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

September 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 7.01 Regulation FD Disclosure.

On September 10, 2022, Cabaletta Bio, Inc. (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 99.1 and is incorporated by reference into this Item 7.01 of this Current Report on Form 8-K.

The information contained in Item 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 8.01 Other Events.

On September 10, 2022, the Company issued a press release announcing that it presented updated clinical and translational data through 6 months of follow-up in cohorts A1 through A4 as well as28-day safety data and DSG3-CAART persistence data through day 29 for cohorts A1 through A5 from the DesCAARTes™ trial at the 31st European Academy of Dermatology and Venereology (EADV) Congress. A copy of the full text of the press release referenced above is filed as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference into this Item 8.01 of this Current Report on Form 8-K.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

99.1	Cabaletta Bio, Inc. Corporate Presentation, dated September 10, 2022, furnished herewith.
99.2	Press Release issued by the registrant on September 10, 2022.
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: September 12, 2022

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

Exhibit 99.1

Cabaletta Bio®

Corporate Presentation

SEPTEMBER 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 technology and CABA™ platform; 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 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; 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 our ongoing Phase 1 DesCAARTes™ trial, 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 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 first 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 DSG3-CAART and MuSK-CAART, 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® overview

Developing highly specific CAAR T products to treat B cell-mediated autoimmune diseases

DesCAARTes™ trial in patients with mucosal pemphigus vulgaris (mPV) ongoing

- Favorable safety profile for DSG3-CAART with no dose-limiting toxicities (DLTs) in cohorts A1 to A5[1]
- DSG3-CAART persistence through day 29 was similar between cohorts A4 and A5 despite a substantial increase in dose[2]
- One cohort A4 subject with sustained persistence had transient improvement in several efficacy assessments at 3 months post-infusion[2]
- Combination sub-study (pre-treatment with IVIg + cyclophosphamide) prioritized to potentially enhance *in vivo* DSG3-CAART exposure

MusCAARTes™ trial in patients with MuSK myasthenia gravis on track to initiate in 2022

- Circulating anti-MuSK antibody titers may be ~90% lower than anti-DSG3 antibody titers in pemphigus vulgaris[3,4,5]

Cell therapy pipeline[6] targeting diseases that affect over 80,000 U.S. patients

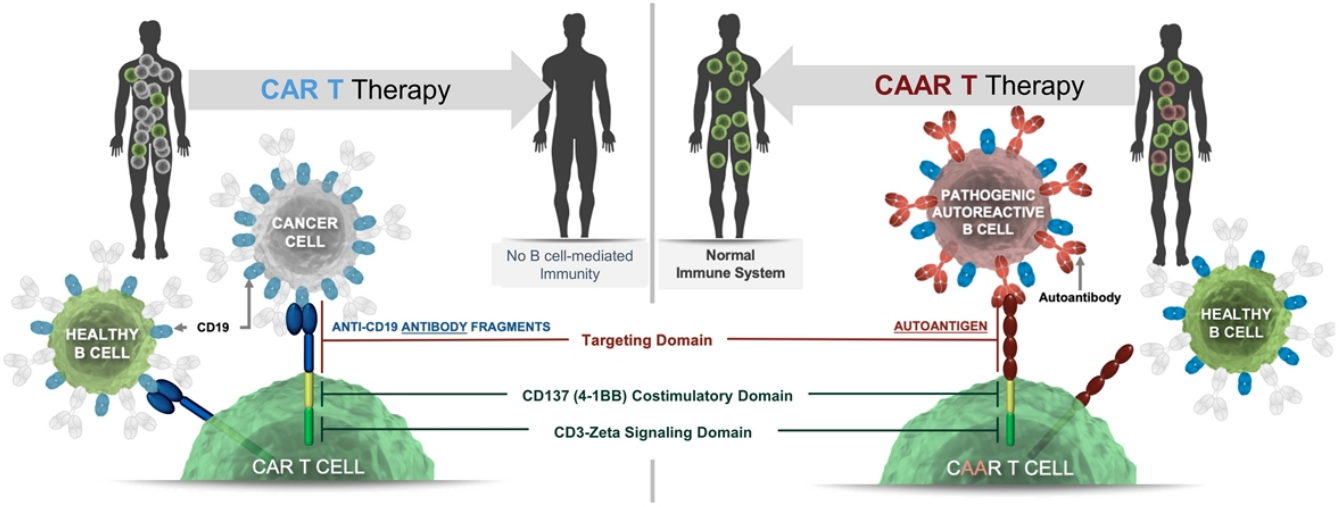
Cash runway through 1Q24 with $96.8M in cash and investments at the end of 2Q22

CRS – Cytokine release syndrome; SAEs – Serious adverse events

1. One subject in cohort A5 developed Grade 1 CRS several hours after each of the 2 infusions which resolved within 2 days (related SAEs). The events were not considered to be DLTs and did not delay study progression
2. Presented at the 31st EADV Congress.
3. Matthews, Ian, et al. "Muscle-specific receptor tyrosine kinase autoantibodies—a new immunoprecipitation assay." Clinica chimica acta 348.1-2 (2004): 95-99.
4. McConville, John, et al. "Detection and characterization of MuSK antibodies in seronegative myasthenia gravis." Annals of neurology 55.4 (2004): 580-584.
5. 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.
6. Includes five disclosed product candidates and two undisclosed pipeline disease targets in our pipeline.

Our scientific platform leverages clinically validated CAR T technology

CAAR T product candidates are designed for selective and specific elimination of the pathogenic B cells



