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

May 18, 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 May 18, 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 Form 8-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 May 18, 2022, the Company issued a press release announcing the presentation of updated clinical and translational data through six months of follow-up in cohorts A1 through A3, safety data through three months and persistence data through one month of follow-up in cohorts A1 through A4 of the DesCAARTes™ Phase 1 clinical trial of DSG3-CAART for the treatment of patients with mucosal pemphigus vulgaris at the American Society of Gene & Cell Therapy 25th Annual Meeting being held in Washington, D.C. 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 May 18, 2022, furnished herewith.
99.2	Press Release issued by the registrant on May 18, 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.

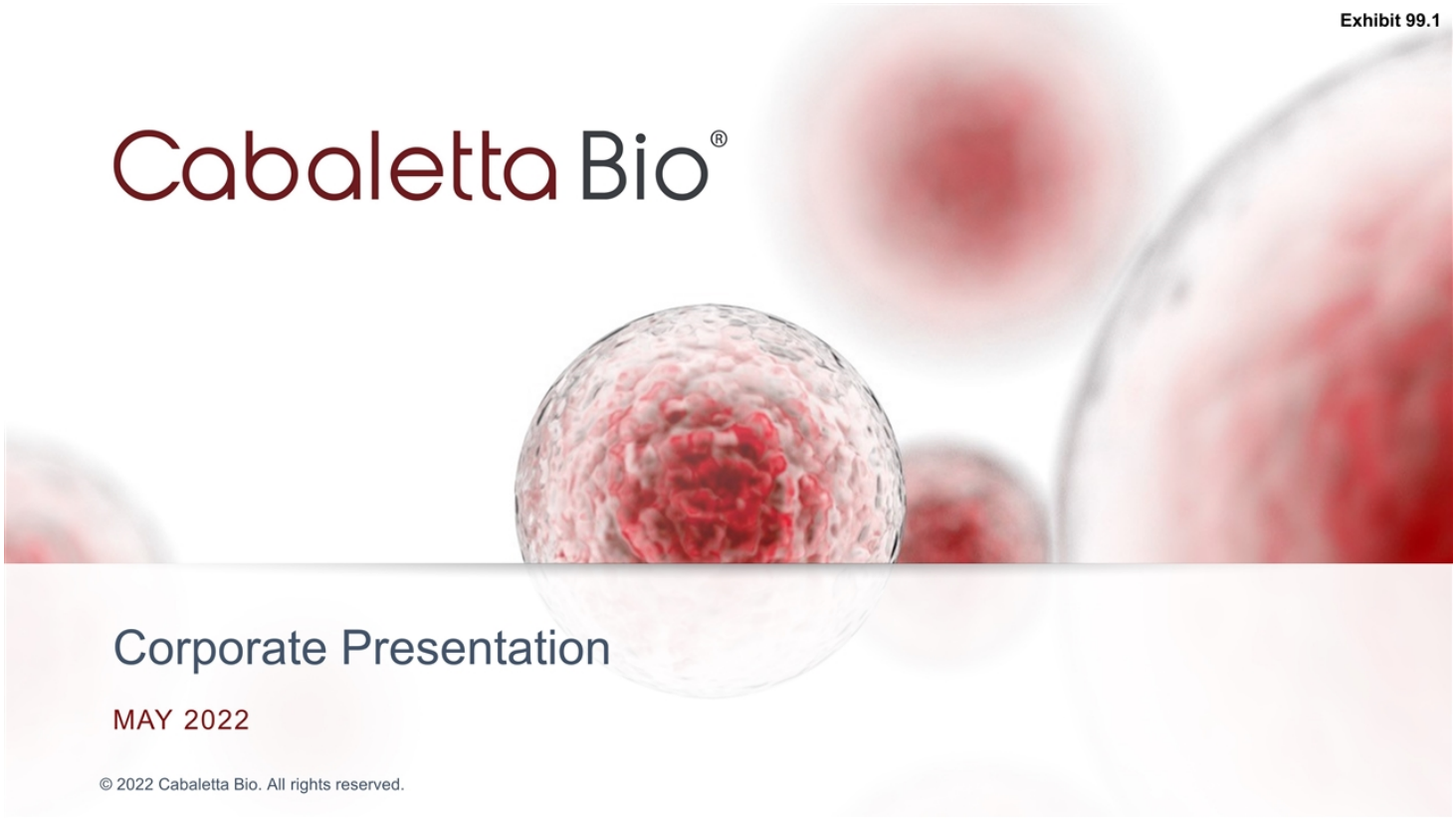
CABALETTA BIO, INC.

