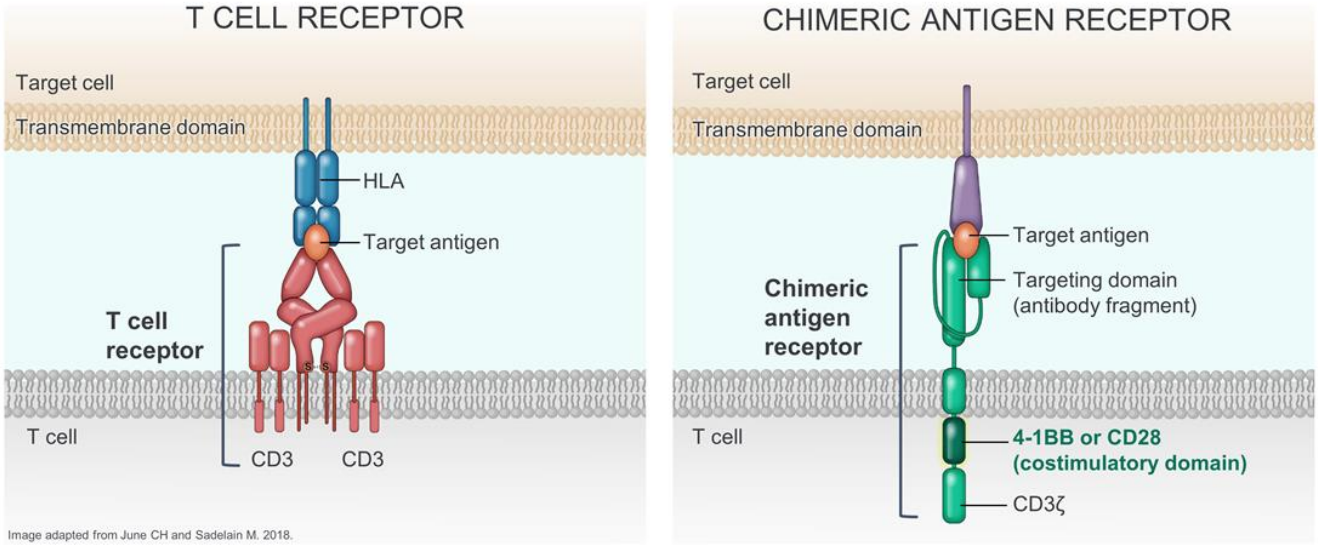


Image adapted from June CH and Sadelain M. 2018.

CD, cluster of differentiation; HLA, human leukocyte antigen.
June CH, Sadelain M. *N Engl J Med.* 2018;379:64-73.

Personalized Manufacturing of CAR T Cells

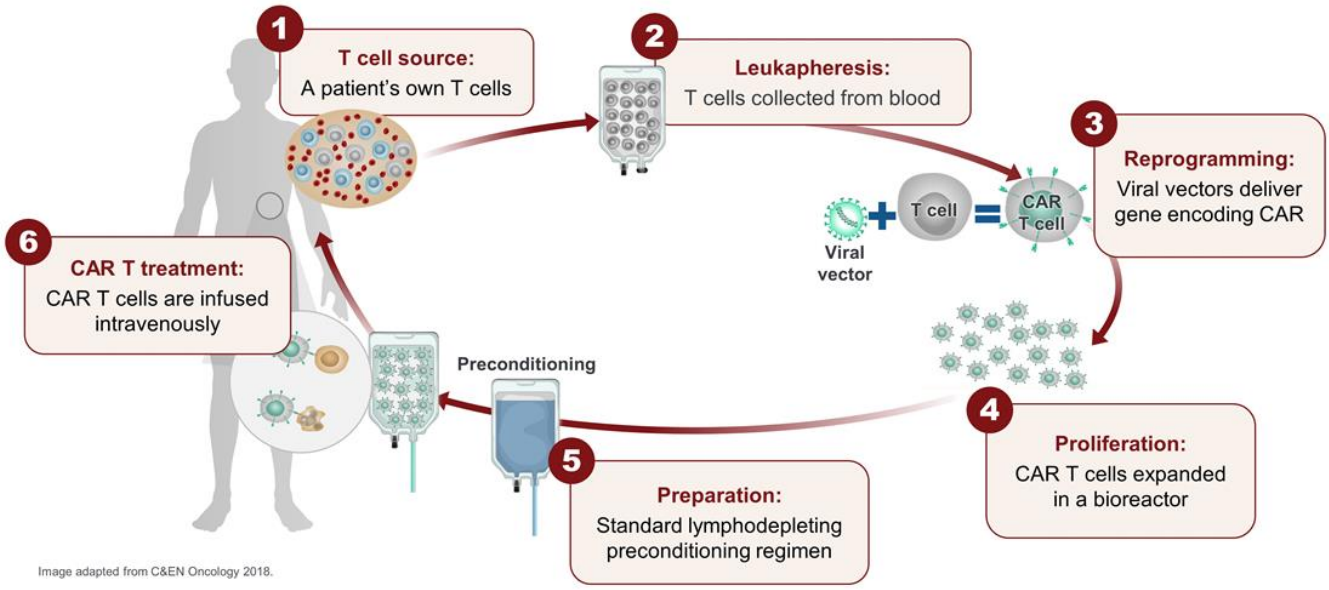


Image adapted from C&EN Oncology 2018.

C&EN Oncology. Accessed June 10, 2024. https://cen.acs.org/pharmaceuticals/oncology/Controlling-CAR-T-scientists-plan/96/i19.

Considerations and Efficacy Outcomes of CAR T in Cancer

Personalized cell therapy product that behaves as a 'living drug' by fully eliminating target cells in the body[1]

- **CAR T is a 'living drug'[1]**
  - Engrafts & expands in the body
  - Penetrates across tissues
- **Activated by target cells[1]**
- **Preconditioning key in oncology[2]**
  - Eliminates cytokine sinks
  - Increases CAR T expansion, persistence & activity

CD19-CAR T cells have been FDA approved for lasting remission of B cell cancers[1]

- **2017** Kymriah (tisagenlecleucel) **4-1BB**
- **2017** Yescarta (axicabtagene ciloleucel) **CD28**
- **2020** Tecartus (brexucabtagene autoleucel) **CD28**
- **2021** Breyanzi (lisocabtagene maraleucel) **4-1BB**

COMPLETE remission rate: **40%-67%**[3-7]

LONG-TERM remission rate: **30%-59%**[6-9]

FDA, US Food and Drug Administration.
1. Holzinger A, Abken H. *Pharmacology*. 2022;107(9-10):446-463. 2. Pietrobon V, et al. *Int J Mol Sci*. 2021;22(19):10828. 3. Maude SL, et al. *N Engl J Med*. 2018;378(5):439-448. 4. Schuster SJ, et al. *N Engl J Med*. 2019;380(1):45-56. 5. Locke FL, et al. *Lancet Oncol*. 2019;20(1):31-42. 6. Abramson JS, et al. *Lancet*. 2020;396(10254):839-852. 7. Wang M, et al. *N Engl J Med*. 2020;382(14):1331-1342. 8. Schuster SJ, et al. *Lancet Oncol*. 2021;22(10):1403-1415. 9. Neelapu SS, et al. *Blood*. 2023;141(19):2307-2315.

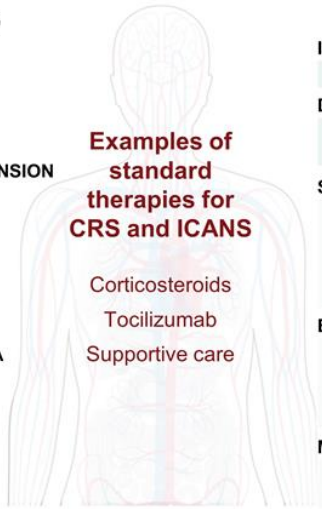
Common Adverse Events Associated With CAR T Cell Therapy

Familiarity with CAR T-associated AEs has increased in oncology, enabling potential outpatient administration

CRS

(cytokine release syndrome)

		Grade 1	Grade 2	Grade 3	Grade 4
Temperature ≥38°C	**FEVER**				
with					
No vasopressors					
Vasopressor +/- vasopressin	**HYPOTENSION**				
Multiple vasopressors					
and/or					
Low-flow nasal cannula or blow-by					
High-flow nasal cannula face mask, nonrebreather mask, or Venturi mask	**HYPOXIA**				
Positive pressure (CPAP, BiPAP)					



Examples of standard therapies for CRS and ICANS

Corticosteroids

Tocilizumab

Supportive care

ICANS

(immune effector cell-associated neurotoxicity syndrome)