Chimeric **A**ntigen **R**eceptor **T** cell

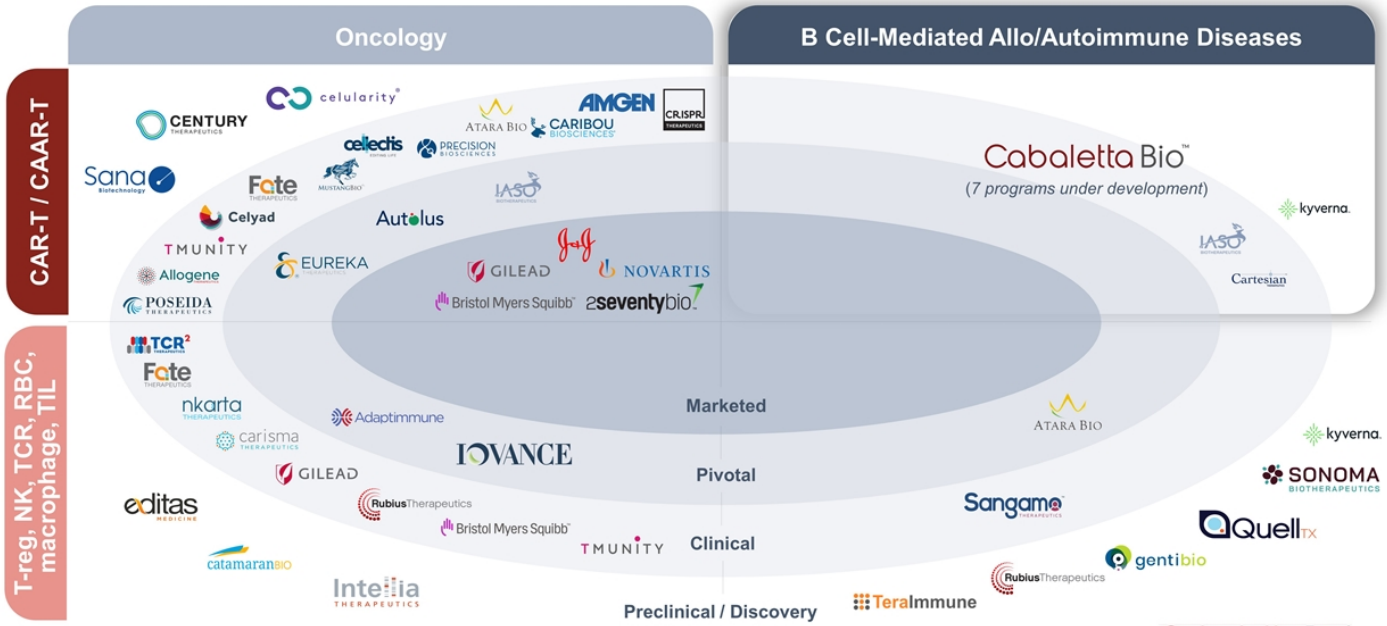
Kymriah

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

CABA CAAR T

Cabaletta: Advancing targeted cell therapy to autoimmunity

Foundational CAR T technology clinically validated in treating B cell-mediated cancers

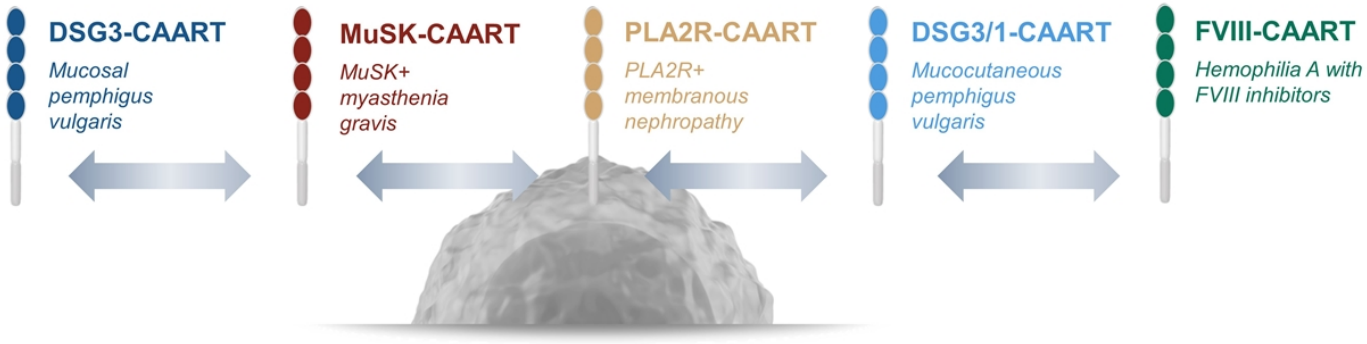


***Note**: Landscape for illustrative purposes only.*

Modular platform with “plug-and-play” architecture

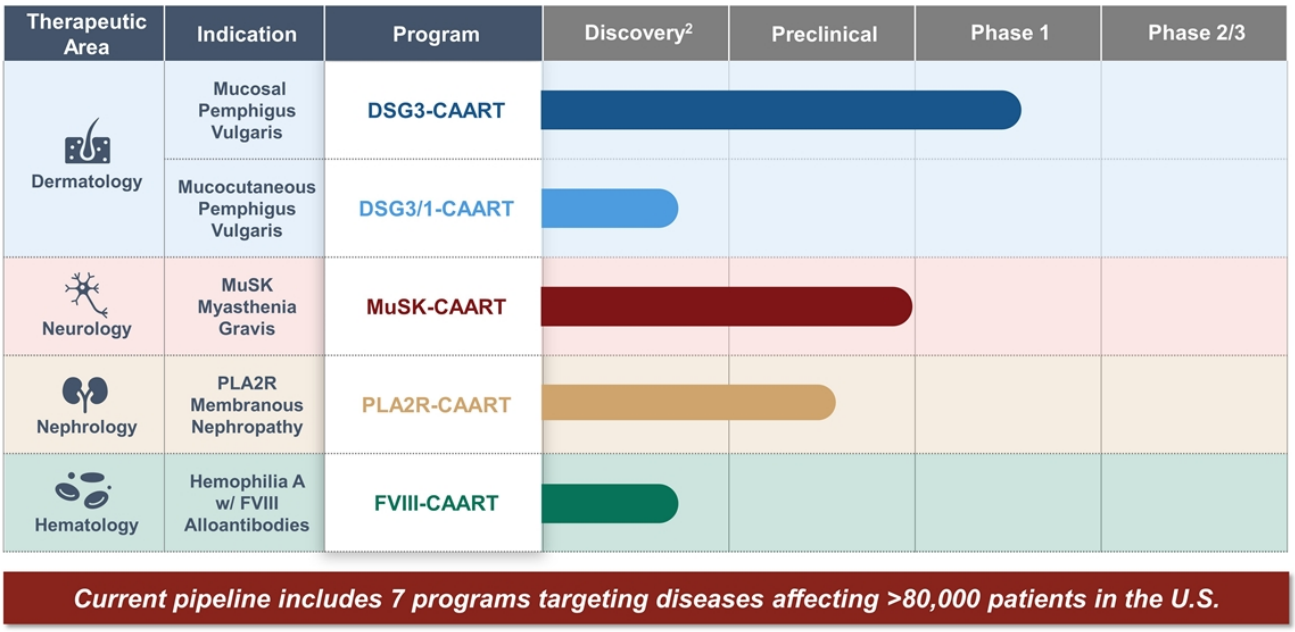
CABA™ platform designed to enable a portfolio of programs targeting B cell-mediated diseases

Swapping the extracellular domain, or autoantigen, creates **new product candidates**



Clinically validated engineered T cell platform is the foundational technology

Pipeline[1] includes multiple disease targets where cure is possible



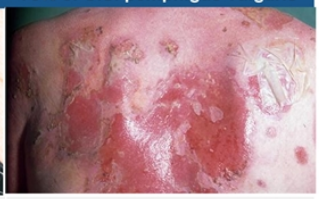
Current pipeline includes 7 programs targeting diseases affecting >80,000 patients in the U.S.