Date: May 18, 2022

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

Exhibit 99.1

Cabaletta Bio®



Corporate Presentation

MAY 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 expected timing and significance of the announcement of 28-day safety for cohort A5 and clinical and translational data for cohort A4 in mid-2022; 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 continue progressing in cohort A5, including the planned addition of an enhanced manufacturing process in cohort A5e; our ability to escalate dosing as high as 10 to 15 billion cells in cohort A6m or otherwise; 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 third quarter of 2023. 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 and clinical trials of DSG3-CAART and MuSK-CAART, 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

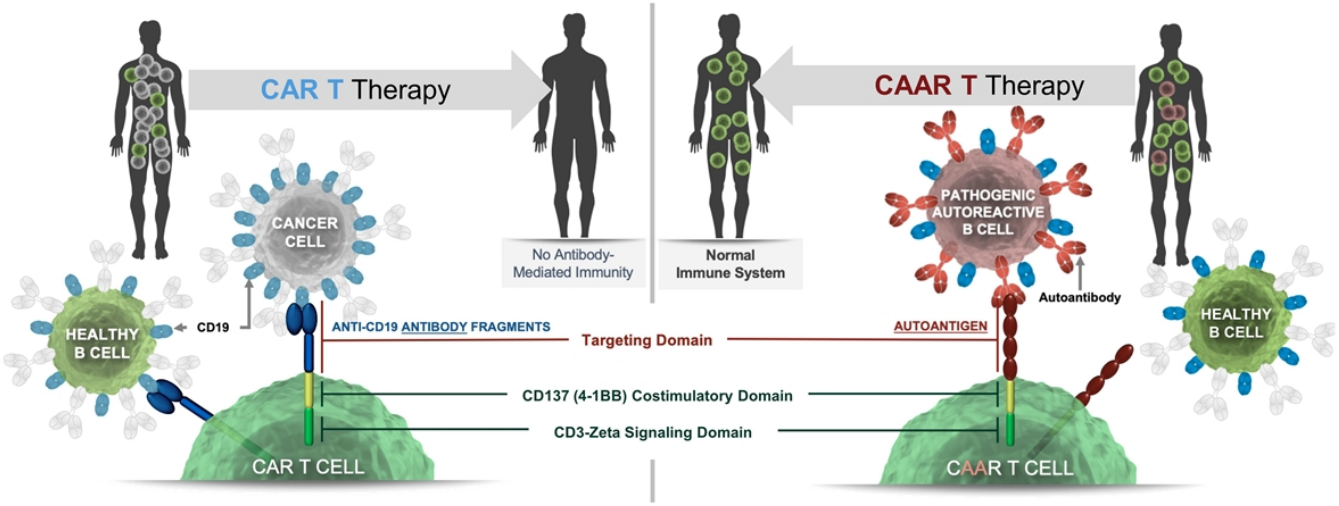
- **Developing highly specific CAAR T products to treat B cell-mediated autoimmune diseases**
- **DesCAARTes™ trial in patients with mucosal pemphigus vulgaris (mPV) ongoing**
  - Favorable safety profile for DSG3-CAART demonstrated in cohorts A1 through A4 at doses up to 2.5 billion cells
    - No CRS, ICANS, dose-limiting toxicities or related SAEs observed in any patient in cohorts A1 to A4
  - Dose-dependent increase in DSG3-CAART persistence observed in cohorts A1 to A4, as presented at 25th Annual ASGCT Conference
    - Cohort A4 persistence approached the lower end of the range seen with anti-CD19 CART with lymphodepletion in oncology[1,2,3]
  - Cohort A5 dosing up to 7.5 billion cells ongoing with multiple additional cohorts possible to enhance in vivo DSG3-CAART exposure
- **MusCAARTes™ trial in patients with MuSK myasthenia gravis on track to initiate in 2022**
- **Cell therapy pipeline[4] targeting diseases that affect over 80,000 U.S. patients**
- **Cash runway through 3Q23 with $109.2M in cash and investments at the end of 1Q22**

CRS – Cytokine release syndrome; ICANS – Immune effector cell-associated neurotoxicity syndrome; SAE – Serious adverse event

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. 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

