UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of The Securities Exchange Act of 1934

November 10, 2022
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 2.02 Results of Operations and Financial Condition.

On November 10, 2022, Cabaletta Bio, Inc. (the "Company") announced its financial results for the third quarter ended September 30, 2022. A copy of the press release is being furnished as Exhibit 99.1 to this Report on Form 8-K.

Item 7.01 Regulation FD Disclosure.

On November 10, 2022, the Company posted to the "Investors & Media" section of the Company's website at*www.cabalettabio.com* an updated corporate presentation providing a corporate overview and updated development plan (the "Corporate Presentation"). A copy of the Corporate Presentation is attached hereto as Exhibit 99.2 and is incorporated by reference into this Item 7.01 of this Current Report on Form 8-K.

The information contained in Items 2.02 and 7.01 of this Current Report on Form8-K is being furnished and shall not be deemed to be "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section and shall not be incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

99.1	Press Release issued by the registrant on November 10, 2022, furnished herewith.
99.2	Cabaletta Bio, Inc. Corporate Presentation, dated November 10, 2022, 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: November 10, 2022

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

Cabaletta Bio®

Cabaletta Bio Reports Third Quarter 2022 Financial Results and Provides Business Update

PHILADELPHIA, Nov. 10, 2022 – Cabaletta Bio, Inc. (Nasdaq: CABA), a clinical-stage biotechnology company focused on developing and launching the first curative targeted cell therapies for patients with autoimmune diseases, today reported financial results for the third quarter ended September 30, 2022, and provided a business update.

"Our recently announced product candidate, CABA-201, a proprietary, fully human CD19-chimeric antigen receptor (CAR) T construct containing a 4-1BB co-stimulatory domain, was purposefully designed to be similar to the4-1BB containing CD19-CAR T construct employed in the recent *Nature Medicine* publication, which demonstrated profound clinical and serologic responses with a generally favorable clinical tolerability profile in five of five systemic lupus erythematosus patients with a single administration. Based on our deep experience with discovery, development and regulatory interactions for CAAR T products in patients with autoimmune diseases, we believe we can efficiently and effectively evaluate CABA-201's potential across a broad range of autoimmune diseases. We are planning to submit an IND application to the FDA in the first half of 2023, and expect initial clinical data, subject to IND clearance by the FDA, by the first half of 2024," said Steven Nichtberger, M.D., Chief Executive Officer and Co-founder of Cabaletta. "We also continue to progress our CAART product candidate portfolio, including prioritizing the enrollment of the combination sub-study in the DesCAARTes™ trial for DSG3-CAART, with 1-month safety and persistence data expected in the first quarter of 2023, and continuing preparations to initiate the MusCAARTes™ trial for MuSK-CAART in the fourth quarter of 2022."

Third Quarter 2022 and Recent Operational Highlights and Upcoming Milestones

Chimeric Antigen Receptor T cells for Autoimmunity (CARTA) Platform

CABA-201: Autologous, engineered T cells with a chimeric antigen receptor containing a fully human CD19 binder and a4-1BB co-stimulatory domain as a potential treatment for a broad range of autoimmune diseases in indications such as systemic lupus erythematosus (SLE), rheumatoid arthritis, myositis and systemic sclerosis, among others where B cells contribute to disease pathogenesis.

- **Obtained exclusive, worldwide license from Nanjing IASO Biotherapeutics, Co., Ltd. (IASO Bio) for binder to be used in new product candidate CABA-201:** In October 2022, Cabaletta obtained the CD19 binder for its new product candidate,CABA-201, through an exclusive, worldwide license with IASO Bio. This CD19 binder is separately being used as part of a dual targeting CAR T therapy that has been evaluated in approximately 20 cancer patients to date in an investigator-initiated trial. Tolerability data generated in these patients support further clinical development in patients with autoimmune diseases.

- **Established an exclusive translational research partnership with Georg Schett, M.D.:** In October 2022, Cabaletta signed an exclusive translational research partnership with Dr. Georg Schett, a pioneer and global leader in the application of CD19-targeting cell therapies in autoimmunity and senior author of the September 2022 *Nature Medicine* publication demonstrating the potential forCD19-CAR T therapy to reset the immune system in five of five patients with refractory SLE. The Company's collaboration is focused on generating additional translational data to gain a deeper understanding of the immunologic mechanisms of response and clinical insights from ongoing and continued clinical studies in multiple autoimmune disease indications. The clinical development of CABA-201 will be informed by this exclusive translational research partnership.
- **Investigational New Drug (IND) application submission planned for 1H 2023:** The Company anticipates submitting an IND to the FDA for CABA-201 in the first half of 2023. Subject to FDA clearance of the IND, the Company expects to report initial clinical data by the first half of 2024.

Chimeric AutoAntibody Receptor T (CAART) Cells Platform

DSG3-CAART: Desmoglein 3 chimeric autoantibody receptor T (DSG3-CAART) cells as a potential treatment for patients with mucosal pemphigus vulgaris (mPV).

- **Presented new interim data from the DesCAARTes™ Phase 1 Trial at the 31st European Academy of Dermatology and Venereology (EADV) Congress and the 29th Annual European Society of Gene & Cell Therapy Congress:** In September 2022 and October 2022, Cabaletta presented updated data supporting a favorable safety profile of DSG3-CAART with no dose-limiting toxicities, and one grade 1 cytokine release syndrome, through cohort A5, which provided a rationale to prioritize the enrollment of the cohort in the combination sub-study (2.5 billion cells in addition to patient pre-treatment with intravenous immunoglobulin [IVIg] and cyclophosphamide), with the goal to address possible cytokine and autoantibody effects on CAART activity. The Company anticipates 1-month safety and persistence data for the combination cohort in the first quarter of 2023.

MuSK-CAART: Muscle-specific kinase (MuSK) chimeric autoantibody receptor T (MuSK-CAART) cells as a potential treatment for patients with MuSK-associated myasthenia gravis.

- **Granted Orphan Drug Designation (ODD) by FDA:** In October 2022, the FDA granted ODD to MuSK-CAART for the treatment of muscle-specific tyrosine kinase myasthenia gravis. The FDA grants ODD to drugs or biologics intended to treat or prevent rare diseases or conditions that affect fewer than 200,000 individuals in the United States. This designation qualifies Cabaletta for certain incentives, which may include partial tax credit for clinical trial expenditures, waived user fees and potential eligibility for seven years of marketing exclusivity.
- **First-in-human trial to initiate in the fourth quarter of 2022:** Cabaletta remains on track to initiate the MusCAARTes™ trial for MuSK-CAART in the fourth quarter of 2022. The trial will be an open-label study consisting of two parts: (i) an accelerated dose escalation phase with a "2+4" dosing scheme designed to determine the maximum tolerated dose, with four additional patients added at the highest selected dose and (ii) a cohort expansion phase at the final selected dose. The trial will incorporate insights and enhancements supported by data from the DesCAARTes™ trial, including the ability to start at a higher initial dose and an earlier initiation of the combination cohort, where patients are planned to be pre-treated with cyclophosphamide. The trial is expected to enroll patients across multiple clinical sites throughout the United States and Canada. Based on current clinical expectations, the Company expects 6-month data for the combination cohort of the MusCAARTes™ trial for MuSK-CAART in the first half of 2024.