1. Two additional undisclosed disease targets currently in discovery stage are not shown in our pipeline portfolio.
2. In our discovery stage, we perform epitope mapping and optimize CAAR construct and design.

Cabaletta Bio®

Overview of pemphigus vulgaris

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

	Mucosal PV[1] 25% of U.S. pemphigus vulgaris	Mucocutaneous PV[2] 75% of U.S. pemphigus vulgaris
		
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
US 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]

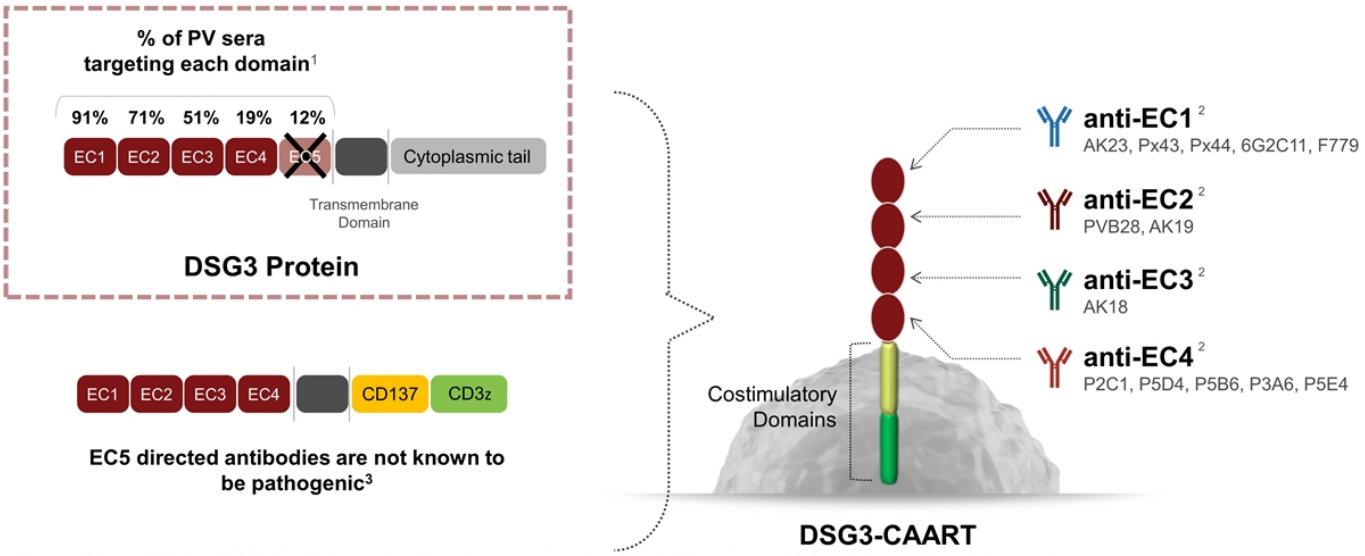
- Response: ~40% of patients achieved a 16-week period with no lesions or medicines during 1 yr[4,5]
- 22% annual serious adverse event (SAE) rate[4]
  - 4-9%[3,4,5] annual risk of severe infection in PV
- Real world data indicate:
  - *Transient* remission ~ 70% CROT[6]:
    - ~30% relapse in 1 year[6]
    - >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 is designed to bind all known pathogenic autoantibodies

Inclusion of all disease-relevant epitopes enables a ‘one-size-fits-all’ approach for patients with mPV



1. Ohyama, Bungo, et al. "Epitope spreading is rarely found in pemphigus vulgaris by large-scale longitudinal study using desmoglein 2–based swapped molecules." Journal of investigative dermatology 132.4 (2012): 1158-1168.
2. Antibodies that target the specific extracellular domain are shown below each extracellular domain.
3. Amagai, Masayuki, et al. "Autoantibodies against the amino-terminal cadherin-like binding domain of pemphigus vulgaris antigen are pathogenic." The Journal of clinical investigation 90.3 (1992): 919-926.

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

Orphan Drug Designation

Fast Track Designation

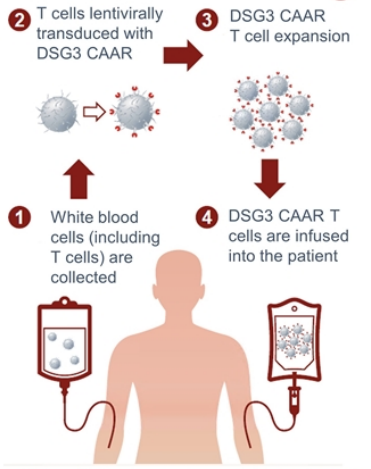
Evaluating DSG3-CAART as monotherapy & in combination with cyclophosphamide and IVIg

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

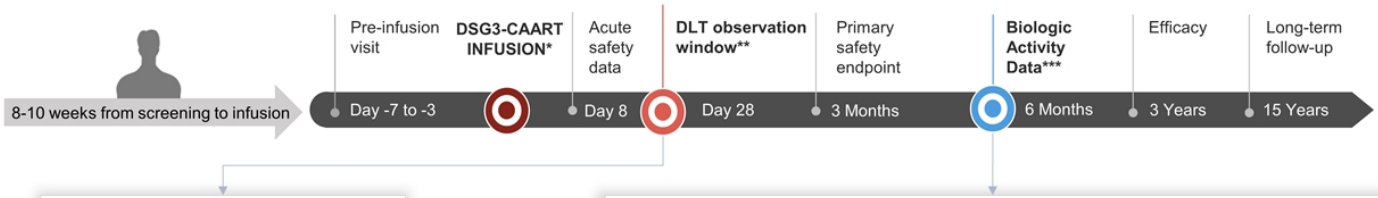
Combination Sub-study	Subjects per Cohort	Dose*
Combo[3,4]	3 (+3)	2.5B

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).*

DesCAARTes™ clinical trial assessments & current timeframes

Safety assessed acutely, at 28 days & at 3 months, with data on biologic activity within 6 months**



Day 28 safety data

Infusion of DSG3-CAART in context of circulating soluble DSG3 antibody

Other safety measures

- CRS / neurotoxicity
- Other adverse events

Primary safety endpoint at 3 months

Potential for disease flare during planned steroid taper +/- discontinuation of immuno-suppressive medications for mPV