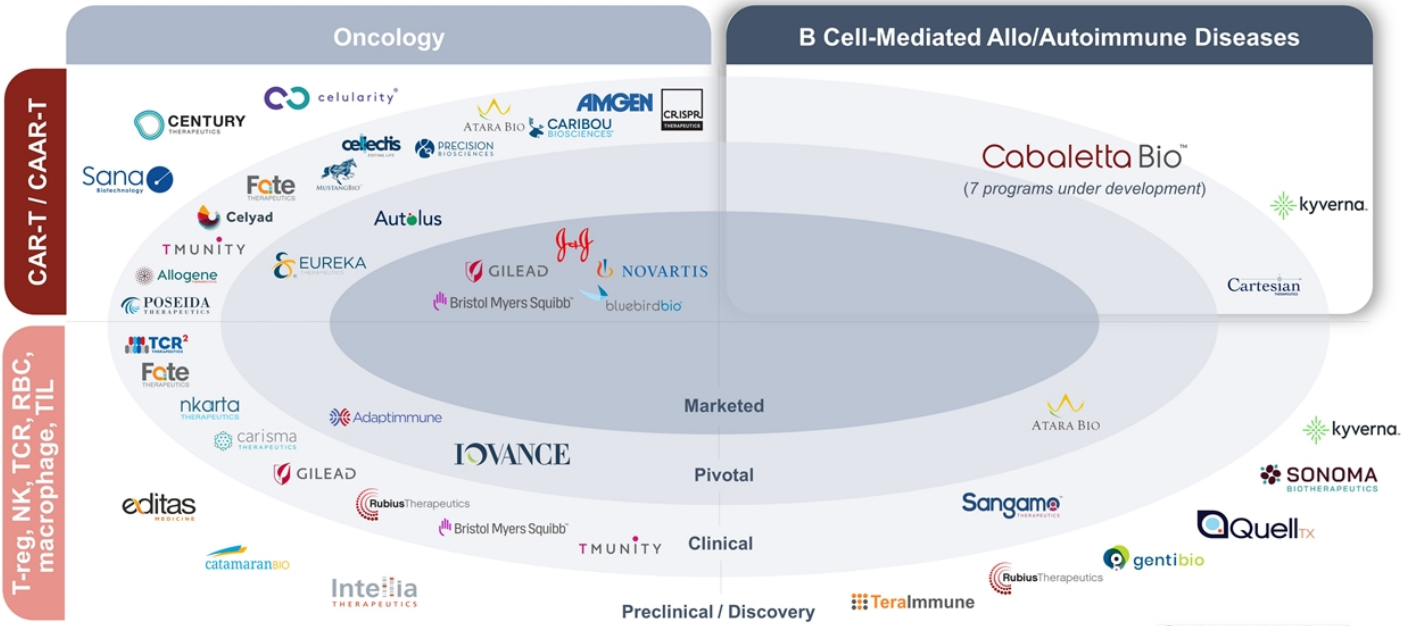
Kymriah

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

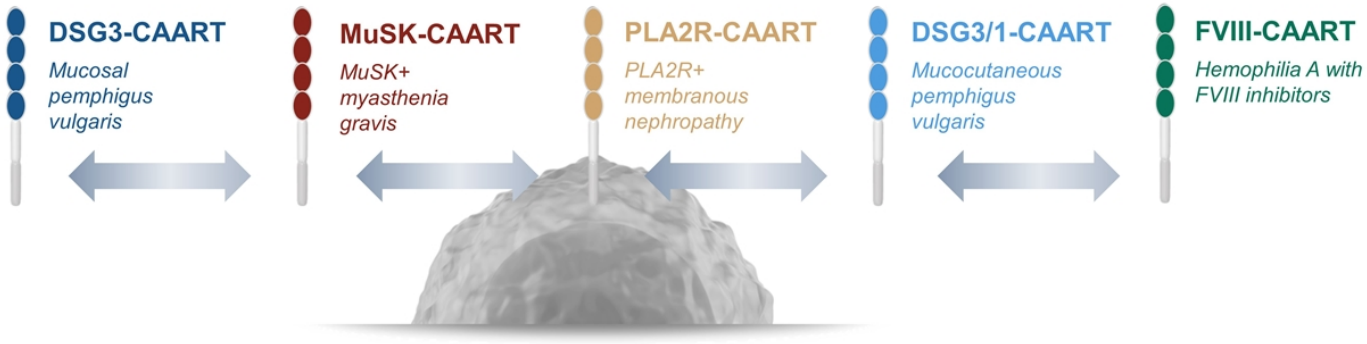


***Note**: Landscape for illustrative purposes only.*

Modular platform with “plug-and-play” architecture

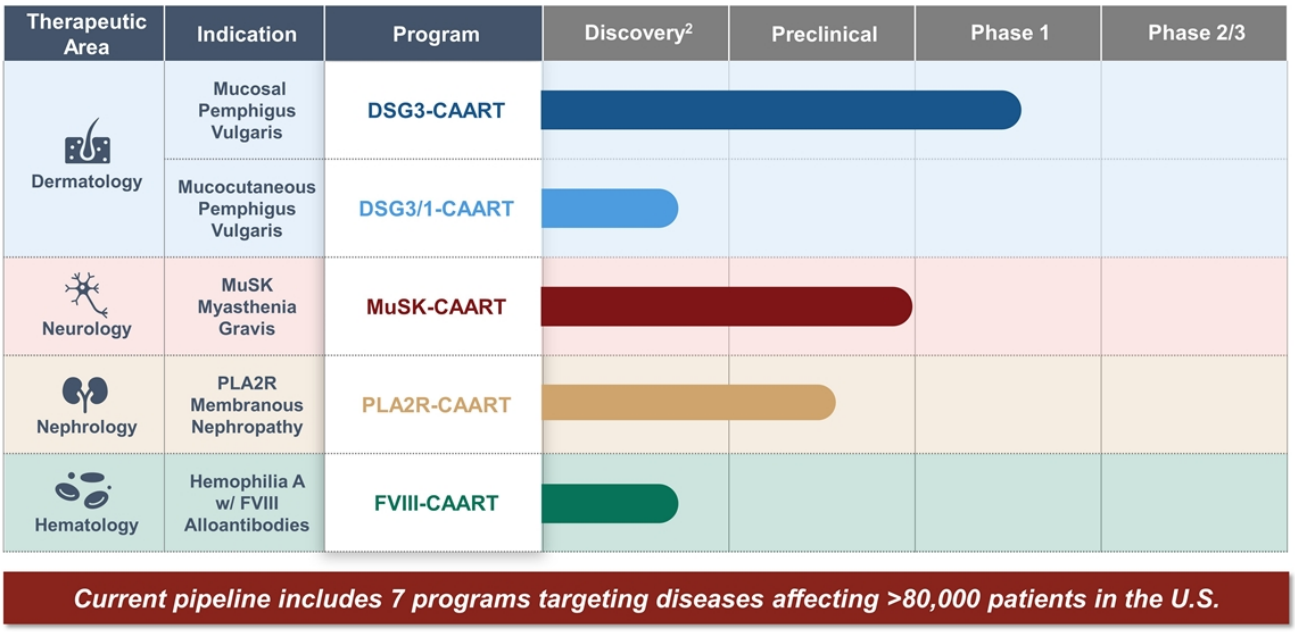
CABA™ platform designed to enable a portfolio of programs targeting B cell-mediated diseases

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



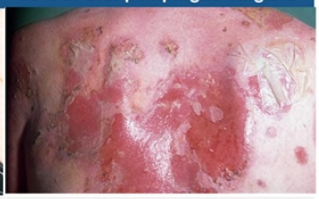
Current pipeline includes 7 programs targeting diseases affecting >80,000 patients in the U.S.