Upcoming Events

Cabaletta will participate in the upcoming 5th Annual Evercore ISI HealthCONx Conference, which is being held virtually from November 29 – December 1, 2022.

Third Quarter 2022 Financial Results

- Research and development expenses were $8.2 million for the three months ended September 30, 2022, compared to $8.2 million for the same period in 2021.
- General and administrative expenses were $3.6 million for the three months ended September 30, 2022, compared to $3.4 million for the same period in 2021.
- As of September 30, 2022, Cabaletta had cash, cash equivalents and investments of $85.9 million, compared to $122.2 million as of December 31, 2021.

The Company expects that its cash, cash equivalents and investments as of September 30, 2022, will enable it to fund its operating plan through the second quarter of 2024.

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 – encompassing chimeric antigen receptor T cells for autoimmunity (CARTA: CABA-201, a 4-1BB-containing CD19-CAR T) and Cabaletta Bio's proprietary chimeric autoantibody receptor T cells (CAART: multiple candidates including DSG3-CAART for mucosal pemphigus vulgaris, MuSK-CAART for MuSK myasthenia gravis) – provides multiple opportunities to treat broad and challenging autoimmune diseases. Cabaletta Bio's headquarters are located in Philadelphia, PA. For more information, visit www.cabalettabio.com and follow us on LinkedIn.

Forward-Looking Statements

This press release contains "forward-looking statements" of Cabaletta Bio within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including without limitation, express or implied statements regarding expectations regarding: Cabaletta's ability to grow its autoimmune-focused pipeline; the ability to capitalize on and potential benefits resulting from the translational research partnership with Professor Georg Schett and the exclusive license agreement with IASO Bio; the company's business plans and objectives; the timing of our planned submission of an IND application for CABA-201 to the FDA and generation of initial clinical data forCABA-201; statements regarding regulatory filings for its development programs, including the planned timing of such regulatory filings and potential review by such regulatory authorities; the expectation that Cabaletta Bio may improve outcomes for patients suffering from mPV, MG, or other autoimmune diseases; the progress and results of its DesCAARTes™ Phase 1 trial, including Cabaletta's ability to enroll the requisite number of patients, dose each dosing cohort in the intended manner, and progress the trial; plans to initiate patient dosing in an open-label Phase 1 clinical trial to evaluate MuSK-CAART safety and tolerability in MuSK MG patients in 2022; the ability to retain and recognize the intended incentives conferred by Orphan Drug Designation for MuSK-CAART for the treatment of muscle-specific tyrosine kinase myasthenia gravis; the ability to accelerate Cabaletta's pipeline and develop meaningful therapies for patients, including in collaboration with academic and industry partners and the ability to optimize such collaborations on its development programs; use of capital, expenses, future accumulated deficit and other financial results in the future; ability to fund operations through the second quarter of 2024; and the anticipated contribution of the members of Cabaletta's executives to the company's operations and progress.

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: 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 DSG3-CAART, MuSK-CAART and CABA-201; the risk that the results observed with the similarly-designed construct employed in the recent*Nature Medicine* publication are not indicative of the results we seek to achieve withCABA-201; risks related to clinical trial site activation or enrollment rates that are lower than expected; risks related to unexpected safety or efficacy data observed during clinical studies; risks related to volatile market and economic conditions; risks related to the impact of public health epidemics affecting countries or regions in which Cabaletta has operations or does business, such as COVID-19; Cabaletta's ability to retain and recognize the intended incentives conferred by Orphan Drug Designation and Fast Track Designation 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; 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.

CABALETTA BIO, INC.
SELECTED FINANCIAL DATA
(unaudited; in thousands, except share and per share data)

Statements of Operations

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
	unaudited		unaudited	
Operating expenses:				
Research and development	$ 8,216	$ 8,169	$ 26,900	$ 22,575
General and administrative	3,562	3,394	10,937	9,845
Total operating expenses	11,778	11,563	37,837	32,420
Loss from operations	(11,778)	(11,563)	(37,837)	(32,420)
Other income:				
Interest income	351	3	554	19
Net loss	(11,427)	(11,560)	(37,283)	(32,401)
Net loss per share of voting and non-voting common stock, basic and diluted	$ (0.39)	$ (0.45)	$ (1.29)	$ (1.31)

Selected Balance Sheet Data

	September 30, 2022	December 31, 2021
	(unaudited)	
Cash, cash equivalents and investments	$ 85,895	$ 122,222
Total assets	91,675	126,336
Total liabilities	5,801	8,380
Total stockholders' equity	85,874	117,956

Contacts:

Anup Marda
Chief Financial Officer
investors@cabalettabio.com

Sarah McCabe
Stern Investor Relations, Inc.
212-362-1200
sarah.mccabe@sternir.com