Early evaluations of efficacy include[1]:

- Persistence of DSG3-CAART detected via qPCR
- DSG3 antibody titer changes (targeting sustained reduction)[2]
- Change in mPV therapy and/or new systemic rescue therapy
- Disease activity changes based on clinically validated scales
  - e.g. PDAI, ODSS

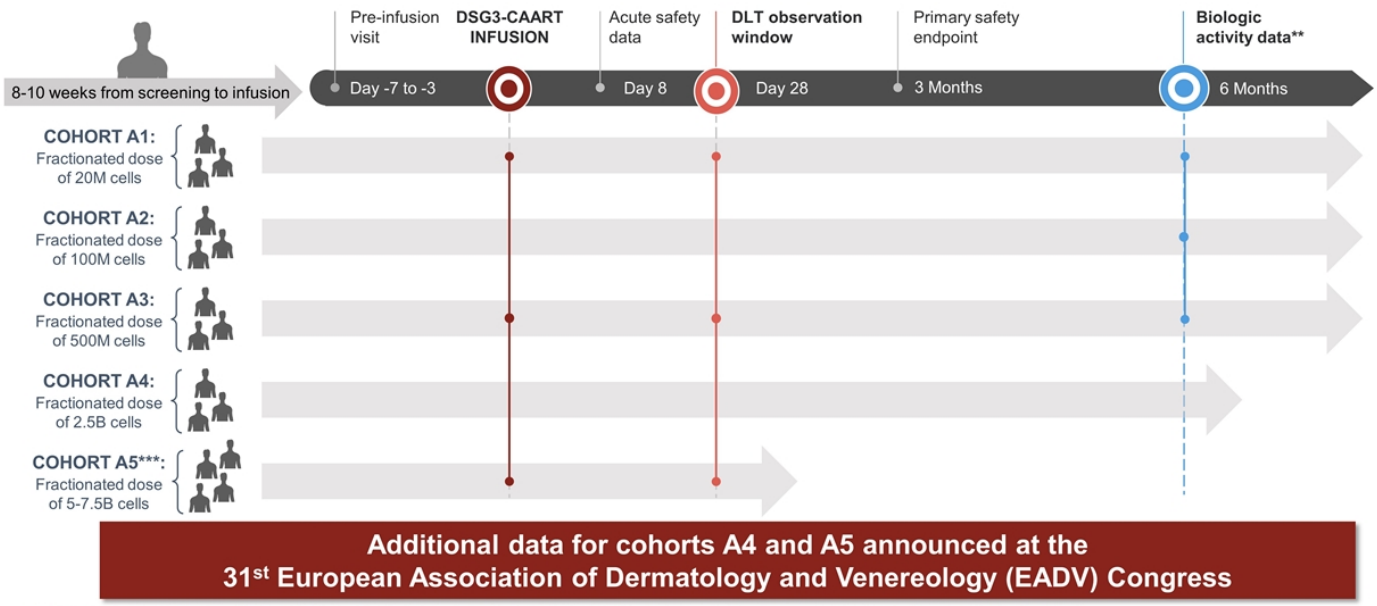
*Data expected within 6 months of completion for each cohort****

** For the combination cohort, patients will be pre-treated with IVIG and cyclophosphamide prior to DSG3-CAART infusion.*
*** Clearance of 28-day observation window without DLTs required to initiate next dosing cohort. DLTs include any grade 3 or 4 CRS or neurotoxicity, or any Grade 2 CRS or neurotoxicity that failed to improve to ≤ Grade 1 or baseline within 7 days.*
****For the combination cohort, we believe data on biologic activity up to 9 months may be required to appropriately assess signals of biologic activity.*

1. This information represents data that we believe can be used to inform potential efficacy endpoints in future clinical development.
2. Spindler, Volker, et al. "Mechanisms causing loss of keratinocyte cohesion in pemphigus." Journal of Investigative Dermatology 138.1 (2018): 32-37.

No DLTs observed in first 5 cohorts of DesCAARTes™ trial

Favorable safety profile at all reported doses of DSG3-CAART, including up to 7.5B cell dose cohort



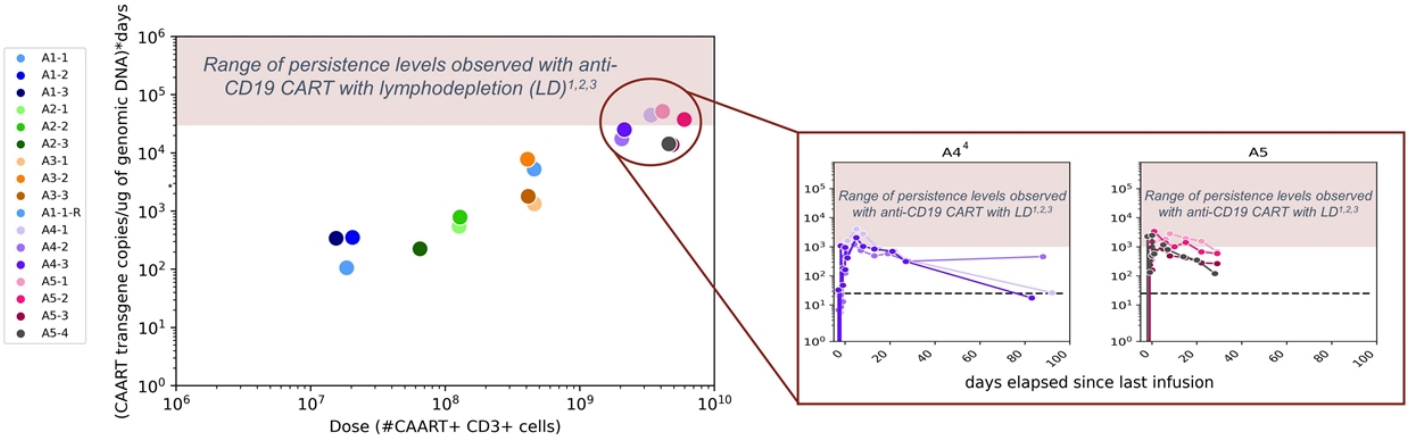
Additional data for cohorts A4 and A5 announced at the 31st European Association of Dermatology and Venereology (EADV) Congress

** 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).*
*** For the combination cohort, we believe data on biologic activity up to 9 months may be required to appropriately assess signals of biologic activity.*
**** A 4th subject was dosed in Cohort A5 to generate additional data.*

Cabaletta Bio®

DSG3-CAART persistence through day 29 in cohorts A1 to A5

Dose dependent persistence observed through cohort A4, but leveling off with cohort A5