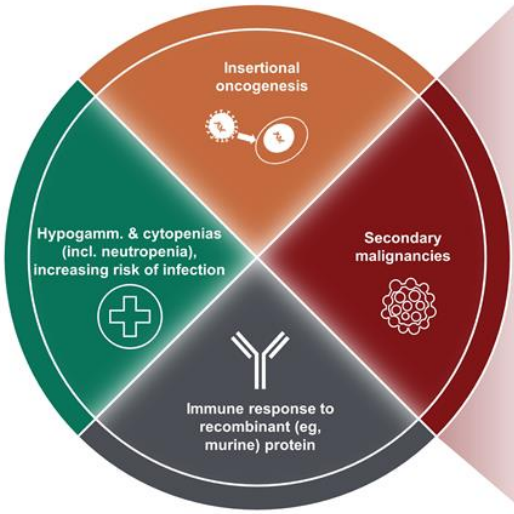
	Grade 1	Grade 2	Grade 3	Grade 4
ICE SCORE	7-9	3-6	0-2	Unarousable/unable to perform ICE
DEPRESSED LEVEL OF CONSCIOUSNESS	Awakens spontaneously	Awakens to voice	Awakens only to tactile stimulus	Unarousable or requires vigorous tactile stimuli to arouse or coma
SEIZURE	None	None	Any clinical seizure that resolves rapidly or nonconvulsive seizure that resolves with intervention	Life-threatening prolonged seizure (>5 min) or repetitive clinical or electrical seizures with no return to baseline in between
ELEVATED ICP/CEREBRAL EDEMA	None	None	Focal/local edema on neuroimaging	Diffuse cerebral edema on neuroimaging; decerebrate or decorticate posturing; or cranial nerve VI palsy; papilledema; or Cushing's triad
MOTOR FINDINGS	None	None	None	Deep focal motor weakness such as hemiparesis or paraparesis

Diagram adapted from Zhang Y, et al. 2023.

AE, adverse event; BiPAP, bilevel positive airway pressure; CPAP, continuous positive airway pressure; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; ICE, immune effector cell encephalopathy; ICP, intracranial pressure.

Zhang Y, et al. *J Clin Med*. 2023;12(19):6124.

Potential Adverse Events After CAR T Cell Therapy in Cancer



Secondary malignancies

- In November 2023, the FDA reported identifying 22 cases of T cell cancers that occurred among the 34,000 patients who previously received treatment with CAR T products[2]
- In April 2024, the FDA required approved CAR T products (CD19 and BCMA targeted) to add a boxed warning for T cell malignancy when used in patients treated for hematologic malignancies[4]
- In January 2024, the Director of FDA's CBER suggested the risk:benefit profile of CAR T is not in question in oncology or in moving forward development programs in autoimmune diseases[5,6]

Image adapted from Bonifant CL, et al. 2016,[1] Verdun N and Marks P. 2024,[2] Adkins S, et al. 2019.[3]

1. Bonifant CL, et al. *Mol Ther Oncolytics*. 2016;3:16011. 2. Verdun N, Marks P. *N Eng J Med*. 2024;390(7):584-586. 3. Adkins S. *J Adv Pract Oncol*. 2019;10(suppl 3):21-28. 4. FDA. Accessed June 10, 2024. https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/fda-requires-boxed-warning-t-cell-malignancies-following-treatment-bcma-directed-or-cd19-directed.
5. Wu L. Accessed June 10, 2024. https://endpts.com/jpm24-fdas-peter-marks-says-some-secondary-cancer-cases-after-car-t-therapy-may-be-causal-but-benefits-still-outweigh-risks/. 6. Expediting the Development of Cell and Gene Therapy. Accessed June 10, 2024. https://www.youtube.com/watch?v=jt3CNgsCXAk.
CBER, Center for Biologics Evaluation and Research.

Differences in CD19-CAR T Constructs

A human CD19 binder and 4-1BB costimulatory domain may be ideal for a CD19-CAR T construct

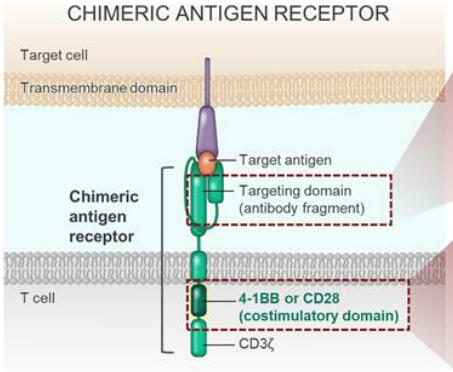


Image adapted from June CH and Sadelain M. 2018.[1]

IMMUNOGENICITY[2]

Sources of CAR constructs

Chimeric

Approved products (FMC63)

Humanized

Fully human

Candidates under development with potentially lower risk of immune responses

Image adapted from Brekke OH and Inger Sandlie. 2003.[2]

Product in lymphoma study[a]	Costim domain	CRS		ICANS		Requiring tocilizumab	Requiring steroids
		All Gr	Gr ≥3	All Gr	Gr ≥3		
Axicabtagene ciloleucel[4]	CD28	93%	13%	64%	28%	43%	27%
Brexucabtagene autoleucel[5]	CD28	91%	15%	63%	31%	59%	22%
Tisagenlecleucel[6]	4-1BB	58%	22%	21%	12%	14%	10%
Lisocabtagene maraleucel[7]	4-1BB	42%	2%	30%	10%	18%	10%

In oncology, a 4-1BB costimulatory domain is associated with a reduced incidence and severity of CRS and ICANS events[6,7]

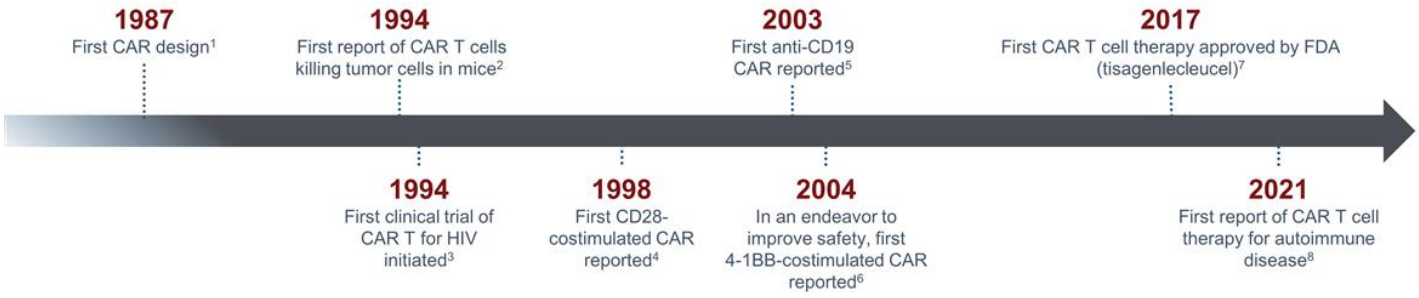
[a]Similar safety outcomes comparing 4-1BB and CD28 costimulatory domains were also demonstrated in patients with B-ALL.[8,9]

B-ALL, B cell acute lymphoblastic leukemia; Costim, costimulatory. Gr, grade.

1. June CH, Sadelain M. *N Engl J Med*. 2018;379:64-73. 2. Brekke OH, Sandlie I. *Nat Rev Drug Discov*. 2003;2(1):52-62. 3. Cappell KM, Kochenderfer JN. *Nat Rev Clin Oncol*. 2021;18(11):715-727. 4. Neelapu SS, et al. *N Engl J Med*. 2017;377(26):2531-2544. 5. Wang M, et al. *N Engl J Med*. 2020;382(14):1331-1342. 6. Schuster SJ, et al. *N Engl J Med*. 2019;380(1):45-56. 7. Abramson JS, et al. *Lancet*. 2020;396(10254):839-852. 8. Zhao X, et al. *Mol Ther Oncolytics*. 2020;18:272-281. 9. Wu L, et al. *Cancers (Basel)*. 2023;15(10):2767.

Success of CAR T in Oncology Established Over Decades

Significant experience with CAR T in B cell cancers provided the foundation for autoimmune application



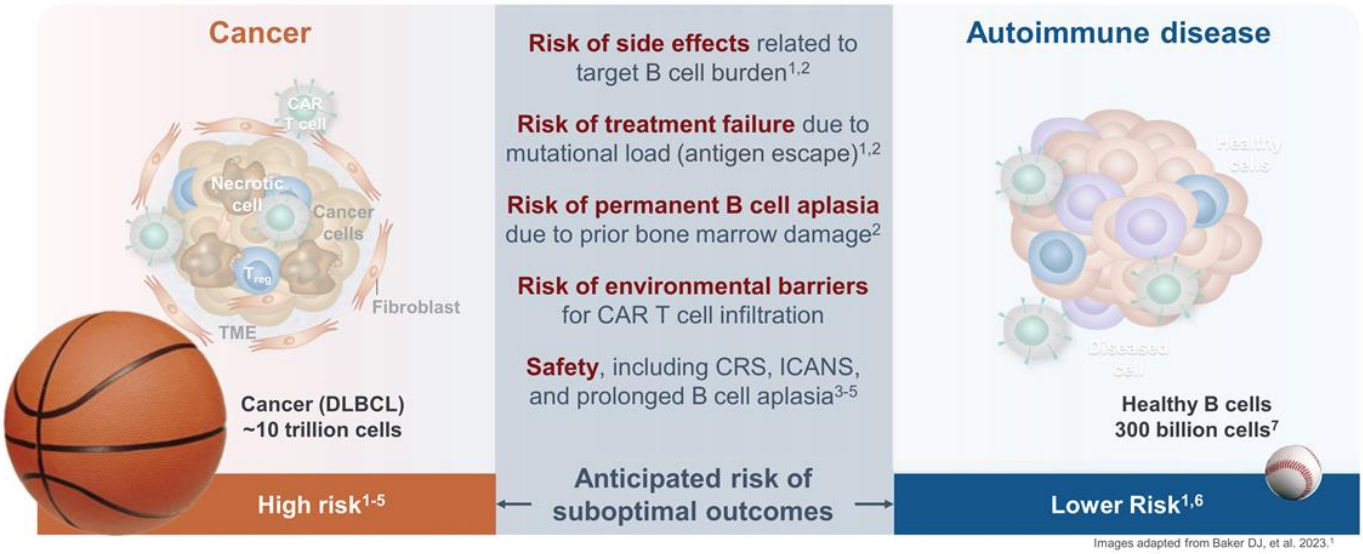
- Multiple types of cell therapies are in phase 1/2 studies, with the majority being autologous CAR T cell therapy[9]
- Over 800 ongoing CAR T trials, with the majority in the US and China[10]

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 June 10, 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 are minimized in 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.