Exhibit 99.2

Cabaletta Bio®

Corporate Presentation

NOVEMBER 2022

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 and CABA™ platform; Cabaletta's ability to grow its autoimmune-focused pipeline; the ability to capitalize on and potential benefits resulting from the translational research partnership with Professor Georg Schett and the exclusive license agreement with IASO Bio; the timing of our planned submission of an investigational new drug application (IND) for CABA-201 to the FDA; statements regarding regulatory filings regarding its development programs; the progress and results of our DesCAARTes™ Phase 1 trial, including the significance and impact around the clinical and translational data updates from cohorts A1 through A4 of our DesCAARTes™ Phase 1 trial; the significance and impact around the 28-day safety for cohort A5 and clinical and translational data for cohort A4 announced at the 31st European Association of Dermatology and Venereology Congress; the therapeutic potential and clinical benefits of our product candidates; the expectation that Cabaletta Bio may improve outcomes for patients suffering from mucosal pemphigus vulgaris, myasthenia gravis, or other autoimmune diseases; our ability to escalate dosing as high as 10 to 15 billion cells in cohort A6m, initiate dosing in a combination cohort or otherwise; Cabaletta's plans to implement a pre-treatment regimen and the potential ability to enhance *in vivo* DSG3-CAART exposure; our ability to advance dose escalation in the DesCAARTes™ Phase 1 trial at the current dose ranges for the current cohorts and any projected potential dose ranges for future cohorts, and to optimize our targeted cell therapy; our ability to evaluate, and the potential significance of, the relationship between DSG3-CAART persistence and potential clinical responses in patients with mPV; our ability to safely retreat additional patients and whether we will continue to observe a lack of immune-mediated clearance of DSG3-CAART cells after retreatment and repeat dosing of patients; our ability to successfully complete our preclinical and clinical studies for our product candidates, including CABA-201, our ongoing Phase 1 DesCAARTes™ trial, and our planned clinical trial of MuSK-CAART, including our ability to enroll the requisite number of patients, dose each dosing cohort in the intended manner, and progress the trial; the ability of MuSK-CAART to target B cells that differentiate into antibody secreting cells, which produce autoantibodies against muscle-specific kinase; 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 Designation for DSG3-CAART for the treatment of pemphigus vulgaris and Orphan Drug Designation and Fast Track Designation for MuSK-CAART to improve activities of daily living and muscle strength in patients with MuSK antibody-positive myasthenia gravis; the further expansion and development of our modular CABA™ platform across a range of autoimmune diseases; our ability to contract with third-party suppliers and manufacturers, 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; our expectations regarding our use of capital and other financial results; and our ability to fund operations through the second quarter of 2024. 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 employed in the recent *Nature Medicine* publication are not indicative of the results we seek to achieve with CABA-201, Cabaletta's 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 CART-19 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 relationship 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 Designation and Fast Track Designations, 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, the impact of COVID-19 on the timing, progress, interpretability of data, and results of ongoing or planned clinical trials and risks relating to as a result of extraordinary events or circumstances such as the COVID-19 pandemic, and any business interruptions to our operations or to those of our clinical sites, manufacturers, suppliers, or other vendors resulting from the COVID-19 pandemic or similar public health crisis. 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 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.

Cabaletta Bio®

Cabaletta®: Pursuing cures for a broad range of autoimmune diseases

Leveraging years of clinical experience with cell therapy for autoimmune diseases to evaluate two strategies

CARTA: CABA-201 (4-1BB CD19-CAR T) on track for 1H23 IND submission

- Builds on recent academic clinical data[1] demonstrating that CD19-CAR T may potentially reset the immune system in patients with SLE
  - Exclusive translational research partnership with lead investigator on the academic study[1] is informing CABA-201 clinical development
- Exclusive global license for clinically-evaluated, fully human CD19 binder with favorable clinical tolerability profile in ~20 oncology patients
  - Similar construct design to CD19-CAR T used in the academic SLE study, including 4-1BB costimulatory domain[1,2]
- Potential to cure many common autoimmune diseases such as SLE, RA, myositis and systemic sclerosis[3]

CAART: Advancing clinical studies to increase CAART activity & explore additional indications

- DesCAARTes™ trial in mPV ongoing: Enrolling combination sub-study (pre-treatment with IVIg & cyclophosphamide)
  - 1 month safety and persistence data anticipated in 1Q23[4]
- MusCAARTes™ trial in MuSK myasthenia gravis: On track to initiate in 4Q22; received FDA Fast Track Designation
  - Higher starting cell dose and early implementation of combination strategy as early as the fifth subject treated in the trial

Cash runway through 2Q24 with $85.9M at the end of 3Q22

- Initial CABA-201 clinical data[5] as well as 6-month combination data from DesCAARTes™ & MusCAARTes™ trials expected by 1H24[4]

CAART – Chimeric AutoAntibody Receptor T cells; CARTA – Chimeric Antigen Receptor T cells for Autoimmunity; IND – Investigational New Drug; SLE – Systemic lupus erythematosus; RA – Rheumatoid arthritis; mPV – Mucosal pemphigus vulgaris

1. Mackensen, Andreas, et al. "Anti-CD19 CAR T cell therapy for refractory systemic lupus erythematosus." Nature Medicine (2022): 1-9.
2. Dai, Zhenyu, et al. "Development and functional characterization of novel fully human anti-CD19 CARs for T-cell therapy." Journal of Cellular Physiology 236.8 (2021): 5832-5847.
3. Mullin, Emily. "How a 'Living Drug' Could Treat Autoimmune Disease." WIRED, 16 Sept 2022.
4. Assumes no dose-limiting toxicities are observed in the cohort, uninterrupted enrollment and no delays due to COVID-19 resurgence occur in the trial.
5. Subject to clearance of CABA-201 IND by the FDA.

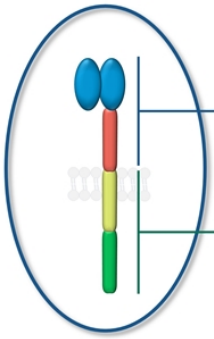
One CABA™ platform, two strategies to address autoimmune diseases

Complementary strategies to optimize clinical outcomes using cellular therapies in autoimmune diseases

CARTA

Chimeric **A**ntigen **R**eceptor **T** cells for **A**utoimmunity

*Potential to '**reset the immune system**' in patients with **autoimmune diseases driven by B cells**, through **generalized transient B cell depletion** and **repopulation of healthy B cells**[1]*



Fully Human Anti-CD19 Targeting Domain

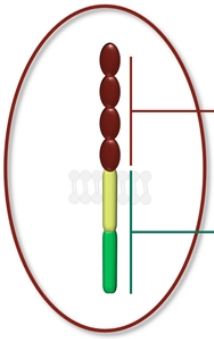
4-1BB Costimulatory Domain & CD3-Zeta Signaling Domain

CABA-201

CAART

Chimeric **A**uto**A**ntibody **R**eceptor **T** cells

*In autoimmune diseases with a **limited number of well-defined pathogenic autoantibodies**, permanent **antigen-specific B cell depletion** may provide an **elegant biologic solution** to disease*[2]



Autoantigen Targeting Domain

4-1BB Costimulatory Domain & CD3-Zeta Signaling Domain

DSG3-CAART

1. Mackensen, Andreas, et al. "Anti-CD19 CAR T cell therapy for refractory systemic lupus erythematosus." *Nature Medicine* (2022): 1-9.
2. Ellebrecht, Christoph T., et al. "Reengineering chimeric antigen receptor T cells for targeted therapy of autoimmune disease." *Science* 353.6295 (2016): 179-184.