DSG3-CAART persistence in cohorts A4 & A5 approached lower end of the range seen with CD19-CART[1,2,3]; combination cohort prioritized to potentially further increase DSG3-CAART exposure

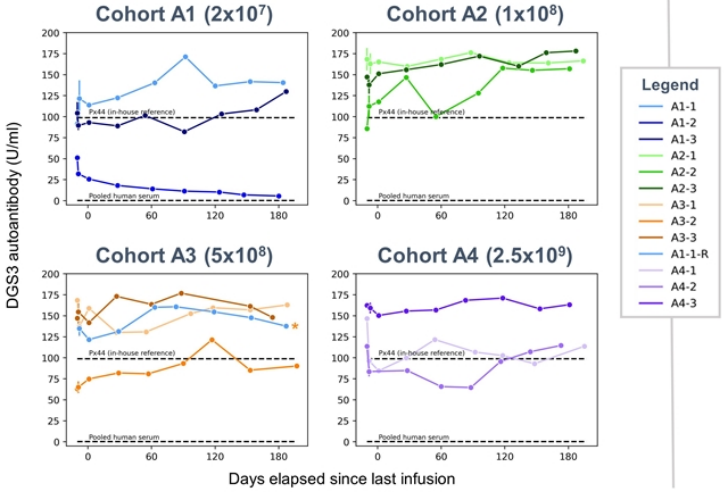
1. Mueller, Karen Thudium, et al. "Cellular kinetics of CTL019 in relapsed/refractory B-cell acute lymphoblastic leukemia and chronic lymphocytic leukemia." Blood, The Journal of the American Society of Hematology 130.21 (2017): 2317-2325.
2. Schuster SJ, Bishop MR, Tam CS, et al. Tisagenlecleucel in 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. For cohort A4, 3 month DSG3-CAART persistence data also shown as presented at the 31st EADV Congress.

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

Anti-DSG3 antibody levels across cohorts A1-A4

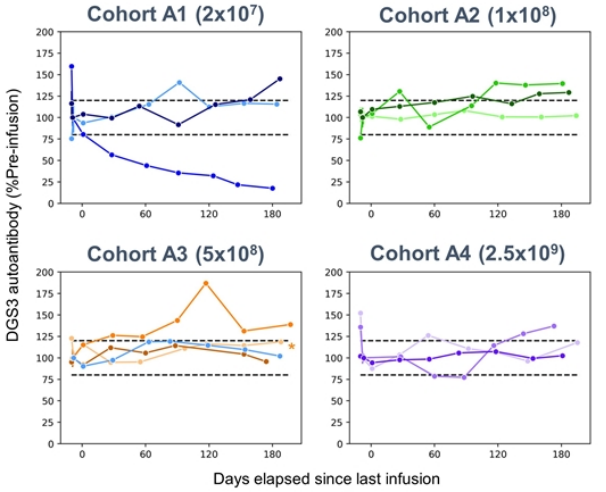
Antibody levels as measured via ELISA generally stable, though patient A4-2 had transient response

Absolute Values



Normalized Values

Dashed lines represent ± 20% from the pre-infusion timepoint



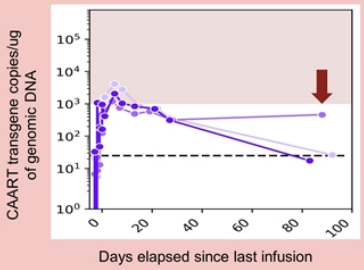
**Subject A1-1-R = Patient A1-1 retreated at the A3 dose level*

Data on Subject A4-2 (2.5x10^9 DSG3-CAART Dose)

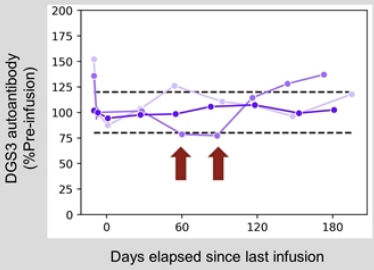
Transient improvement in disease activity by 3 months & steroid taper during that period

1 DSG3-CAART persistence detected at 3 months

(not observed in other subjects in Cohorts A1-A4)



2 Anti-DSG3 antibody levels decreased >20% at 2- & 3-months post-infusion



3 PDAI Mucous Membrane score decreased from 1 to 0 at 3- & 4-months post-infusion

4 Prednisone tapered from 10mg daily to 1mg daily over the 4 months after DSG3-CAART infusion

Disease Activity Measure	Screen	Pre-Infusion	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6
PDAI	1	1 PRD	1	1	0	0 PRD	8	0
ODSS[1]	10	5	5	6	0	0	26	1

1. Oral Disease Severity Score

Strategy and rationale for planned cohorts in DesCAARTes™ trial

Combo sub-study prioritized to potentially overcome possible cytokine & autoantibody effects on CAART activity

Combination sub-study cohort

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

- Dose-dependent increase in DSG3-CAART persistence through cohort A4 that leveled off with cohort A5
- Cyclophosphamide (CY) reduces 'cytokine sink,' potentially enhancing DSG3-CAART activation & proliferation
- Potential reduction in anti-DSG3 autoantibodies that may inhibit or reduce DSG3-CAART activity
- CY & IVIg likely to provide transient disease improvement limited to the first few months after infusion[1,2,3,4,5]
  - Evaluation up to 9 months post-infusion may be required to assess independent DSG3-CAART clinical effect

Cohort A6m

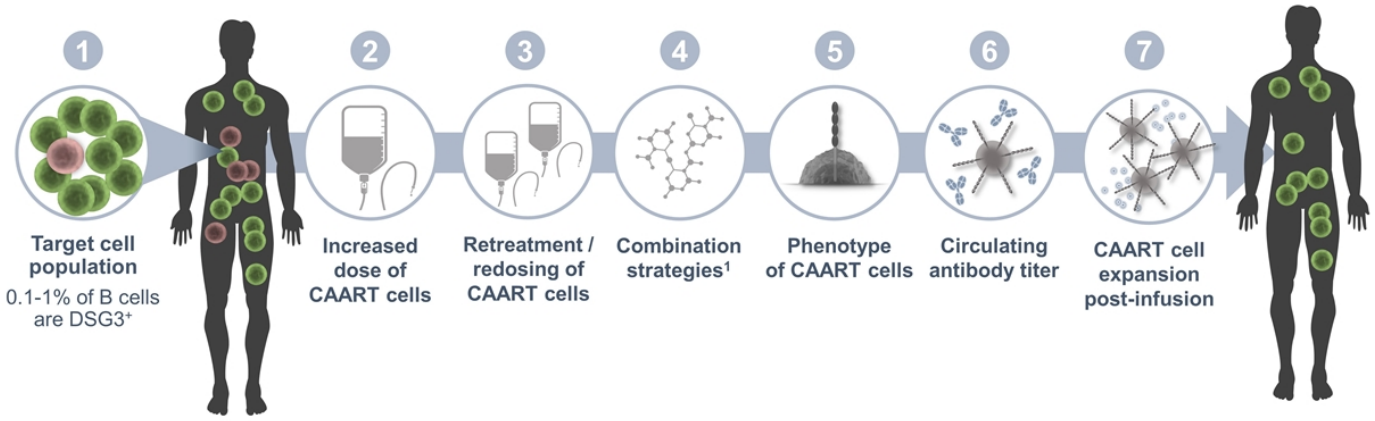
2x A5 dose ($1\text{-}1.5x10^{10}$ cells)