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]

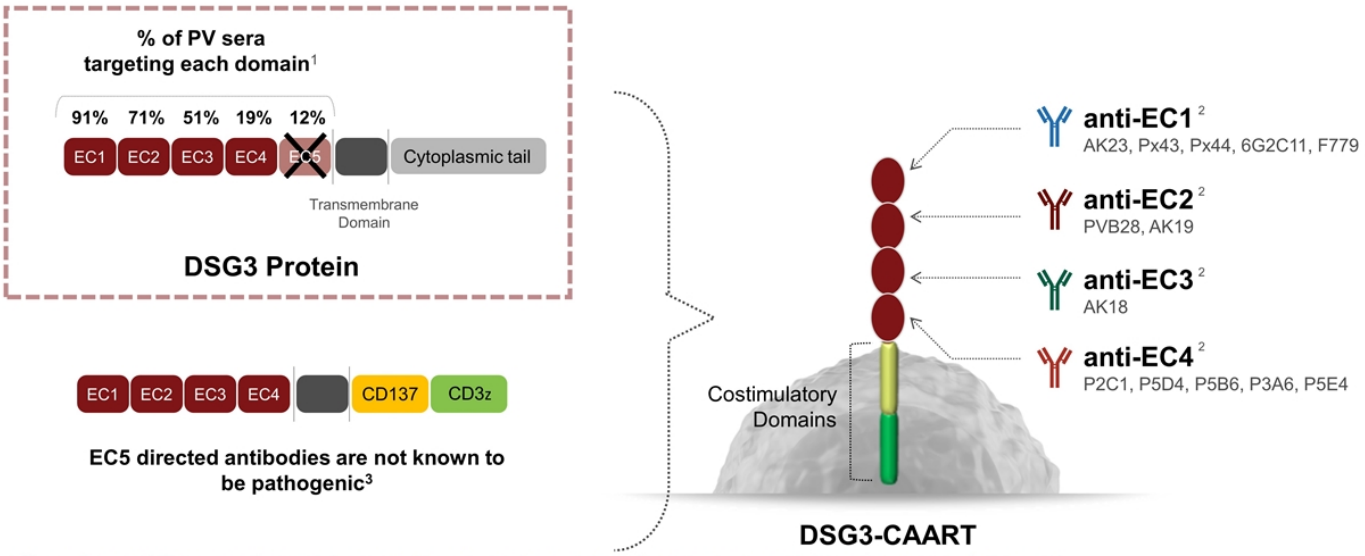
- Response: ~40% of patients achieved a 16-week period with no lesions or medicines during 1 yr[4,5]
- 22% annual serious adverse event (SAE) rate[4]
  - 4-9%[3,4,5] annual risk of severe infection in PV
- Real world data indicate:
  - *Transient* remission ~ 70% CROT[6]:
    - ~30% relapse in 1 year[6]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

Trial in patients with mPV evaluating up to 750x dose range (20M up to 10-15B cells)