CABA™ platform may apply across a range of autoimmune diseases

Biologic opportunity for cure or treatment may be possible in dozens of B-cell mediated autoimmune diseases*

Neurology
- **Myasthenia Gravis[1,2,3,5]**
- Multiple Sclerosis[6]
- Neuromyelitis Optica[3]
- Chronic Inflammatory Demyelinating Polyneuropathy[1,2]
- Anti-NMDAR Encephalitis[3,6]
- Lambert-Eaton Syndrome[5]

Rheumatology
- **Systemic Lupus Erythematosus[3,4,5,6]**
- Rheumatoid Arthritis[2,3,4]
- **Myositis[5]**
- **Systemic sclerosis[6]**
- ANCA-Associated Vasculitis[3,4,5]

Dermatology
- **Pemphigus Vulgaris[1,2,3]**
- Pemphigus Foliaceus[1,2,3]
- Epidermolysis Bullosa Acquisita[3]
- Bullous Pemphigoid[1,2,3]

Hematology
- Immune Thrombocytopenic Purpura[3]
- Thrombotic Thrombocytopenic Purpura[1,2,3]
- Antiphospholipid Syndrome[4,5]
- Autoimmune Hemolytic Anemia[3]

Nephrology
- **Lupus Nephritis[3,4]**
- Membranous Nephropathy[1,2,3]
- Goodpasture's Syndrome[1,2,3,4]

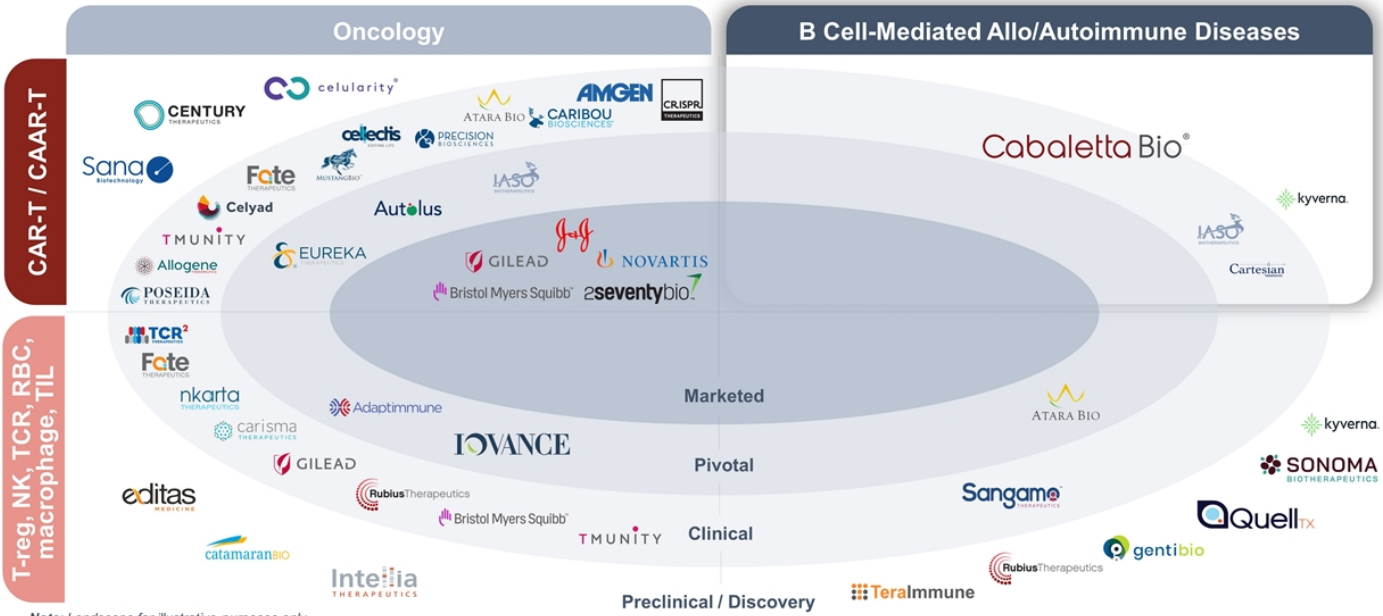
Endocrinology
- Type 1 Diabetes[3,6]
- Graves' Disease[3,5]
- Hashimoto's Disease[5]

- *Illustrative list of diseases where biologic opportunity for cure or treatment with CAART or CARTA approach may be possible.*
- *Diseases **in bold** represent where clinical studies are underway or plan to be initiated by Cabaletta or by Professor Schett*

1. Koneczny, Inga. "Update on IgG4-mediated autoimmune diseases: new insights and new family members." Autoimmunity Reviews (2020): 102646.
2. Huijbers, Maartje G., et al. "IgG4-mediated autoimmune diseases: a niche of antibody-mediated disorders." Annals of the New York Academy of Sciences 1413.1 (2018): 92.
3. Ludwig, Ralf J., et al. "Mechanisms of autoantibody-induced pathology." Frontiers in immunology 8 (2017): 603.
4. Suurmond, Jolien, and Betty Diamond. "Autoantibodies in systemic autoimmune diseases: specificity and pathogenicity." The Journal of clinical investigation 125.6 (2015): 2194-2202.
5. Xiao, Ze Xiu, Joseph S. Miller, and Song Guo Zheng. "An updated advance of autoantibodies in autoimmune diseases." Autoimmunity Reviews (2020): 102743.
6. Hampe, Christiane S. "B cells in autoimmune diseases." Scientifica 2012 (2012).

Cabaletta: Advancing targeted cell therapy to autoimmunity

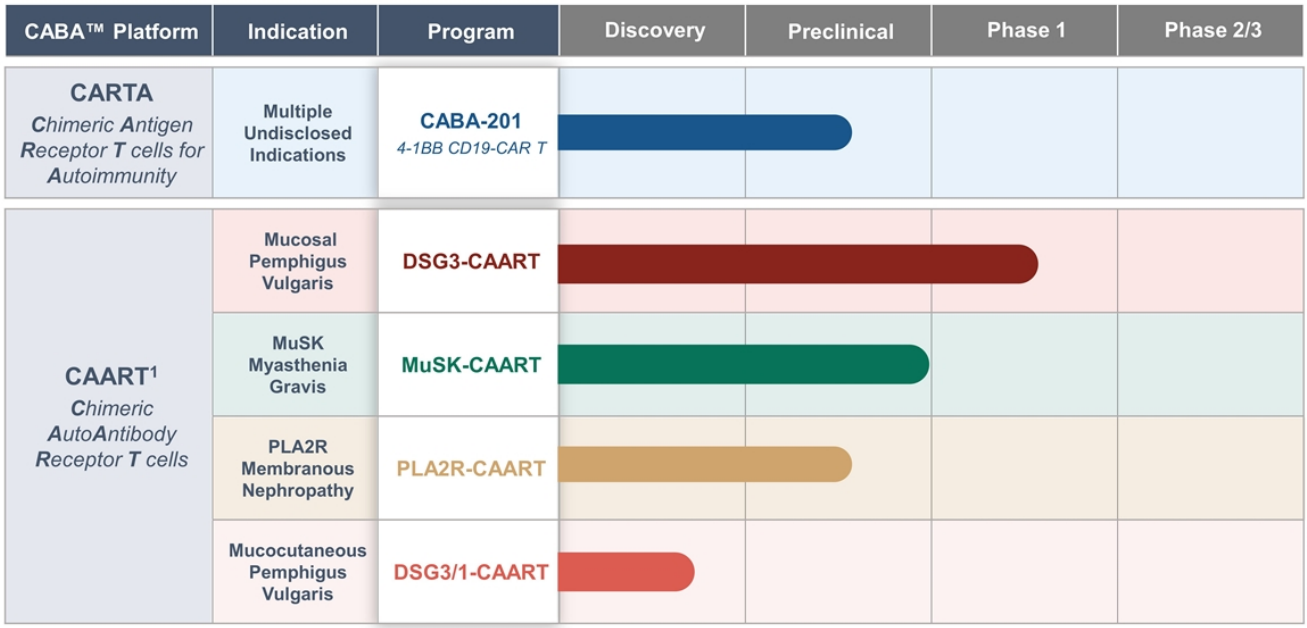
Foundational CAR T technology clinically validated in treating B cell-mediated cancers and SLE[1]