Key Takeaways

Evolving the Potential of CAR T Cell Therapies to Autoimmunity

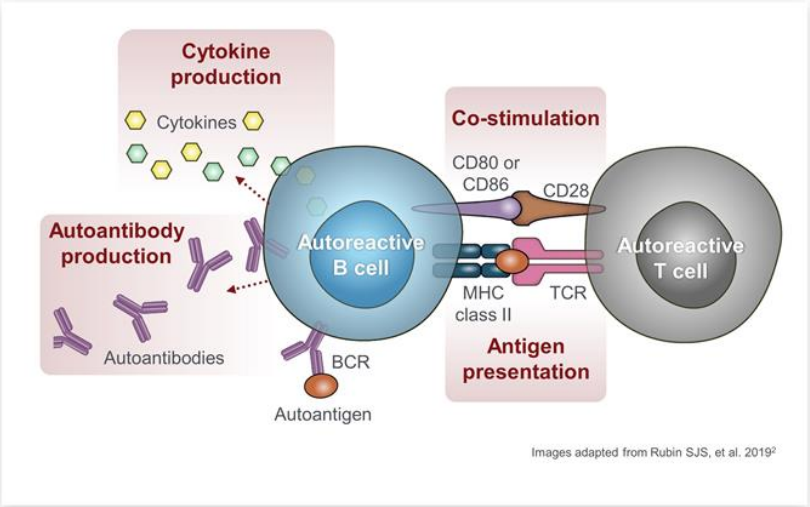
- CAR T cells are engineered T cells that are designed to combine the targeting ability of antibodies with the cell-killing machinery of T cells[1]
- Key learnings from oncology have the potential to accelerate the adoption of CAR T cell therapy for autoimmune disease[2,3]
- Differences in CD19-CAR T costimulatory domains seem to impact safety in cancer[3-5]
- Many factors that drive adverse events & disease relapse post-CAR T are not at play in autoimmune disease driven by B cells[3,6]
  - Potentially lower risk of CRS & ICANS due to lower B cell burden

1. Holzinger A, Abken H. *Pharmacology*. 2022;107(9-10):446-463. 2. Baker DJ, et al. *Nature*. 2023;619(7971):707-715. 3. Cappell KM, Kochenderfer JN. *Nat Rev Clin Oncol*. 2021;18(11):715-727. 4. Davey AS, et al. *Cancers*. 2021;13(38). 5. Zhao X, et al. *Molecular Therapy Oncolytics*. 2020;18. 6. Müller F, et al. *N Engl J Med*. 2024;390(8):687-700.


Resetting the Immune System of Patients
With Autoimmune Disease
15

B Cells Play a Central Role in the Pathogenesis of Autoimmune Diseases

- **B cells contribute to autoimmunity through a variety of mechanisms[1,2]**
  - Autoantibody production
  - Antigen presentation
  - T cell co-stimulation
  - Production of proinflammatory cytokines
- **While circulating B cells are sensitive to depletion, tissue-resident B cells easily escape depletion[2]**

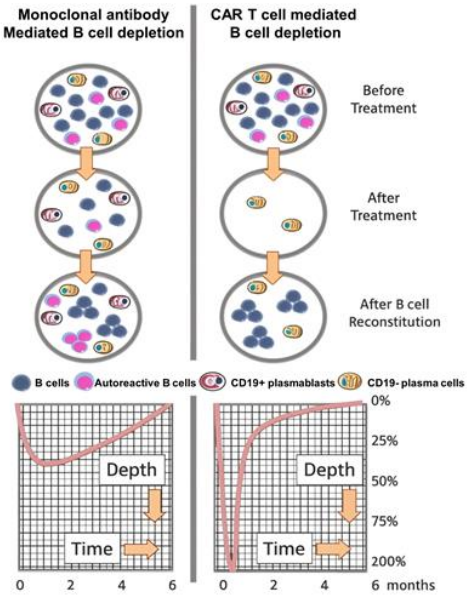


BCR, B cell receptor; MHC, major histocompatibility complex.

1. Barnas JL, et al. *Curr Opin Immunol.* 2019;61:92-99. 2. Rubin SJS, et al. *Nat Rev Rheumatol.* 2019;15(5):303-315.

Current Therapies for B Cell Driven Autoimmune Disease Rarely Achieve Drug-Free Remission

- **Current challenges**
  - Despite good peripheral B cell depletion, bispecific and antibody-based B cell targeting therapies rarely induce stable drug-free remission in autoimmune disease
  - Shallow B cell depletion that does not tackle resident autoimmune B cell clones may be the reason for this limitation
- **Goals of newer therapies**
  - Deeper B cell depletion with a 'living drug' to allow targeting resident autoimmune B cell clones, enabling potential immune tolerance such that long-term drug therapy is not needed
  - Reversibility of B cell depletion enabling a good safety profile



1. Schett G, et a. *Ann Rheum Dis.* 2024. PMID: 38777374. 2. Bucci, L. et al. *Nat Med.* 2024; PMID 38671240.

Emerging Academic Evidence of CD19-CAR T in Autoimmunity

15 patients with refractory systemic autoimmune disease

- Age range of 18 to 60 years; 60% female
- All patients with disease duration >12 months
- All patients had inadequate response to ≥2 lines of therapy
- ~50% of patients received B cell depletion therapy

Myositis (n=3)	Muscle and lung involvement median CK of 4298 U/L
SLE (n=8)	Median SLEDAI-2K score of 13; all had LN class III or IV
SSc (n=4)	All had active skin and lung involvement

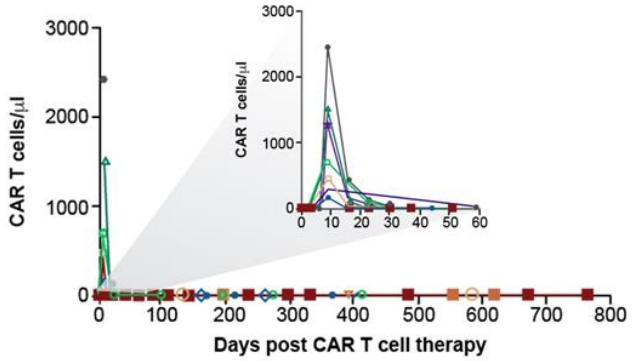
All patients received a single dose of 1x10^6/kg CD19-CAR T cells following Flu/Cy preconditioning

CK: creatinine kinase; Flu/Cy, fludarabine/cyclophosphamide; LN, lupus nephritis; SLE, systemic lupus erythematosus; SLEDAI-2K, systemic lupus erythematosus disease activity index 2K.

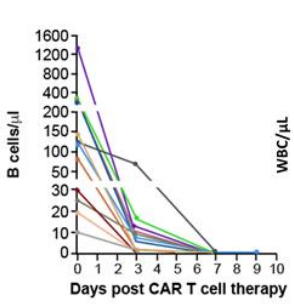
Müller F, et al. *N Engl J Med.* 2024;390(8):687-700.