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

1. 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.
2. Arnold, D. F., et al. "An 'n-of-1'placebo-controlled crossover trial of intravenous immunoglobulin as adjuvant therapy in refractory pemphigus vulgaris." British Journal of Dermatology 160.5 (2009): 1098-1102.
3. 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.
4. Fleischli, Mary E., Rachel H. Valek, and Amit G. Pandya. "Pulse intravenous cyclophosphamide therapy in pemphigus." Archives of dermatology 135.1 (1999): 57-61.
5. Lolis, Margarita, et al. "Effect of intravenous immunoglobulin with or without cytotoxic drugs on pemphigus intercellular antibodies." Journal of the American Academy of Dermatology 64.3 (2011): 484-489.

Optimizing DSG3-CAART product and patient profiles

Range of strategies being implemented and/or under consideration to increase *in vivo* activity of DSG3-CAART



Many options exist to optimize product and patient profiles; ongoing evaluation to enhance DSG3-CAART exposure in DesCAARTes™ trial

CAART cell

Pathogenic autoreactive B cell

Healthy B cell

1. Combination strategies reflect regimens that include preconditioning and/or immunomodulatory medications prior to administration of DSG3-CAART.

Cabaletta Bio®

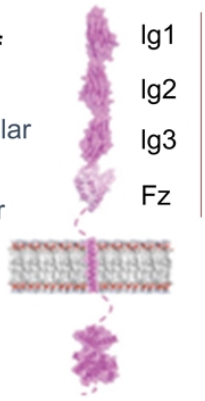
High unmet need in MuSK myasthenia gravis; a valuable CAAR target

All known extracellular domains can be 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]

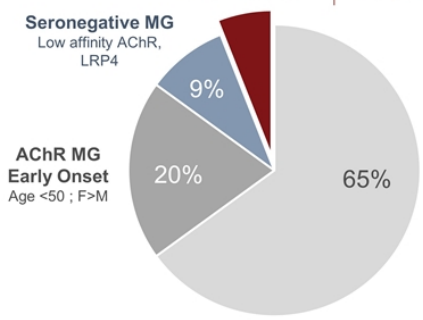
Similarities to pemphigus support clinical potential of CAAR T in MuSK MG

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

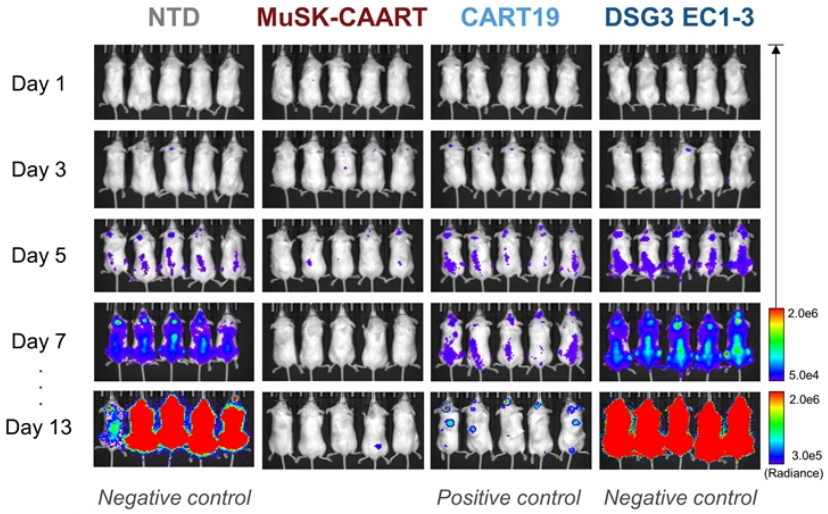


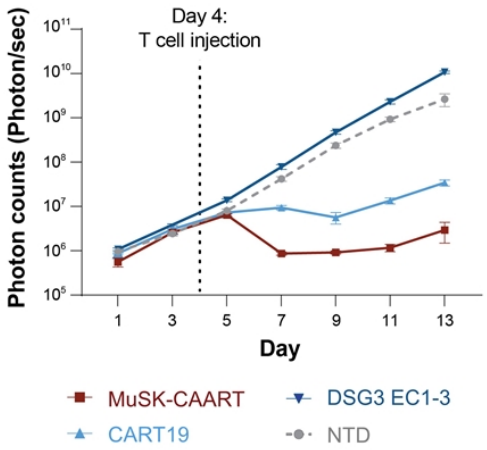
Total US MG Prevalence: 50,000 to 80,000 patients

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 demonstrated specific *in vivo* target engagement[1]

MuSK-CAART eliminated anti-MuSK target cells[2] in an animal model where CART19 cells were a positive control





MuSK-CAART IND open; planning to initiate first-in-human MuSK-CAART trial in 2022

1. https://cabalettabio.com/technology/posters-publications; recently presented at AAI Immunology 2022, MGFA International and ASGCT 2022 conferences in May 2022.
2. Target cells represent a B cell tumor line (CD19 positive) that has been modified to express the anti-MuSK antibody.