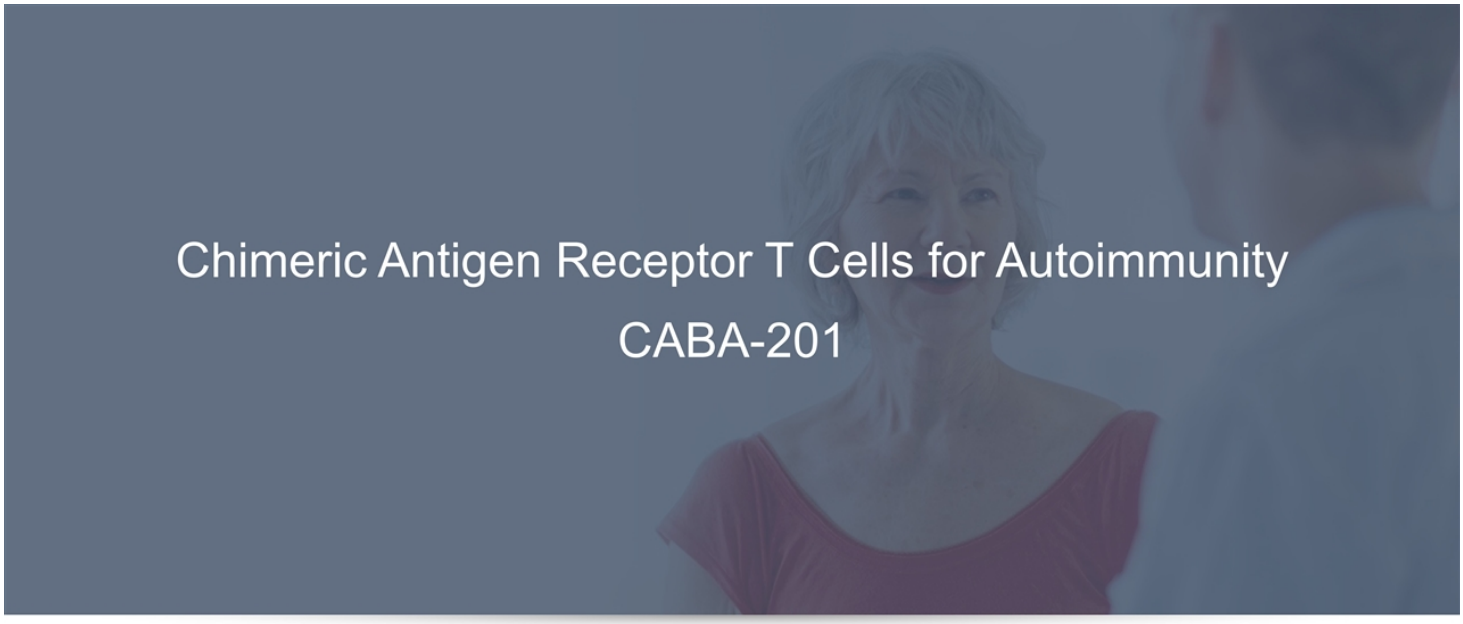
***Note**: Landscape for illustrative purposes only.*

1. Mackensen, Andreas, et al. "Anti-CD19 CAR T cell therapy for refractory systemic lupus erythematosus." Nature Medicine (2022): 1-9.

Pipeline targeting autoimmune diseases where cure is possible



1. Additional disease targets in discovery stage in our CAART pipeline portfolio include hemophilia and two undisclosed indications.



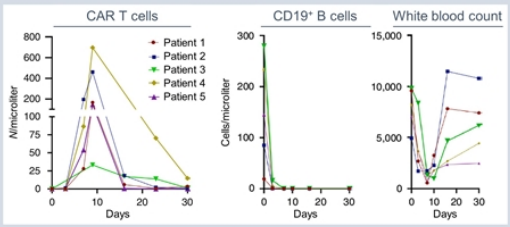
Cabaletta Bio®

Academic clinical data: Immune system reset in 5/5 SLE patients[1]

Exclusive translational research partnership with lead investigator informing our CD19 clinical strategy

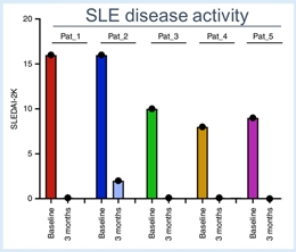
5/5 refractory SLE patients treated with 4-1BB CD19-CAR T[2] resulting in rapid, deep and transient depletion of CD19+ B cells[1]

- All 5 patients with moderate to severe disease
- Preconditioning with standard Flu/Cy regimen[2]
- Dose of $1x10^6$ CD19-CAR T cells/kg
- CD19 binder: 4-1BB costimulatory domain & FMC63 scFv



Clinical & serologic responses by 3 mo. after 4-1BB CD19-CAR T therapy with promising safety profile[1]

- Anti-dsDNA antibodies undetectable in 5/5
  - All SLE-associated antibodies reduced
  - Complement levels normalized
- No – or only mild – CRS observed
  - Grade 1 fever in 3/5 patients
- No neurotoxicity / ICANS



Repopulation of healthy B cells[1]

- New B cells reappeared in 5/5 patients between 2-5 months
- Limited decline in vaccination titers

Durable clinical responses[1]

- 5-17 months of follow up
- Responses maintained with no need for SLE-associated medications