CD19-CAR T Cells Can Result in Targeted B Cell Depletion

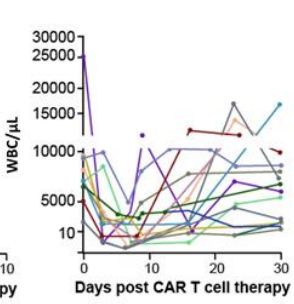
Preconditioning results in transient WBC decrease, though B cell depletion is sustained



Circulating CAR T cell numbers after CD19-CAR T treatment (N=15)



Circulating CD19⁺ B cells within first 10 days after treatment (N=15)

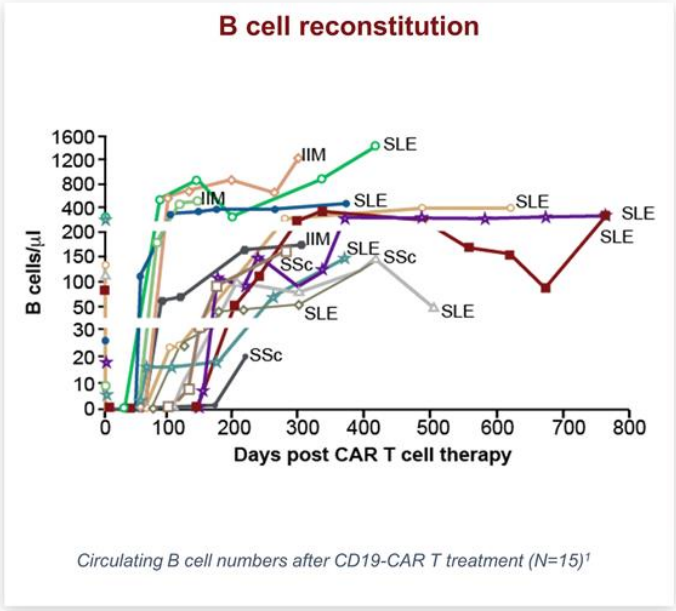


Circulating total WBCs within first 30 days after treatment (N=15)

WBC, white blood cell.

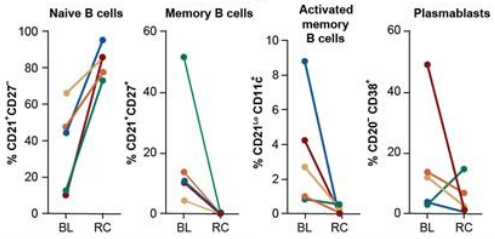
Müller F, et al. *N Engl J Med*. 2024;390(8):687-700.

Reconstitution With Naïve B Cells Within 7 Months[1]

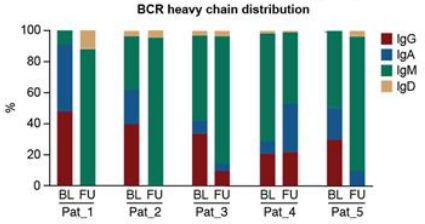


Circulating B cell numbers after CD19-CAR T treatment (N=15)[1]

Changes in B cell subtype numbers from baseline to B cell reconstitution (n=5)[2]



Distribution of heavy chain in the BCRs at baseline and after B cell reconstitution by mRNA sequencing (n=5)[2]

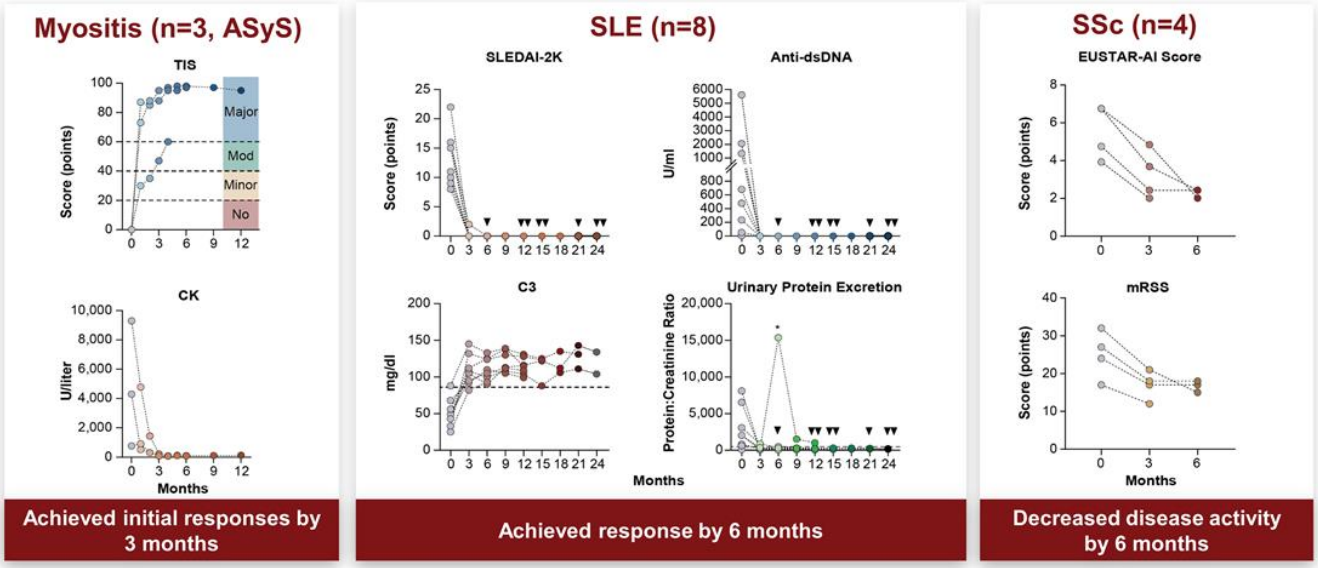


BL, baseline; FU, follow-up; Ig, immunoglobulin; IIM, idiopathic inflammatory myopathy; RC, reconstitution.

1. Müller F, et al. *N Engl J Med.* 2024;390(8):687-700. 2. Mackensen, Andreas A, et al. *Nature Medicine*. 2022;28(10):1-9.

Long-term Efficacy Outcomes With CD19-CAR T Cells

Patients maintained off immunosuppressive therapies, suggesting an ‘immune reset’ is possible



Achieved initial responses by 3 months	Achieved response by 6 months	Decreased disease activity by 6 months

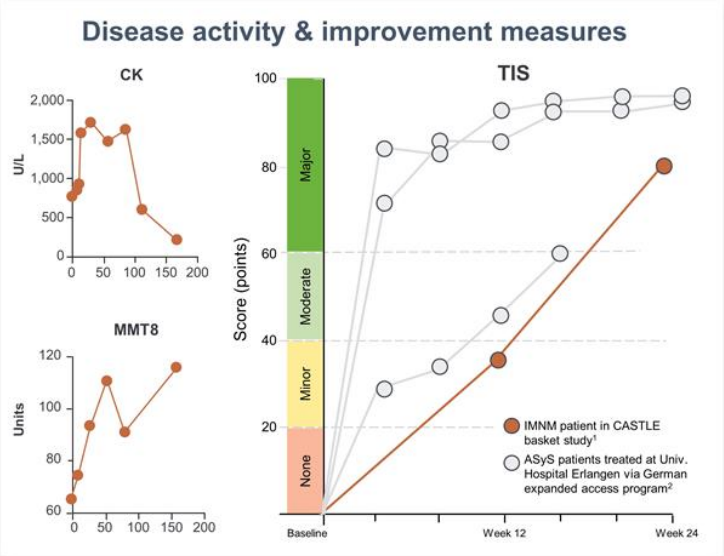
Figures adapted from Müller F, et al. 2024.
C3, complement component 3; EUSTAR-AI, European Scleroderma Trials and Research Group activity index; dsDNA, double stranded DNA; mRSS, modified Rodnan skin score; TIS, total improvement score.
Müller F, et al. *N Engl J Med*. 2024;390(8):687-700.

Initial HMGCR IMNM Patient Treated With CD19-CAR T[1]

Preliminary academic data suggests potential slower IMNM improvement due to muscle-predominant disease[1,2]

- 81-year-old woman with HMGCR IMNM
  - Myositis subtype involving primarily muscle
  - Manifestations may affect response kinetics
- Treated with CD19-CAR T in CASTLE study

Potential for disease-specific timing & magnitude of response to CD19-CAR T



1. Patient treated in CASTLE Phase I/II basket study. CK and MMT8 data as presented at the Global Conference on Myositis in March 2024 and TIS data at Week 12 and 24 provided via personal communication with Dr. Georg Schett. 2. Müller F, et al. *N Engl J Med.* 2024;390(8):687-700.

Safety & Tolerability of CD19-CAR T in Autoimmunity[1]

AE profile consisted primarily of fever in 4-1BB costimulatory domain-containing CD19-CAR T

Cytokine release syndrome

- **67%** (10 of 15 patients) with only grade 1 (**fever**)
- **1 patient with myositis with grade 2**
  - Preexisting ILD with increased oxygen requirement for 1 day while febrile
- 6 patients received tocilizumab

ICANS

- Possible **grade 1 ICANS in 1 ASyS patient**
  - Mild dizziness at 2w post-infusion
  - Resolved following oral steroids

Hypogammaglobulinemia

- **5 patients** developed hypogamm.[a]
- 2 patients required IVIg supplementation[b]
- **Vaccine titers remained stable**

Infection

- **1 hospitalization due to pneumonia**[c]
- All other infections were mild and mostly manifested as URTIs (including COVID)
- 2 events of herpes zoster reactivation

[a]2 patients (1 SLE, 1 myositis) had preexisting hypogammaglobulinemia due to previous rituximab exposure [b]1 patient had preexisting hypogammaglobulinemia. [c]Pneumonia occurred in an SLE patient 7 weeks after CAR T cell therapy.
ILD, interstitial lung disease; IVIG, intravenous immunoglobulin; URTI, upper respiratory tract infection.
1. Müller F, et al. *N Engl J Med.* 2024;390(8):687-700.