MusCAARTes™ study of MuSK-CAART

Strategy for upcoming trial evaluating MuSK-CAART informed by learnings from DesCAARTes™ study

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

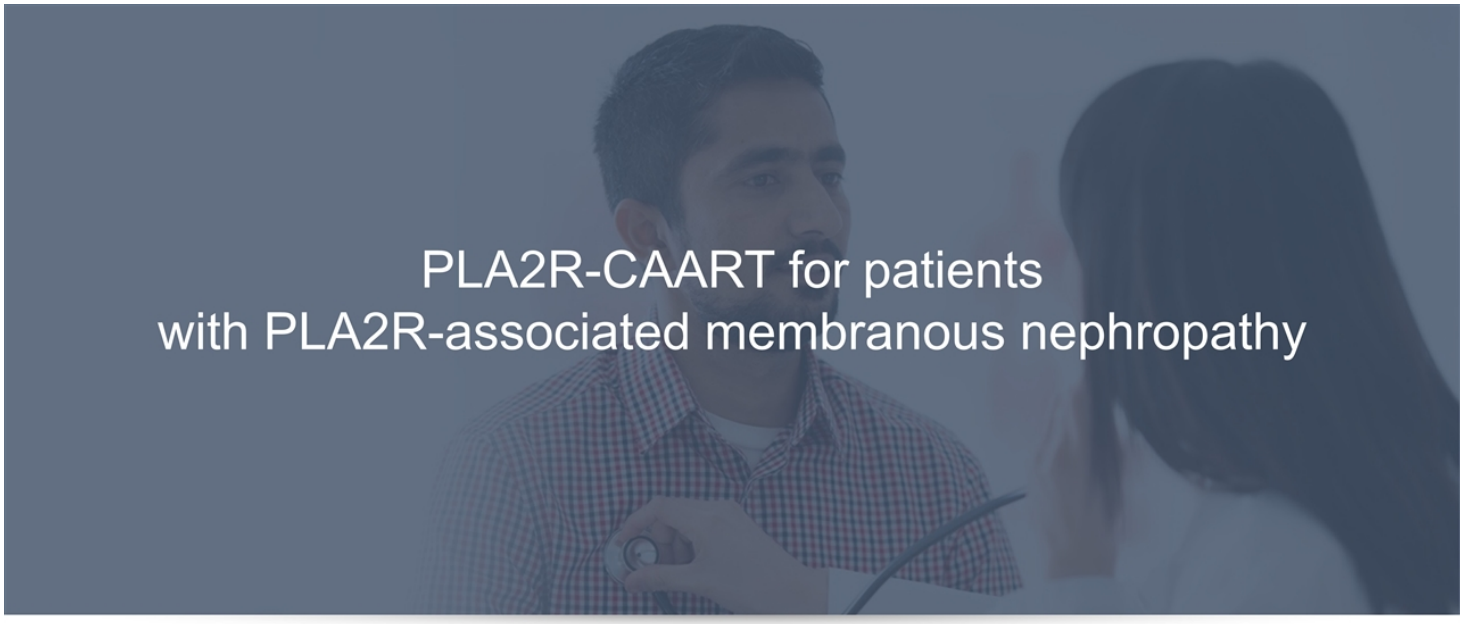
Primary Endpoint: Adverse Events, including DLT

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.



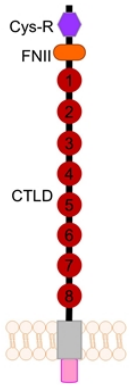
Cabaletta Bio®

Preclinical stage CAART program in membranous nephropathy

Primary MN is an immune-mediated kidney disease with anti-PLA2R antibodies in ~75% of patients

Accumulating evidence of a correlation between PLA2R antibodies and disease activity, remission and relapse in primary MN

1. PLA2R autoantibody levels routinely used as diagnostic and prognostic markers
2. Autoantibody titer shown to rise rapidly before clinical manifestations
3. Co-localization of antigen & PLA2R antibodies at site of damage in kidney



PLA2R+ MN is attractive for CAAR development

- Epitopes are well-defined
- IgG4-dominant disease, similar to PV and MuSK MG
- Eligible US population
  - prevalence of ~4,000-8,000;
  - incidence of ~700-1,400 / yr

PLA2R-CAART showed *in vitro* antigen-specific cytotoxicity[1]

- PLA2R CAARs demonstrated activity in the presence of physiologic levels of anti-PLA2R autoantibodies
- Candidate CAAR contains targets that bind >95% of anti-PLA2R autoantibodies
- Demonstrated no off-target binding interactions in membrane protein array

1. As presented at the ASN Kidney Week 2021.

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.
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

Jay Siegel, M.D.

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

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.

Multiple potential data catalysts with possible pipeline read-through

DesCAARTes™ trial: Prioritizing combination cohort to potentially enhance DSG3-CAART *in vivo* exposure

- 31st EADV Congress: 6 month clinical & translational data for cohort A4 and 1 month safety & persistence data for cohort A5
  - DSG3-CAART persistence through day 29 was similar between cohorts A4 and A5 despite a substantial increase in dose
  - One subject in cohort A4 with sustained persistence demonstrated transient improvement in several efficacy assessments at 3 months
- Combination cohort (pre-treatment with IVIg + cyclophosphamide) to potentially enhance *in vivo* DSG3-CAART exposure

MuSK-CAART: IND cleared within routine 30-day period; received FDA Fast Track Designation

- Circulating anti-MuSK antibody titers may be ~90% lower than anti-DSG3 antibody titers in pemphigus vulgaris[2,3,4]
- 500M MuSK-CAART cells is planned initial dose (25x higher compared to starting dose in DesCAARTes™ trial)

Cash runway through 1Q24 with $96.8M in cash and investments at the end of 2Q22

Multiple anticipated near-term milestones for the pipeline

- DesCAARTes™ Trial: Initial combination sub-study cohort data to be presented at a scientific or medical meeting in 1Q23[1]
  - 1 month safety and DSG3-CAART persistence data
- MuSK-CAART: On track to initiate first-in-human trial in 2022

1. Assumes no dose-limiting toxicities are observed in the cohort, uninterrupted enrollment and no delays due to COVID-19 resurgence occur in the trial.
2. Matthews, Ian, et al. "Muscle-specific receptor tyrosine kinase autoantibodies—a new immunoprecipitation assay." Clinica chimica acta 348.1-2 (2004): 95-99.
3. McConville, John, et al. "Detection and characterization of MuSK antibodies in seronegative myasthenia gravis." Annals of neurology 55.4 (2004): 580-584.
4. 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.

* *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).*

Cabaletta Bio®

Corporate Presentation

SEPTEMBER 2022

Cabaletta Bio®

Cabaletta Bio Presents New Interim Data from the DesCAARTes™ Phase 1 Trial at the 31st EADV Congress

PHILADELPHIA, Sept. 10, 2022 — Cabaletta Bio, Inc. (Nasdaq: CABA), a clinical-stage biotechnology company focused on the discovery and development of targeted cell therapies for patients with autoimmune diseases, today presented updated clinical and translational data through 6 months of follow-up in cohorts A1 through A4 as well as28-day safety data and DSG3-CAART persistence data through day 29 for cohorts A1 through A5 from the DesCAARTes™ trial at the 31st European Academy of Dermatology and Venereology (EADV) Congress, which is being held in Milan, Italy from September 7-10, 2022.