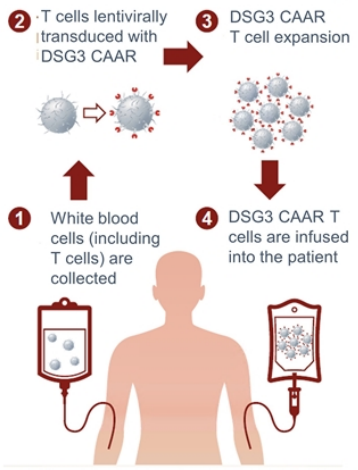
Screening → Apheresis → DSG3-CAART INFUSION → TREATMENT & FOLLOW-UP PERIOD → Next Patient

Major Inclusion Criteria

- Age: ≥18, confirmed diagnosis
- Inadequately managed by standard immunosuppressive therapies
- Confirmed diagnosis
- 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[2,3]	Subjects	Dose*
A1	3 (+3)	20M
A2	3 (+3)	100M
A3	3 (+3)	500M
A4	3 (+3)	2.5B
A5	3 (+3)	5.0B to 7.5B
A5e[4]	*3 (+3)*	*5.0B to 7.5B*
A6m[5]	*3 (+3)*	*10B to 15B*

Up to 750-fold dose escalation

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

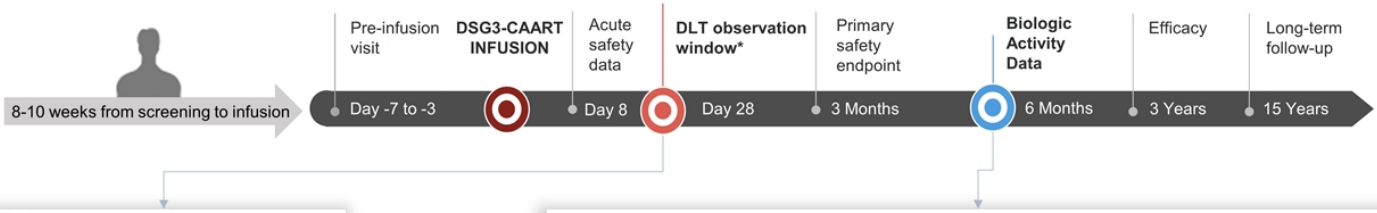
Secondary objectives:
- Manufacturing success rate
- DSG3-CAART persistence
- Anti-DSG3 antibody titer changes
- Concomitant medication changes
- Clinical disease activity score changes

1. Phase 1 Trial (NCT04422912).
2. 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.
3. Cohort progression following A5 (e.g. A5e or A6m) is to be prioritized according to emerging data and discussions with the FDA, as applicable.
4. Cohort A5e reflects an enhanced manufacturing process designed to amplify the already present cell subtypes in the product in order to potentially improve product potency and trafficking.
5. Cohort A6m reflects a multi-dose regimen where patients will receive a total of 10 to 15 billion cells.

* *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 A (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)
- Change in mPV therapy and/or new systemic rescue therapy
- Disease activity changes based on clinically validated scales
  - e.g. PDAI, ODSS

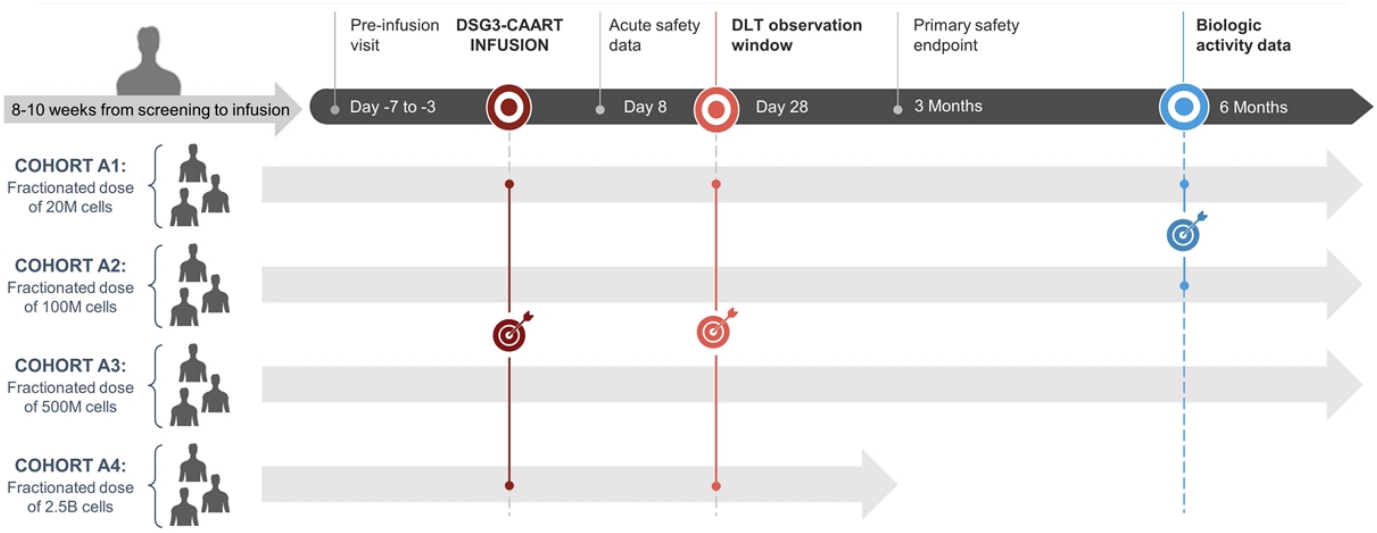
Data expected within 6 months of completion for each cohort