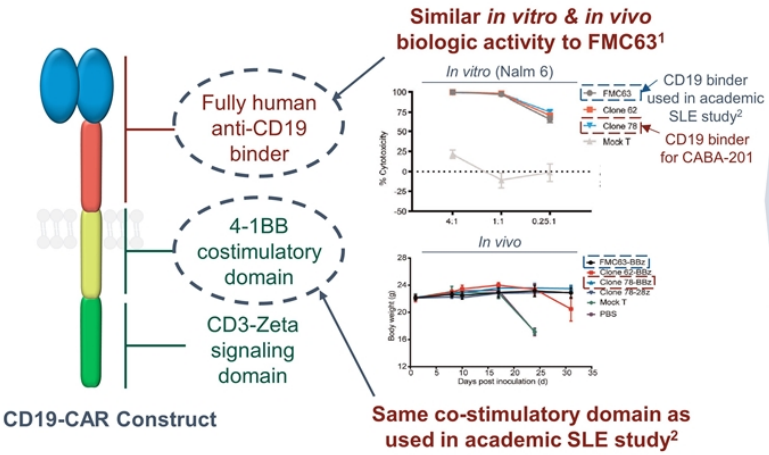
SLE – Systemic lupus erythematosus; scFv – Single chain variable fragment; SLEDAI-2K – Systemic Lupus Erythematosus Disease Activity Index 2000; CRS – Cytokine release syndrome; ICANS – Immune effector cell-associated neurotoxicity syndrome

1. Mackensen, Andreas, et al. "Anti-CD19 CAR T cell therapy for refractory systemic lupus erythematosus." Nature Medicine (2022): 1-9.
2. The construct utilized in this study has a similar design to CABA-201, sharing the 4-1BB costimulatory domain, but is a different construct.
3. Fludarabine (Flu) 25 $mg/m^2/d$ intravenously day -5 to day -3; Cyclophosphamide (Cy) 1,000 $mg/m^2/d$ intravenously on day -3

CABA-201: CD19-targeting CAR T therapy for autoimmune diseases

Cabaletta's CD19 binder with similar *in vitro* & *in vivo* activity to FMC63[1] (binder used in academic SLE study[2])

CABA-201



Clinical Data for Licensed CD19 Binder[3]

Fully human binder
Evaluated within dual-CAR combined with CD22 binder with standard Flu/Cy preconditioning

Evaluated in ~20 patients to date[3]
Under evaluation in patients with B cell leukemia and lymphoma in IIT in China

Promising tolerability data to date[3]
Used in oncology patients with high target cell burden

SLE – Systemic lupus erythematosus; IIT – Investigator-initiated trial; Flu/Cy – Fludarabine/Cyclophosphamide; CRS – Cytokine release syndrome; ICANS – Immune effector cell-associated neurotoxicity syndrome

1. Dai, Zhenyu, et al. "Development and functional characterization of novel fully human anti-CD19 chimeric antigen receptors for T-cell therapy." Journal of Cellular Physiology 236.8 (2021): 5832-5847.
2. Mackensen, Andreas, et al. "Anti-CD19 CAR T cell therapy for refractory systemic lupus erythematosus." Nature Medicine (2022): 1-9.
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

Accelerating development of CABA-201 for autoimmune diseases

Differentiated asset, exclusive translational insights & track record of timely CAART clinical implementation

1 Cabaletta is uniquely positioned to efficiently advance CABA-201 in autoimmune diseases

- Expertise in conducting complex, interdisciplinary autoimmune-focused cell therapy clinical trials
- Track record of positive regulatory interactions to support cell trials in autoimmune diseases since 2018
  - 2 INDs cleared within routine 30-day period; multiple clinical protocol modifications, Fast Track designations granted
- Successful track record manufacturing novel cell therapy products with academic and industry partners
- Deep understanding of autoimmunity allows potential application across broad range of diseases

2 Clinically-evaluated binder & translational research partnership support CABA-201 development

- CABA-201 leverages similar design to 4-1BB-containing CD19-CAR T in seminal academic SLE study[1]
- Exclusive research partnership with lead investigator for SLE study provides early and actionable insights

IND submission for CABA-201 anticipated in first half of 2023

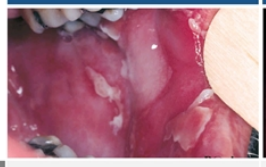
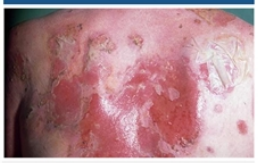
SLE – Systemic lupus erythematosus

1. Mackensen, Andreas, et al. "Anti-CD19 CAR T cell therapy for refractory systemic lupus erythematosus." Nature Medicine (2022): 1-9.

Cabaletta Bio®

Overview of pemphigus vulgaris

Current treatments require broad immunosuppression associated with safety risks and transient efficacy

	Mucosal PV[1] (25%)	Mucocutaneous PV[2] (75%)
		
Associated Antibody	**Anti-DSG3**	**Anti-DSG3 + Anti-DSG1**
Clinical Signs	Painful blisters of the mucous membranes (mouth, nose, larynx, esophagus, eyes, genitalia, rectum)	Blisters on orifices and skin
U.S. Disease Prevalence	**3,250 to 4,750**	**9,750 to 14,250**

Current Treatment Landscape

Broad immunosuppression[3,6]

- Modestly effective & poorly tolerated

Rituximab plus steroids (~3,500 mg/yr)[4]

- Response: ~40% of patients achieved a 16-week period with no lesions or medicines during 1 yr[4,5]
- 22% annual serious adverse event (SAE) rate[4]
  - 4-9%[3,4,5] annual risk of severe infection in PV
- Real world data indicate:
  - *Transient* remission ~ 70% CROT[6]:
    - ~30% relapse in 1 year[6]
    - >50% relapse within 2 years[6]
  - ~30% never achieve CROT[6]
  - ~1.9% lifetime risk of fatal infection[7]

CROT = 8+ weeks without lesions while off systemic therapy

1. Image credit: D@nderm.
2. http://www.vgrd.org/archive/cases/2004/pv/DSCN4996%20copy.JPG
3. Joly, Pascal, et al. "First-line rituximab combined with short-term prednisone versus prednisone alone for the treatment of pemphigus (Ritux 3): a prospective, multicentre, parallel-group, open-label randomised trial." The Lancet 389.10083 (2017): 2031-2040.
4. Werth, Victoria P., et al. "Rituximab versus Mycophenolate Mofetil in Patients with Pemphigus Vulgaris." New England Journal of Medicine (2021).
5. Rituximab label, 08/2020 revision.
6. Kushner, Carolyn J., et al. "Factors Associated With Complete Remission After Rituximab Therapy for Pemphigus." JAMA dermatology (2019).
7. Tony, Hans-Peter, et al. "Safety and clinical outcomes of rituximab therapy in patients with different autoimmune diseases: experience from a national registry (GRAID)." Arthritis research & therapy 13.3 (2011): 1-14.