Key Takeaways

Academic Data Demonstrates Drug-free and Durable Responses in Patients With Myositis, SLE and SSc

- Case series provides preliminary support for the feasibility, efficacy and safety of a 4-1BB CD19-CAR T in patients with autoimmune disease[1,2]
  - Durable disease- and drug-free remission
  - Acute adverse events post-CAR T consisted primarily of fever
  - Repopulation with naïve B cells within 7 months
  - Most infections were mild in severity, with only one case of pneumonia requiring hospitalization

1. Müller F, et al. *N Engl J Med.* 2024;390(8):687-700. 2. Mackensen, Andreas A, et al. *Nat Med.* 2022;28(10):1-9.


Unlocking the Potential of CD19-CAR T Cell Therapy
in Myositis and Lupus
25

REstoring **SE**lf-**T**olerance (**RESET™**) Development Program

Designed to replicate and expand on the academic clinical data that generated interest in the field

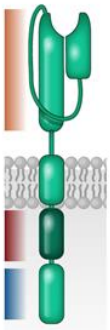
CABA-201 designed to optimize the potential safety and efficacy of CD19-CAR T for patients with autoimmune disease

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

Safety data in ~20 oncology patients evaluated and reported by IASO as part of a dual-CAR[3]

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

CD3-zeta signaling domain



CABA-201

Key Questions for RESET Phase 1/2 Studies

Safety of CABA-201
- CABA-201 AE profile
- *CRS, ICANS, SAEs*

Dose selection
1 x 10^6 cells/kg
- PK – CAR T persistence
- PD – B cell depletion
- Autoantibody reduction
- Clinical outcomes

PK, pharmacokinetics; PD, pharmacodynamics, SAEs: serious adverse events

1.Peng, BinghaoJ, et al. Presented at: American Society Gene and Cell Therapy 26th Annual Meeting; 2023 May 19; Los Angeles, CA. 2. Dai, Zhenyu, et al. *Journal of Cellular Physiology*. 2021;236(8): 5832-5847. 3. Evaluated as part of CT120, a dual-CD19xCD22 CAR T product candidate under development by Nanjing IASO Biotherapeutics, Co., Ltd. (IASO Bio).

Phase 1/2 Myositis Study for CABA-201[1]

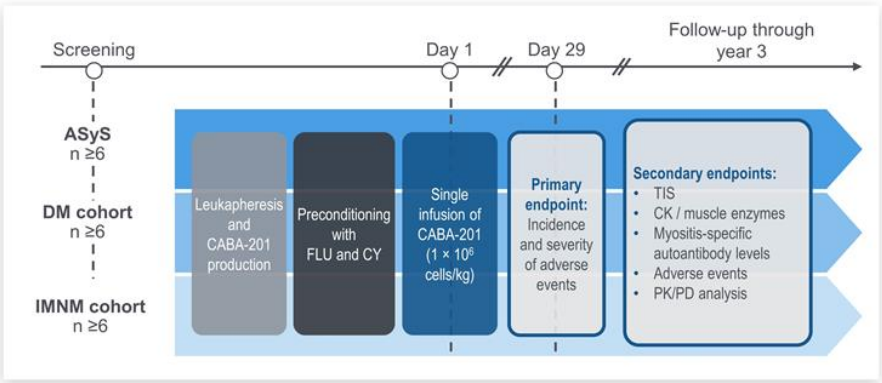
RESET Myositis™

Key inclusion criteria

- Age ≥18 and ≤75 with a definite or probable clinical diagnosis of IIM (2017 EULAR/ACR classification criteria)
- Diagnosis of antisynthetase syndrome (ASyS), dermatomyositis (DM), or immune-mediated necrotizing myopathy (IMNM) based on presence of serum myositis-specific antibodies
- Evidence of active disease despite prior or current treatment with standard of care

Key exclusion criteria

- Cancer-associated myositis
- Significant lung or cardiac impairment
- B cell-depleting agent within prior ~6 months
- Previous CAR T cell therapy and/or HSCT



Juvenile IIM cohort recently incorporated into trial

CY, cyclophosphamide; EULAR/ACR, European Alliance of Associations for Rheumatology/America College of Rheumatology; FLU, fludarabine; HSCT, hematopoietic stem cell transplantation. TIS, Total Improvement Score.

1. ClinicalTrials.gov. Accessed June 10, 2024. https://classic.clinicaltrials.gov/ct2/show/NCT06154252.

Phase 1/2 Lupus Study for CABA-201[1]

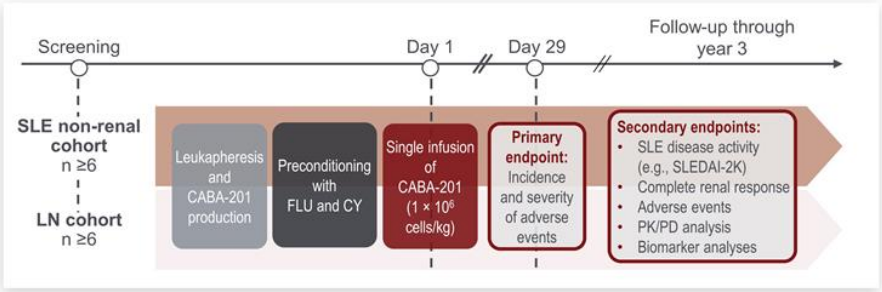
RESET SLE

Key inclusion criteria

- Age ≥18 to ≤65 with an SLE diagnosis (2019 EULAR/ACR classification criteria)
- ANA+ or anti-dsDNA+ at screening
- For SLE (non-renal) cohort: active, moderate to severe SLE, SLEDAI-2K ≥8 despite standard therapy
- For Lupus Nephritis cohort: active, biopsy-proven LN class III or IV, ± class V

Key exclusion criteria

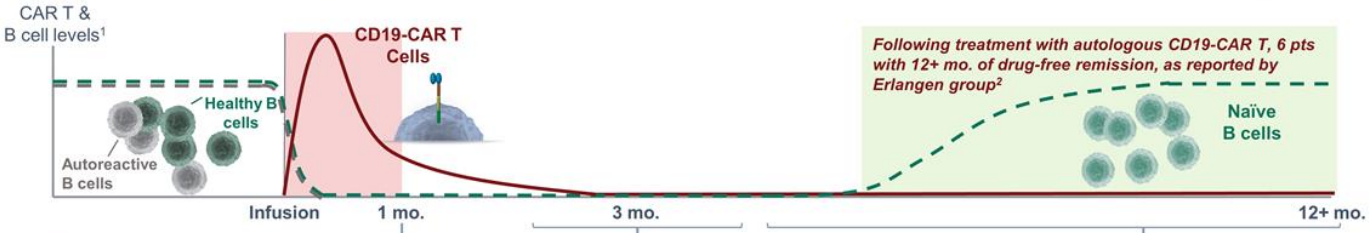
- B cell-depleting agent within prior ~6 months
- Previous CAR T cell therapy and/or HSCT
- Presence of kidney disease other than LN



ANA, antinuclear antibody; SELENA-2K, Systemic Lupus Erythematosus Disease Activity Index-2K.
1. ClinicalTrials.gov. Accessed June 10, 2024. https://classic.clinicaltrials.gov/ct2/show/NCT06121297.

Metrics To Assess Outcomes of B Cell Depletion In Autoimmunity

Translational & clinical parameters inform framework to evaluate advanced modalities in autoimmunity



Metrics of evaluation	Within 1 month	~3 months	Up to 12+ months
Translational measures	☑ B cell depletion: Timing & depth ☑ CAR T expansion: Magnitude & timing	☑ Autoantibody changes ☑ Vaccine titer changes ☑ Inflammatory marker changes	☑ Time to B cell repopulation ☑ B cell phenotype[a] ❑ Autoantibody changes
Clinical data	☑ Rate of CRS more severe than fever ☑ Rate & grade of ICANS ☑ Rate & severity of infection	☑ Early efficacy signals ☑ Rate & severity of infection	❑ Durability of clinical activity ❑ Rate & severity of infection
Patient experience	☑ Hospitalization requirements ☑ Apheresis & preconditioning ☑ Single vs. multiple infusions	☑ Chronic maintenance therapy / concomitant medications, if any	❑ Chronic maintenance / concomitant medications, if any

✓Indicates data being presented for either or both of the first two patients in the RESET™ clinical program.
[a]Flow phenotyping data; confirmatory analyses ongoing.
1. Illustrative graphic, adapted from Taubmann J, et al. OPO141. Abstract presented at: EULAR; May 31, 2023; Milan, Italy. 2. Müller F, et al. *N Engl J Med.* 2024;390(8):687-700.