** 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*

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 to date in first 4 cohorts of DesCAARTes™ trial

Favorable safety profile at all reported doses of DSG3-CAART, including the 2.5B cell dose cohort

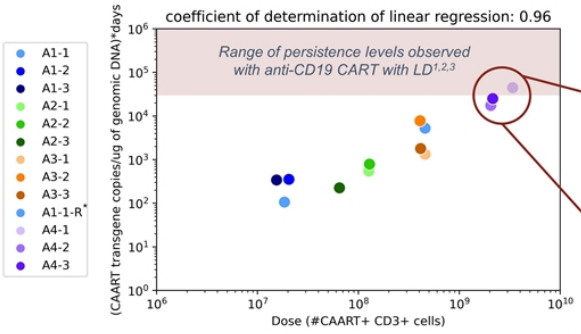


Cohort A5 (two-split fractionated dose of 5.0-7.5B cells) progressing; additional clinical data for cohort A4 expected to be provided at a scientific meeting in mid-2022

** 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).*

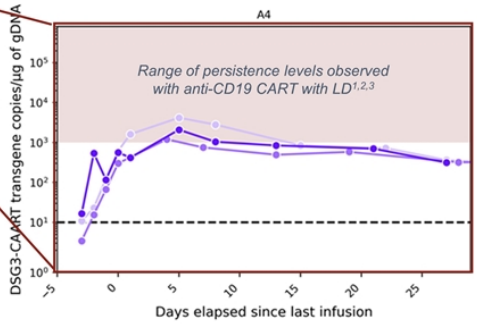
Dose-dependent persistence of DSG3-CAART in cohorts A1 to A4

DSG3-CAART persistence in cohort A4 approached levels seen in CART-19 with lymphodepletion in oncology



Persistence 'area under the curve' throughout 29 days post infusion was dose dependent

Persistence in cohort A4 approached the lower end of the range observed with anti-CD19 CART with lymphodepletion in oncology[1,2,3]



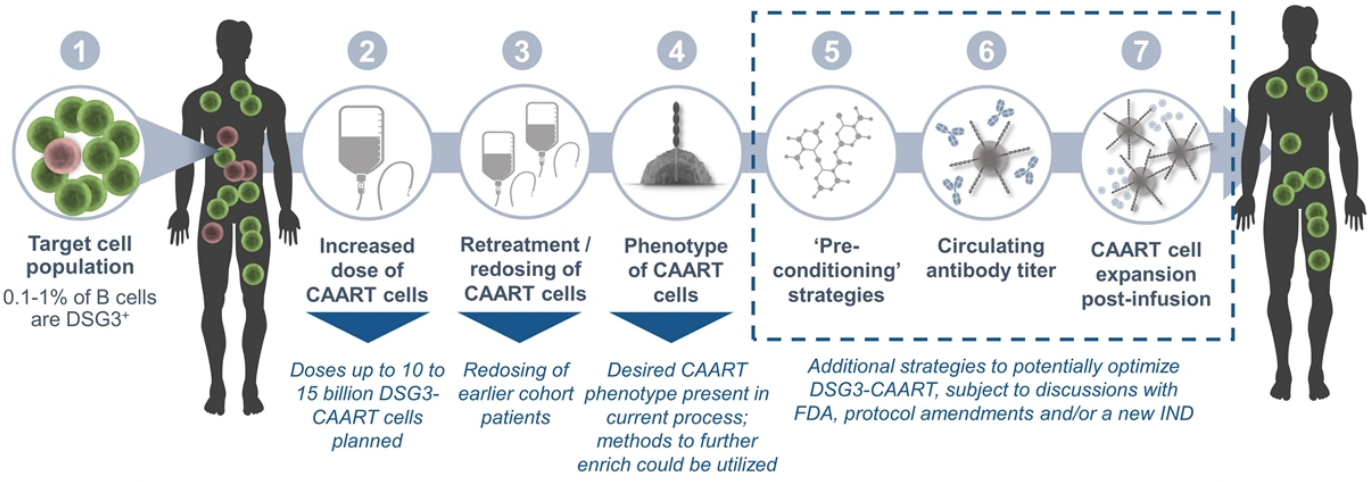
Ongoing & planned cohorts designed to further increase DSG3-CAART exposure

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.