"The new data continue to support the favorable safety profile of DSG3-CAART, with no dose-limiting toxicities, and one grade 1 cytokine release syndrome through cohort A5, at a dose of up to 7.5 billion DSG3-CAART cells. No clear trends in antibody levels or disease activity reduction were observed, though one subject in cohort A4 had no disease activity by three months post-infusion while reducing steroid usage during that period, an antibody titer that dropped more than 20% by three months post-infusion, and was the only patient in the first four cohorts that had detectable DSG3-CAART persistence at the 3 month time point following initial DSG3-CAART infusion," said David J. Chang, M.D., Chief Medical Officer of Cabaletta. "The 2 to 3 fold increase in infusion dose in cohort A5 relative to cohort A4 did not result in a dose-dependent increase in one month DSG3-CAART persistence, suggesting strategies beyond single dose escalation may be required to potentially further increase DSG3-CAART in vivo exposure and generate durable clinical responses. We believe these data support a multiple infusion approach, and provide a rationale to prioritize the combination sub-study, which will employ pre-treatment with intravenous immunoglobulin and cyclophosphamide to potentially increase the in vivo expansion, persistence and activity of DSG3-CAART."

The updated interim data included 16 treated subjects, four cohorts with three patients per cohort and one cohort with four patients, with twelve having completed six months of follow-up after DSG3-CAART infusion, and four having completed 28-day follow-up after DSG3-CAART infusion. The presentation is available on the Company's website at https://www.cabalettabio.com/technology/posters-publications. The data demonstrate:

- Doses up to 7.5 billion DSG3-CAART cells (cohort A5) were generally well tolerated, with no DLTs, and one grade 1 CRS.
- There was a dose-dependent increase in DSG3-CAART persistence through day 29 in cohorts A1 to A4. DSG3-CAART persistence through day 29 in cohort A5 was similar to that observed in cohort A4.
- In cohorts A1 to A4:

- Through six months post DSG3-CAART infusion, no clear pattern was observed in changes in anti-DSG3 Ab levels (ELISA) or disease activity (PDAI) through cohort A4.
- One subject in cohort A4 demonstrated a transient improvement in several assessments of efficacy, including DSG3-CAART persistence at 3 months, decrease of anti-DSG3 Ab levels >20% at 2- and 3-months post-infusion, improvement in PDAI score, and decreased steroid usage.

The rationale for prioritization of the next planned dosing cohorts is as follows:

- Combination sub-study: A4 dose ($2.5x10^9$ cells) combined with cyclophosphamide (CY) and intravenous immunoglobulin (IVIg) pre-treatment has been prioritized based on leveling off of DSG3-CAART persistence through day 29 from cohorts A4 to A5.
  - CY may reduce cells that compete for cytokines necessary for DSG3-CAART activation & proliferation.
  - This combination is designed to reduce anti-DSG3 autoantibodies, which may block DSG3-CAART.
    - CY may reduce pathogenic autoantibody-secreting B cells.
    - IVIg may facilitate this reduction through several mechanisms, including binding and blocking the autoantibodies.
- Cohort A6m: 2-fold higher than A5 dose ($1\text{-}1.5x10^{10}$ cells): Two A5 infusions will be administered 3 weeks apart to potentially increase the duration of *in vivo* exposure and persistence of DSG3-CAART.

The trial is currently being conducted across multiple clinical sites throughout the United States and is enrolling patients in the combination sub-study. If no DLTs are observed, 28-day safety and persistence data through day 29 for the combination sub-study cohort are anticipated to be shared at a scientific or medical meeting during the first quarter of 2023.

About the DesCAARTes Phase 1 Trial

Cabaletta's DesCAARTes™ Phase 1 trial is an open-label, dose escalation, multi-center study of DSG3-CAART in adults with mucosal-dominant pemphigus vulgaris (mPV). The trial is designed to determine the maximum tolerated dose of DSG3-CAART in adult subjects with active, anti-DSG3 Ab positive, biopsy confirmed mPV that is inadequately managed by one or more standard therapies. The primary endpoint is incidence of adverse events (AEs), including dose-limiting toxicities (DLTs), such as certain events of cytokine release syndrome (CRS) and neurotoxicity, related to DSG3-CAART within three months of infusion. Secondary endpoints include CAART persistence (qPCR), anti-DSG3 Ab levels (ELISA) and disease activity (PDAI).

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, in combination with Cabaletta Bio's proprietary technology, has advanced a growing pipeline that currently includes potential treatments for patients with mucosal pemphigus vulgaris, MuSK-associated myasthenia gravis, PLA2R-associated membranous nephropathy, mucocutaneous pemphigus vulgaris and hemophilia A with FVIII alloantibodies. Cabaletta Bio's headquarters are located in Philadelphia, PA. For more information, visit www.cabalettabio.com and follow us on LinkedIn and Twitter.

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: the company's business plans and objectives; 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; the expected significance and impact around the clinical and translational data updates provided at the scientific meeting described herein and the expected timing and significance around additional clinical data updates from the DesCAARTes™ trial at additional scientific meetings throughout 2022 and 2023; the expectation that Cabaletta may improve outcomes for patients suffering from mPV; Cabaletta's ability to escalate dosing as high as 10 to 15 billion cells in a planned future cohort, 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; Cabaletta's 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 its targeted cell therapy; Cabaletta's ability to evaluate, and the potential significance of, the relationship between DSG3-CAART persistence and potential clinical responses in patients with mPV; expectations regarding the design, implementation, timing and success of its current and planned clinical trials and the successful completion of nonclinical studies; planned potential timing and advancement of its preclinical studies and clinical trials and related regulatory submissions; ability to optimize the impact of its collaborations on its development programs; the impact of COVID-19 on the timing, progress, interpretability of data, and results of ongoing or planned preclinical and clinical trials; statements regarding the timing of regulatory filings regarding its development programs; the ability to accelerate Cabaletta's pipeline and develop meaningful therapies for patients, including in collaboration with academic and industry partners; 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; Cabaletta's plans to evaluate additional cohorts in the DesCAARTes™ trial, including a cohort implementing a pre-treatment regimen; 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; risks related to unexpected safety or efficacy data observed during clinical studies; 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

DSG3-CAART for the treatment of pemphigus vulgaris; risks related to Cabaletta's ability to protect and maintain its intellectual property position; 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 commercialized; and the risk that the 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.

Contacts:

Anup Marda
Chief Financial Officer
investors@cabalettabio.com

Sarah McCabe
Stern Investor Relations, Inc.
sarah.mccabe@sternir.com