IMNM: High Unmet Need & Limited Therapeutic Options[1]

Idiopathic inflammatory myopathy (IIM, myositis)

♀ > ♂

Immune-mediated necrotizing myopathy

Dermatomyositis

Antisynthetase syndrome

- IMNM-associated antibodies include anti-SRP & anti-HMGCR
- Muscle disease (weakness, elevated CK) predominant
- No therapies approved by the FDA or EMA for IMNM
- Often refractory despite combination therapy (e.g., IVIg, rituximab)

Myositis Prevalence: ~1 million globally[2]

HMGCR IMNM patient treated in CASTLE CD19-CAR T study with minor response by 3 months improved to major response at 6 months with no additional therapy[3]

Cohort for first patient treated with CABA-201

DM, dermatomyositis; EMA, European Medicines Agency; ESRD, end-stage renal disease; IMNM, immune-mediated necrotizing myopathy; HMGCR: HMG-CoA reductase

1. Suh J, et al. *Muscle Nerve*. Published online May 27, 2024. doi:10.1002/mus.28114. 2. Khoo T, et al. *Nat Rev Rheumatol.* 2023;19(11):695-712. 3. Patient treated in third-party CASTLE Phase I/II basket study.

SLE: Variable Disease Course & Limited Treatments[1-6]

Systemic lupus erythematosus (SLE)

- Highly heterogenous with potentially life-threatening complications
- Two biologic therapies approved with 52-week efficacy endpoint
- Incomplete responses & need for long-term therapy very common
- ~40% with LN, with Class V LN often resistant to therapy

Non-renal systemic lupus erythematosus

Lupus nephritis

♀ > ♂

Academic CD19-CAR T data in SLE patients with predominantly renal disease suggest potential for clinical response by 3 months[7]

SLE Prevalence: >3 million globally[1]

Cohort for first patient treated with CABA-201

LN, lupus nephritis.

1. Tian J, et al. *Ann Rheum Dis.* 2023;82(3):351-356. 2. Hoover PJ, Costenbader KH. *Kidney Int.* 2016;90(3):487-92. 3. Benlysta. Package insert. GSK; 2018. 4. Saphnelo. Package Insert. AstraZeneca. 2021. 5. Hahn BH, et al. *Arthritis Care Res (Hoboken).* 2012; 64(6): 797–808. 6. Aziz F, Chaudhary, K. *Curr Clin Pharmacol.* 2018;13(1):4-13. 7. Mackensen, Andreas A, et al. Nature Medicine. 2022;28(10):1-9.

IMNM #1 SLE #1

Baseline Characteristics of First Two Patients in RESET Trials

Both patients had refractory disease, including to B cell-targeting antibodies & other agents

	RESET-Myositis Patient #1	RESET-SLE Patient #1
Age (years), sex	33, male	26, male
Cohort	IMNM	Non-renal SLE
Disease duration	~2 years	~6 years
Prior disease-specific therapy	IVIG, rituximab, MTX, glucocorticoids	Cyclophosphamide, voclosporin, belimumab, tacrolimus
Disease-specific therapy at screening	MTX, glucocorticoids	MMF, hydroxychloroquine, glucocorticoids
Autoantibodies	SRP, Ro-52	ANA, dsDNA
Disease activity[a]	MMT-8: 130, CK: 617	SLEDAI-2K: 26
Disease manifestations[a,b]	Muscle weakness, dysphagia	Vasculitis, arthritis, alopecia, hematuria, proteinuria (isolated class V LN), low complement

Expanding CD19-CAR T experience in IMNM & non-renal SLE

[a]Baseline=pre-preconditioning visit. [b]Disease manifestations were according to Myositis Disease Activity Assessment Tool (MDAAT) and SLEDAI-2K for myositis and SLE, respectively.
dsDNA, double-stranded DNA; IMNM, immune-mediated necrotizing myopathy; MMF, mycophenolate mofetil; MMT-8, manual muscle testing of 8 muscles; MTX, methotrexate; Ro-52, ribonucleoprotein 52; SRP, signal recognition particle.

IMNM #1 SLE #1

CABA-201 was Well-tolerated in Initial Patients

No CRS, ICANS or infections reported through follow-up period[a]

		RESET-Myositis Patient #1	RESET-SLE Patient #1
Dose of CABA-201		83 million (1 x 10^6/kg) CAR$^+$ cells	63 million (1 x 10^6/kg) CAR$^+$ cells
Duration of inpatient monitoring[b]		4 days	4 days
Adverse events[d]	CRS	None	None
	ICANS	None	None
	Infections	None	None
	Hypogammaglobulinemia	None	None
	Serious adverse events	None	None
Concomitant disease-specific therapy		Discontinued MTX prior to infusion; Prednisone discontinued day 3 post-infusion	Discontinued MMF and HCQ prior to infusion; Ongoing taper from prednisone 10mg daily by 8 weeks[c]
Duration of follow-up[a]		84 days	28 days

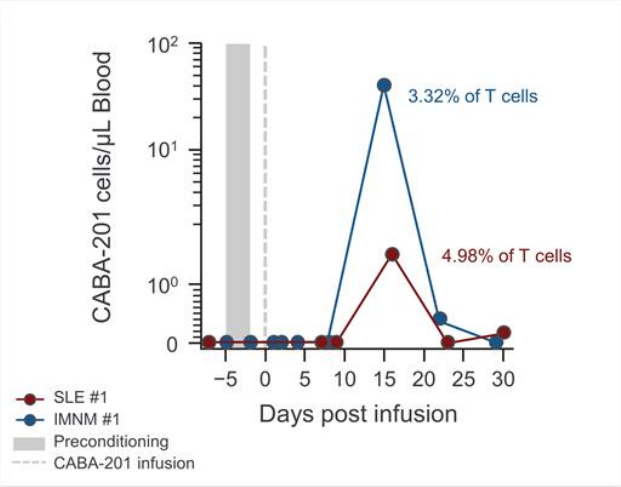
Both patients discharged after 4 days of monitoring post-infusion & neither received tocilizumab

[a]Data cut-off as of 28 May 2024. [b]Protocol requires a minimum of 4-day hospitalization for monitoring. [c]PI-directed taper from 10mg daily prednisone. [d]Grade 4 leukopenia, neutropenia and lymphopenia reported for SLE Patient #1, the Grade 4 cytopenias resolved and were attributed to the preconditioning regimen (fludarabine and cyclophosphamide).

IMNM #1 SLE #1

CABA-201 Expansion in Anticipated Range

CABA-201 exhibited anticipated profile of expansion and contraction[1-5]



- Expansion of CAR T cells to anticipated range suggests target engagement
- Peripheral peak CAR T expansion occurred at approximately 2 weeks[a]
- Rapid contraction suggests systemic B cell aplasia has been achieved

[a]Response appears to be consistent with published data of cryopreserved CAR T products as well as the expansion profile of BCMA-CAR T products in patients with multiple myeloma, in which the number of target cells is more similar to autoimmune disease than to B cell leukemias and lymphomas

BCMA, B cell maturation antigen.

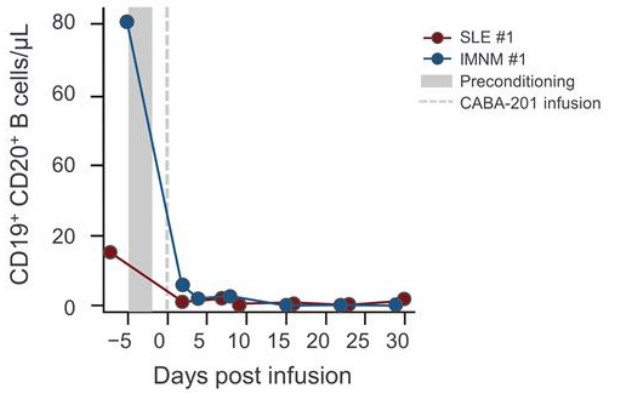
1. Shah BD, et al. *Lancet.* 2021;398(10299):491-502. 2. Awasthi R, et al. *Blood Adv.* 2020;4(3):560-572. 3. Munshi NC, et al. *N Engl J Med.* 2021;384(8):705-716. 4. Cohen AD, et al. *Blood Cancer J.* 2022;12(2):32. 5. Müller F, et al. *N Engl J Med.* 2024;390(8):687-700.