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

Optimizing DSG3-CAART product and patient profiles

Range of strategies to consider for targeted cell therapy approaches in patients with autoimmune diseases



Many options exist to optimize product and patient profiles, ongoing evaluation of strategies to enhance DSG3-CAART exposure

CAART cell
Pathogenic autoreactive B cell
Healthy B cell

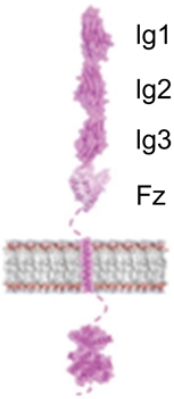
Cabaletta Bio®

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

All known extracellular domains can be included in the CAAR design

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

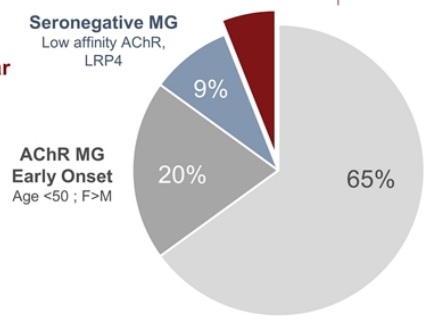
1. IgG4-dominant disease, similar to PV
2. Autoantibody titers drop after rituximab[1,2]
3. Pathogenic B cells are incompletely eliminated by rituximab and persist during relapse[3]



MuSK has similar modular structure and size as DSG3

MuSK MG
6.0 - 7.5%

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

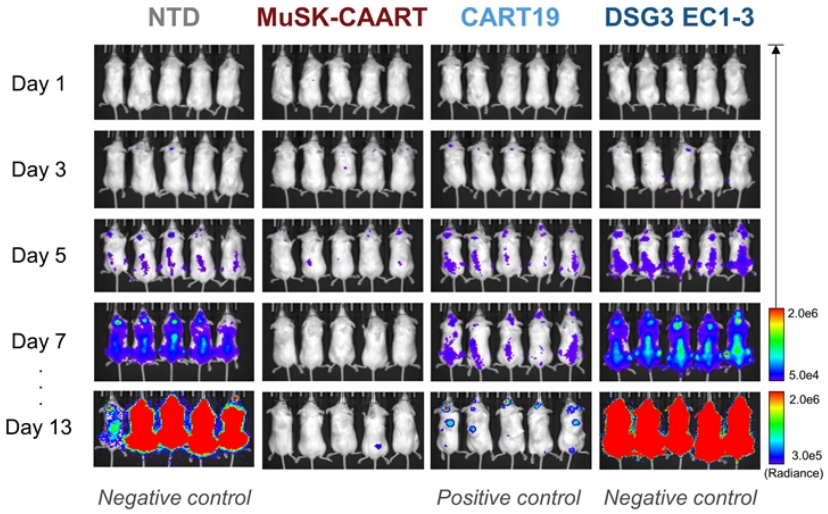


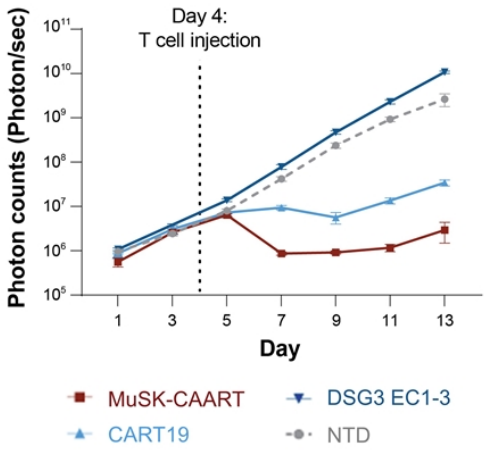
Total US MG Prevalence: 50,000 to 80,000 patients

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).

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 and 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 progression of 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

2 *Single dose rather than fractionation*

Part	Cohort	# Subjects
A – Dose Escalation Increasing dose levels with 2 (+4) design *(A1 – 100M*; A2 – 500M*; A3 – 2.5B*)*	A1-A3	2 (+4) per cohort
Highest planned selected dose[1] *(A4 – 5 to 7.5B*)*	A4	6
B – Expansion Expanded subject enrollment at final selected dose	B	~12