DSG3-CAART

DesCAARTes™ Phase 1 study of DSG3-CAART[1]

Orphan Drug Designation

Fast Track Designation

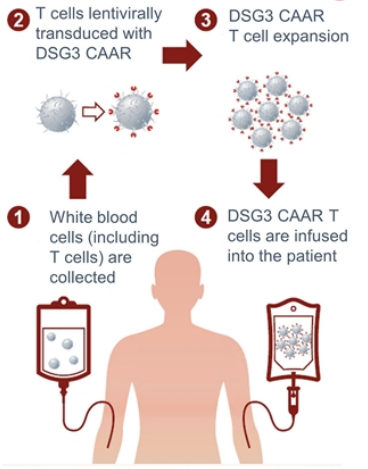
Evaluating DSG3-CAART as monotherapy & in combination with cyclophosphamide and IVIg

Major Inclusion Criteria

- Age: ≥18, confirmed diagnosis
- Inadequately managed by standard immunosuppressive therapies
- Active disease
- Anti-DSG3 antibody positive

Major Exclusion Criteria

- Recent rituximab
- Prednisone > 0.25 mg/kg/day
- Other autoimmune disorder requiring immunosuppressive therapies
- Recent investigational treatment
- ALC < 1,000 at screening



Adjunctive immunosuppressants are stopped; prednisone tapered to low dose prior to infusion

Part A Cohorts[1]	Subjects per Cohort	Dose*
A1 – A6m[2,3]	3 (+3)	20M to 15B

Primary objective:
Determine the maximum tolerated dose of DSG3-CAART

Primary endpoint:
Adverse events, including dose-limiting toxicities (DLTs), related to DSG3-CAART within 3 months of infusion

Combination Sub-study	Subjects per Cohort	Dose*
Combo[3,4]	3 (+3)	2.5B

1. FDA has requested, and the Company has agreed, that we will share data from part A to inform a discussion on the optimal design of part C. According to FDA advice, the submission of part A data is not gating to planned enrollment in part B.
2. Cohort A6m reflects a two-dose regimen of 5.0 to 7.5 billion cells, 3 weeks apart, for a total of 10 to 15 billion cells, which is designed to prolong exposure time of DSG3-CAART *in vivo*.
3. Combination cohort reflects a cell dose of 2.5 billion cells in addition to pre-treatment with intravenous immunoglobulin (IVIg) and cyclophosphamide prior to DSG3-CAART infusion.
4. Combination cohort has been prioritized relative to A6m based on emerging data in cohorts A4 and A5. This is subject to the finalization of the protocol.

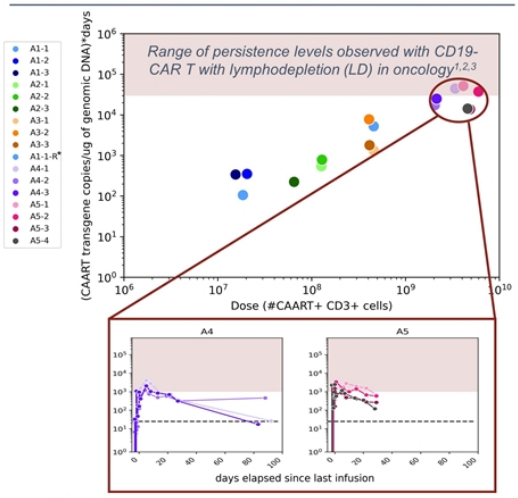
* *20M, 100M, 500M, 2.5B, 5.0B to 7.5B and 10B to 15B refers to the number of DSG3-CAART cells infused for patients in dosing cohorts A1 to A6m (M – millions; B – billions).*

DSG3-CAART

Dose-dependent persistence flattens; aim to increase CAART exposure

Combination sub-study prioritized to address possible cytokine & autoantibody effects on CAART activity

DSG3-CAART Persistence to 29d in Cohorts A1-A5



Combination sub-study cohort

A4 dose ($2.5x10^9$ cells) + cyclophosphamide (CY) & IVIg

- Dose-dependent increase in CAART persistence leveled off with cohort A5
- CY reduces 'cytokine sink,' potentially enhancing CAART activation & proliferation
- Potential reduction in anti-DSG3 autoantibodies that may inhibit or reduce activity
- CY & IVIg likely to provide transient improvement in first few months after infusion[4,5,6,7,8]
  - Up to 9 mo post-infusion may be required to assess DSG3-CAART clinical effect

Cohort A6m | *2x A5 dose (1-1.5x10^{10} cells)*

- Two A5 infusions 3 weeks apart
  - To potentially increase the duration of maximal exposure to DSG3-CAART

1. Mueller, Karen Thudium, et al. "Cellular kinetics of CTL019 in relapsed/refractory B-cell acute lymphoblastic leukemia and chronic lymphocytic leukemia." Blood. 130.21 (2017): 2317-2325.
2. Schuster SJ, Bishop MR, Tam CS, et al. Tisagenlecleucel in Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma. N Engl J Med. 2019;380(1):45-56. doi:10.1056/NEJMoa1804980.
3. The range of persistence observed with anti-CD19 CART therapy in oncology has not been confirmed to be necessary or sufficient for clinical responses in patients with mPV.
4. Amagai, Masayuki, et al. "A randomized double-blind trial of intravenous immunoglobulin for pemphigus." Journal of the American Academy of Dermatology 60.4 (2009): 595-603.
5. Arnold, D. F., et al. "An 'n-of-1'placebo-controlled crossover trial of IVIg as adjuvant therapy in refractory pemphigus vulgaris." British Journal of Dermatology 160.5 (2009): 1098-1102.
6. Zhang, Wenjing, et al. "Short-Term Intravenous Infusion of Cyclophosphamide in the Treatment of Refractory Pemphigus Vulgaris: A Retrospective Study." Dermatology 237.2 (2021): 185-190.
7. Fleischli, Mary E., Rachel H. Valek, and Amit G. Pandya. "Pulse intravenous cyclophosphamide therapy in pemphigus." Archives of dermatology 135.1 (1999): 57-61.
8. Lolis, Margarita, et al. "Effect of IVIg with or without cytotoxic drugs on pemphigus intercellular antibodies." Journal of the American Academy of Dermatology 64.3 (2011): 484-489.

** A1-1-R refers to a subject in cohort A1 who was retreated at the cohort A3 dose (500 million cells).*

MuSK-CAART

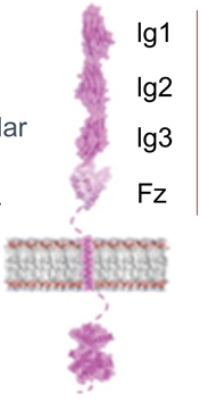
High unmet need in MuSK myasthenia gravis; a valuable CAAR target

All known extracellular domains are included in the CAAR design

MuSK has similar modular structure and size as DSG3, but circulating anti-MuSK ab titers may be ~90% lower than anti-DSG3 ab in PV[4,5,6]

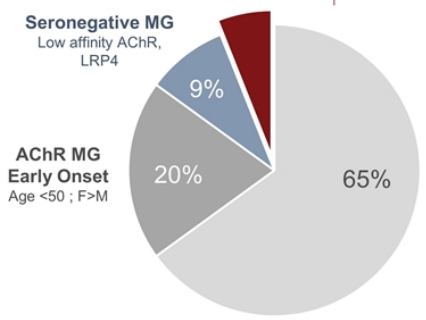
Similarities to pemphigus support clinical potential of CAAR T in MuSK MG