IMNM #1 SLE #1

Systemic B Cell Depletion With CABA-201

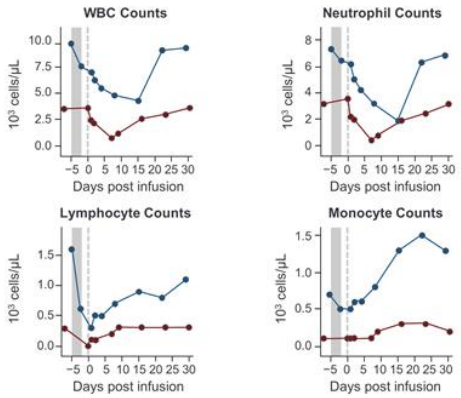
Complete B cell depletion achieved by day 15 on flow cytometry & maintained in context of WBC recovery

$CD19^+$ $CD20^+$ B cell count



B cell depletion was achieved & maintained in follow up or until naïve B cell recovery

Leukocyte counts

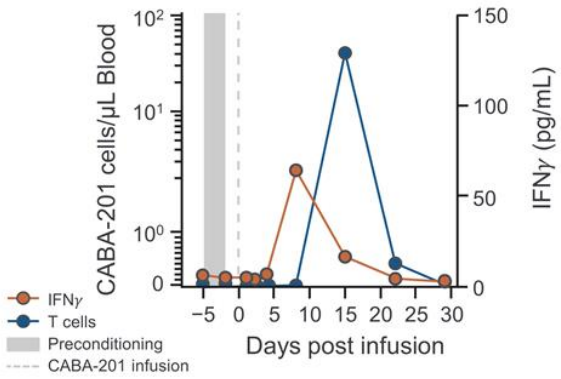


Early, transient leukopenia observed in both patients, as expected with preconditioning[a]

[a]Nadir of lymphocyte count following fludarabine and cyclophosphamide administration estimated based on respective product labels.[1,2]
WBC, white blood cell.
1. Fludarabine phosphate injection. Prescribing information. 2010. https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/022137s003lbl.pdf. 2.Cyclophosphamide. Prescribing information. 2013. https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/012141s090,012142s112lbl.pdf.

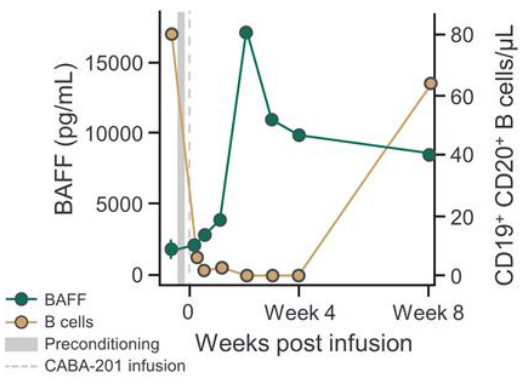
Immunologic Effects of CABA-201

CABA-201 pharmacokinetics



IFNγ peak prior to peripheral CABA-201 peak suggests tissue-resident B cell cytotoxicity

CABA-201 pharmacodynamics



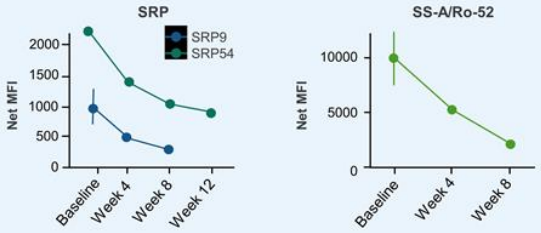
Systemic B cell depletion triggers BAFF to encourage bone marrow B cell repopulation

CK Reduction & Clinical Improvement Observed in SRP IMNM

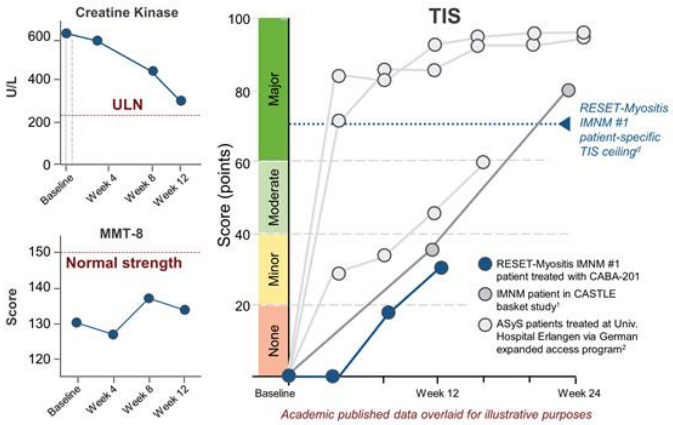
Antibody reduction & clinical improvement in disease activity as anticipated with follow-up of 12 weeks

- Discontinued all disease-specific therapies
- Disease markers continuing to trend positively
- Patient reported symptoms as much improved

Quantitative translational assay shows ongoing reduction in SRP & Ro-52 antibodies[b,c]



Disease activity & improvement measures



12-week TIS consistent with IMNM case report[1]

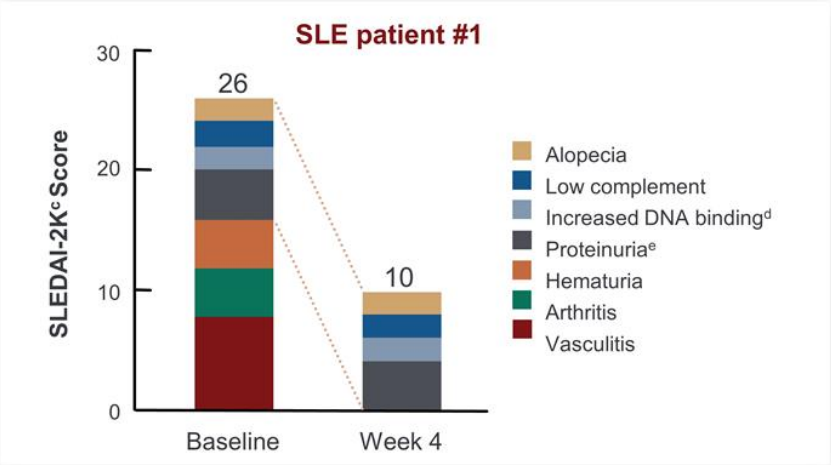
[a]Data cut-off as of 28 May 2024. [b]Luminex assay developed and performed by Cabaletta Labs. [c]Qualitative commercial assay (Myositis Antigen Panel, performed at National Jewish Health Advanced Diagnostic Laboratories) suggests SRP54 antibody remains strongly positive at Week 12; Ro-52 normalizes by week 8. [d]Based on patient's moderate level of muscle disease at baseline, mild-moderate disability and limited extramuscular manifestations, the maximum achievable score is 70 points on the 100-point TIS scale.

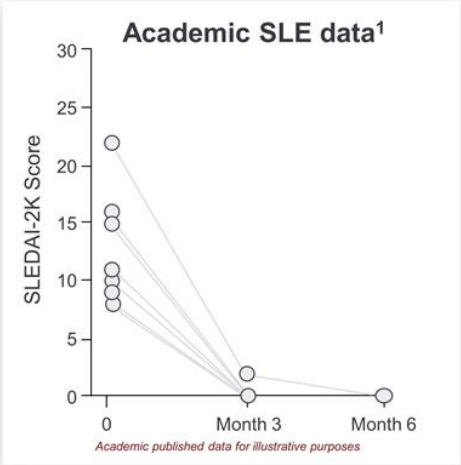
1. Patient treated in third-party CASTLE Phase I/II basket study, TIS data at Week 12 and 24 provided via personal communication with and as presented by Dr. Georg Schett. 2. Müller F, et al. *N Engl J Med*. 2024;390(8):687-700.

SRP9, signal recognition particle 9; SSA, Sjögren's syndrome–related antigen A autoantibody; TRIM21, tripartite motif 21; ULN, upper limit of normal; CK, creatine kinase.

Early Efficacy Signals in Non-Renal SLE[a]

Trend toward improvement in disease manifestations with follow up of 4 weeks[b]



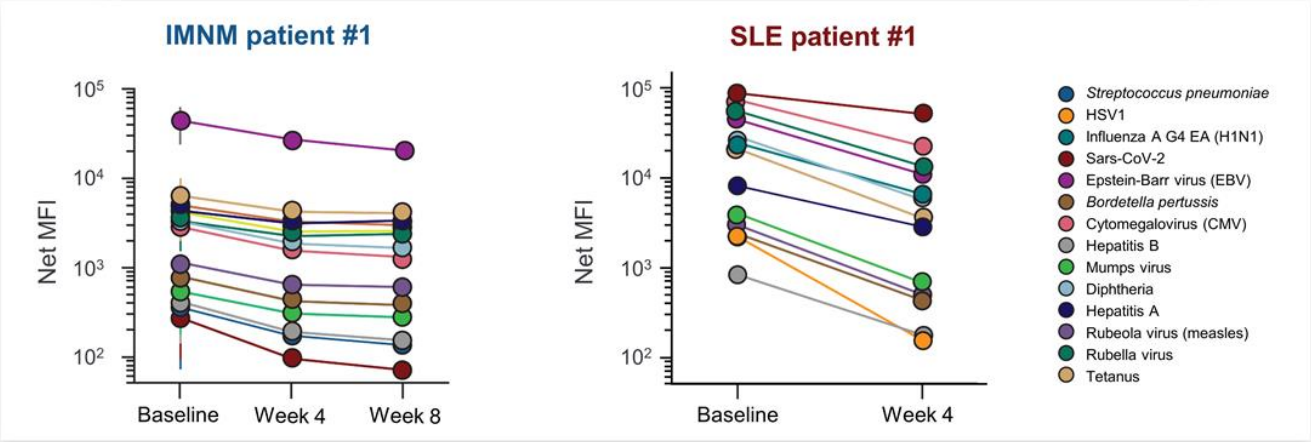


Vasculitis, arthritis and hematuria resolved within 4 weeks despite discontinuation of all therapies at infusion other than ongoing taper from prednisone 10mg per day

[a]Patient in non-renal SLE cohort due to isolated Class V LN. [b]Data cut-off as of 28 May 2024. [c]Baseline and Day 29 SLEDAI-2K score are reflective of disease activity at study visit day. [d]Urine Protein Creatinine Ratio decreased from 1.08 to 0.80 from Baseline to Week 4. [e]Anti-dsDNA antibody titer decreased from 1:40 to 1:10 from Baseline to Week 4.