1. IgG4-dominant disease, similar to PV
2. Autoantibody titers drop after rituximab[1,2]
3. Pathogenic B cells are incompletely eliminated by rituximab and persist during relapse[3]



MuSK MG
6.0 - 7.5%

- Typically more severe
- Limited treatment options
- Early onset – 7:1 females



Total US MG Prevalence: 50,000 to 80,000 patients

1. Hain, Berit, et al. "Successful treatment of MuSK antibody–positive myasthenia gravis with rituximab." Muscle & Nerve: Official Journal of the American Association of Electrodiagnostic Medicine 33.4 (2006): 575-580.
2. Illa, Isabel, et al. "Sustained response to Rituximab in anti-AChR and anti-MuSK positive Myasthenia Gravis patients." Journal of neuroimmunology 201 (2008): 90-94.
3. Jiang, Ruoyi, et al. "Single-cell repertoire tracing identifies rituximab-resistant B cells during myasthenia gravis relapses." JCI insight 5.14 (2020).
4. Matthews, Ian, et al. "Muscle-specific receptor tyrosine kinase autoantibodies—a new immunoprecipitation assay." Clinica chimica acta 348.1-2 (2004): 95-99.
5. McConville, John, et al. "Detection and characterization of MuSK antibodies in seronegative myasthenia gravis." Annals of neurology 55.4 (2004): 580-584.
6. Marino, Mariapaola, et al. "Long-lasting rituximab-induced reduction of specific—but not total—IgG4 in MuSK-positive myasthenia gravis." *Frontiers in immunology* 11 (2020): 613.

MuSK-CAART

MusCAARTes™ study of MuSK-CAART

Strategy for upcoming trial informed by learnings from DesCAARTes™ study

Orphan Drug Designation

Fast Track Designation

Open-label study to determine the maximum tolerated dose & to evaluate safety of MuSK-CAART

Major Inclusion Criteria

- Age: ≥18
- MG severity Class I-IVa
- MGC ≥ 4
- Anti-MuSK antibody positive
- Negative anti-AChR antibody test

Major Exclusion Criteria

- Prednisone > 0.25-0.5 mg/kg/day
- Other autoimmune disorder requiring immunosuppressive therapies

SCREENING → MANUFACTURING → TREATMENT (SINGLE INFUSION) → MONITORING (2-4 WEEKS) → Next Patient

25x higher than DesCAARTes™ starting dose

1

Combination cohorts based on DesCAARTes™ study

2

Part	Cohort	# Subjects
A – Dose Escalation[1] Increasing dose levels with 2 (+4) design *(A1 – 500M; A2 – 2.5B; A3[2] – 7.5B)*	A1-A3	2 (+4) per cohort
A – Adaptive Combination Cohorts[1] Combination cohorts, starting at A2 CAART dose *(A4[2] – 2.5B + Cyclophosphamide)*	A4+	2 (+4) per cohort
B – Expansion Expanded subject enrollment at final selected dose	B	~12

Study Endpoint & Objectives

Primary Endpoint: Adverse Events, including DLT

Secondary & Tertiary Objectives: CAAR T expansion/persistence, effect on serum anti-MuSK antibody titer, use of concomitant systemic medications, effect on clinical symptoms, manufacturing success rate

** 500M, 2.5B, 7.5B refers to the number of MuSK-CAART cells infused for patients in dosing cohorts A1 to A3 (M – millions; B – billions).*

1. A total of 6 subjects will need to have received the final selected dose in Part A of the study.

2. Cohorts A3 and A4 will be enrolled concurrently after cohort A2 is well-tolerated with a preference for enrollment into A4.

CAART

Manufacturing strategy

Three-stage approach allows for efficient allocation of capital while leveraging experienced partners

1. Penn-sponsored CD19 CAR IND CMC data has been cross-referenced in DSG3-CAART IND to provide additional data reflecting alignment; cross reference not required for MuSK-CAART IND.

Cabaletta Bio®

Cabaletta Bio leadership

LEADERSHIP TEAM

Steven Nichtberger, M.D.
President, CEO & Chairman

MERCK · tengion · Penn

Samik Basu, M.D.
Chief Scientific Officer

Adaptimmune · MERCK

Gwendolyn Binder, Ph.D.
President, Science & Technology

Adaptimmune · Penn

David J. Chang, M.D., M.P.H., FACR
Chief Medical Officer

AstraZeneca · Penn

Arun Das, M.D.
Chief Business Officer

Goldman Sachs · Children's Hospital of Philadelphia

Michael Gerard
General Counsel

Spark · SANDOZ A Novartis Division

Heather Harte-Hall
Chief Compliance Officer

Adaptimmune · Pfizer

Anup Marda
Chief Financial Officer

Bristol-Myers Squibb

Martha O'Connor
Chief HR Officer

Bristol-Myers Squibb · accentureconsulting

BOARD OF DIRECTORS

Steven Nichtberger, M.D.

Catherine Bollard, M.D.

Scott Brun, M.D.

Richard Henriques, M.B.A.

Mark Simon, M.B.A.

SCIENTIFIC ADVISORY BOARD

Aimee Payne, M.D., Ph.D.
Co-Founder and Co-Chair

Brian Daniels, M.D.

Carl June, M.D.

Iain McInnes, Ph.D., FRCP, FRSE, FMedSci

Michael C. Milone, M.D., Ph.D.
Co-Founder and Co-Chair

Georg Schett, M.D.

Jay Siegel, M.D.

Drew Weissman, M.D., Ph.D.

Track record of operational success in employing novel cell therapies in autoimmunity across preclinical, clinical, manufacturing & regulatory domains

Multiple potential clinical catalysts anticipated in next 12-18 months[1]

	Anticipated Timing	Anticipated Milestone
CABA-201 *4-1BB CD19-CAR T*	1H 2023	IND filing
	1H 2024[2]	Initial clinical data[2]
DSG3-CAART *Mucosal-dominant pemphigus vulgaris*	1Q 2023	1-month safety & persistence data for combination cohort in DesCAARTes™ trial
	3Q 2023	6-month data for combination cohort
MuSK-CAART *MuSK-associated myasthenia gravis*	4Q 2022	Initiate first-in-human MusCAARTes™ trial
	1H 2024	6-month data for combination cohort

Cash runway extended through 2Q 2024 with $96.8M at the end of 2Q 2022

1. Assumes no dose-limiting toxicities are observed in any cohort, uninterrupted enrollment and no delays due to COVID-19 resurgence occur in the trial.
2. Subject to clearance of CABA-201 IND by the FDA.

Cabaletta Bio®

Corporate Presentation

NOVEMBER 2022