1. SLE patients treated at Univ. Hospital Erlangen via German expanded access program; Müller F, et al. *N Engl J Med.* 2024;390(8):687-700.

CABA-201 Effects on Vaccine & Infection Antibody Titers

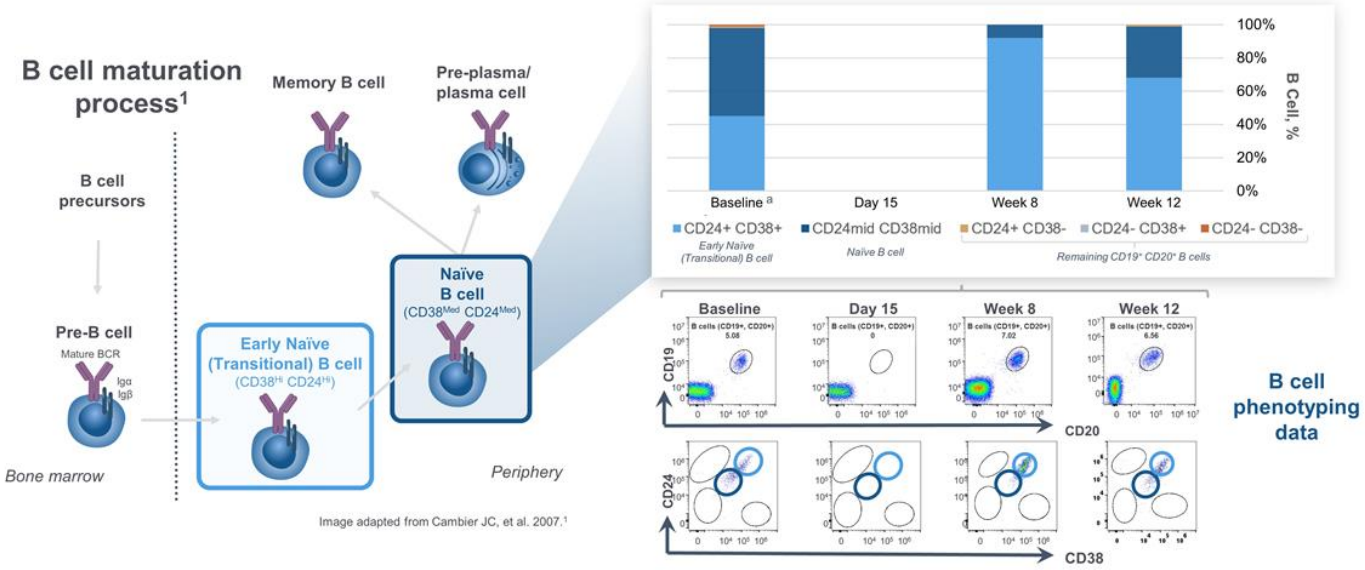


Titers preserved post-infusion, with no reported infections in the duration of follow-up period[a]

[a]Data cut-off as of 28 May 2024.

B Cell Repopulation with Naïve B Cells

Initial patient phenotyping data consistent with potential immune system reset; confirmatory analyses ongoing



Note: Flow plot gating reflects CD19+ CD20+ live lymphocytes. [a]Patient received multiple courses of rituximab, with most recent dose approximately 9 months prior to CABA-201 infusion.
BCR, B cell receptor.

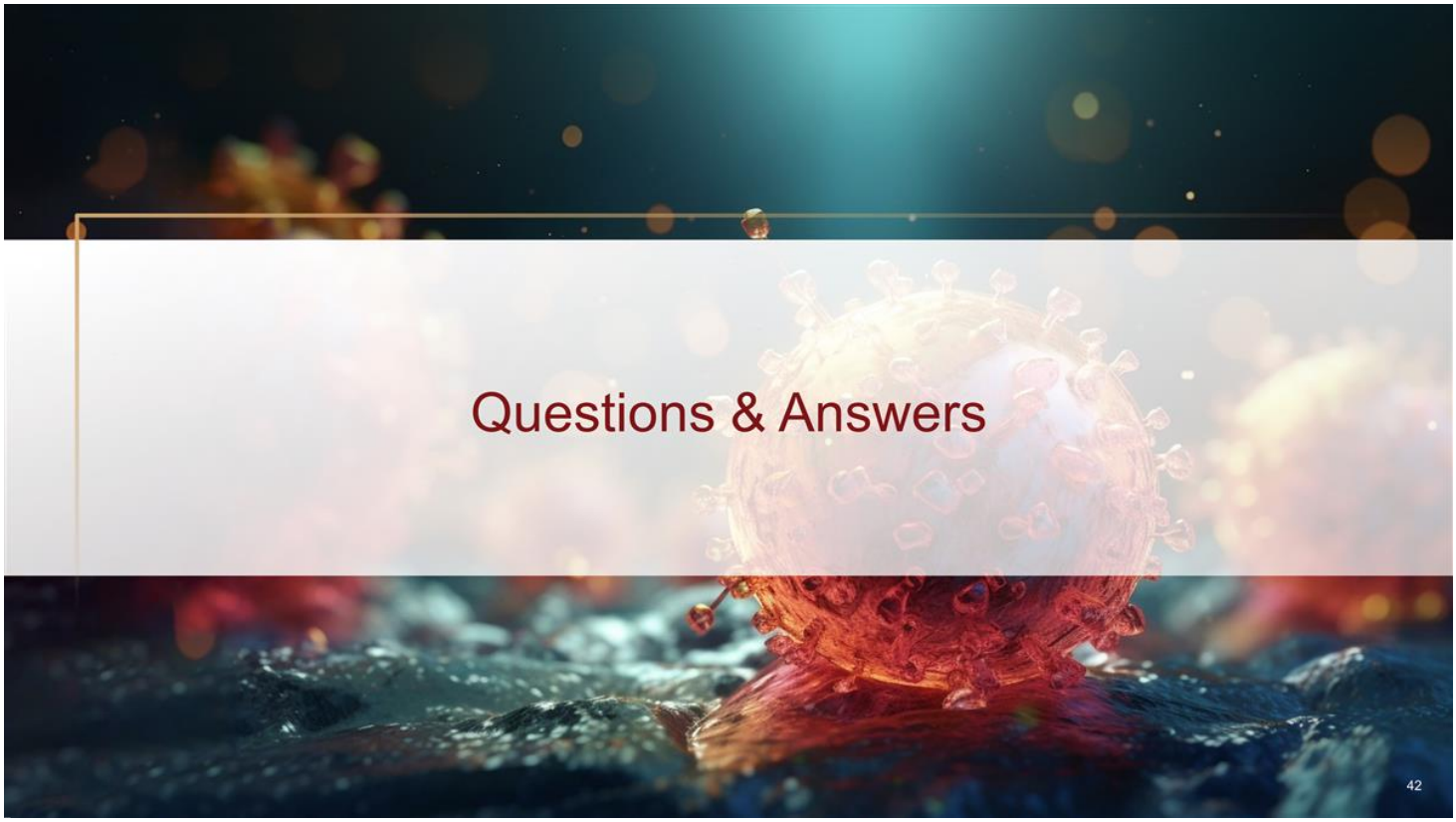
1. Cambier JC, et al. *Nat Rev Immunol.* 2007;7(8):633-643.

Key Takeaways

- **CABA-201**: Designed for autoimmune patients to optimize the potential product profile of CD19-CAR T
- **Safety**: In the first 2 patients (IMNM & SLE), CABA-201 was well-tolerated
  - No CRS, ICANS or infections reported through follow-up period
- **Dose**: Clinical & translational data support the selected dose of CABA-201
  - PK: IFNγ peak prior to peak of CABA-201 suggests tissue-level B cell cytotoxicity
  - PD: Systemic B cell depletion followed by repopulation with naïve B cells
  - Autoantibody levels: Decline generally consistent with Univ. Hospital Erlangen data[1]
  - Clinical & translational data: Improvement consistent with reported CD19-CAR T data[1,2]

18 clinical sites now enrolling patients in the CABA-201 RESET™ program with four trials open – myositis, SLE/LN, systemic sclerosis and myasthenia gravis

1. Müller F, et al. *N Engl J Med.* 2024;390(8):687-700. 2. Castle Phase 1/2 basket study.


Questions & Answers
42

You are invited to stop by at Booth S18-19 for additional engagement with Cabaletta Bio!

Please use the EULAR app to complete an evaluation form

To learn more, please visit **CabalettaBio.com** &
contact us at **clinicaltrials@cabalettabio.com**