1 *Higher starting dose*

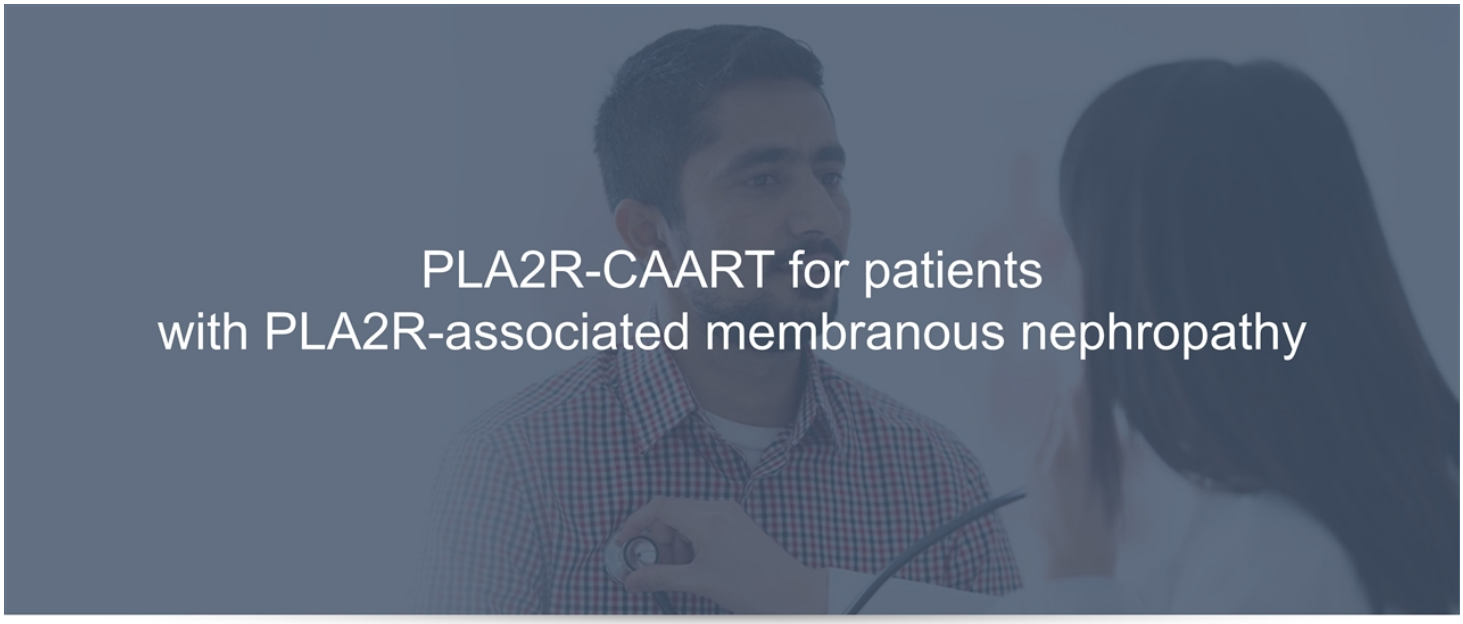
3 *versus 3 (+3) design in DesCAARTes™ trial*

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

** 100M, 500M, 2.5B and 5.0B to 7.5B refers to the number of MuSK-CAART cells infused for patients in dosing cohorts A1 to A4 (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.



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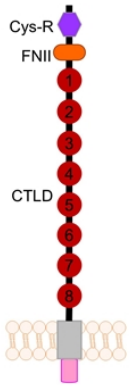
Preclinical stage CAART program in membranous nephropathy

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.

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Manufacturing strategy

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

Stage 1: Penn[1]	**Stage 2:** CDMOs & CABA Process	**Stage 3:** Cabaletta Facility Commercialization & Scale-Up
2019 –	2021 –	Data-gated, staged investment
Penn; Children's Hospital of Philadelphia	OxfordBioMedica; WuXi AppTec	Cabaletta Bio®
• Cell processing capacity secured through Penn partnership • SOPs previously used to develop an FDA approved product • Clinical vector validated	• CDMOs for vector and cell processing with commercial support capabilities	• Leasing followed by engineering and build out of Cabaletta-owned manufacturing facility

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.

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Cabaletta Bio leadership

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tengion
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Adaptimmune
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Gwendolyn Binder, Ph.D.
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Multiple potential data catalysts with possible pipeline read-through

DesCAARTes™ trial ongoing: Currently progressing cohort A5 (5.0-7.5B cells)

- Data presented at ASGCT 2022 demonstrate dose-dependent increase in persistence
  - Cohort A4 persistence approached the lower end of the range seen in anti-CD19 CART with LD in oncology[1,2,3]
  - Demonstrated a favorable safety profile in cohorts A1 to A4
- Additional data from the DesCAARTes trial anticipated at scientific meetings in mid-2022
  - Clinical and translational data for cohort A4[4]
  - 28-day safety data for cohort A5[4]
- Multiple additional planned cohorts designed to enhance DSG3-CAART exposure

MuSK-CAART: Plan to initiate first-in-human trial in 2022; received FDA Fast Track Designation

Expanding network of academic & industry partners

WuXi AppTec, ARTISANBIO, Penn, Yale, Stanford Medicine, OxfordBioMedica, Children's Hospital of Philadelphia, UC Davis, Iowa

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. Assumes no dose-limiting toxicities are observed during each cohort, uninterrupted enrollment and no delays due to COVID-19 resurgence occur in the trial.

* *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).*

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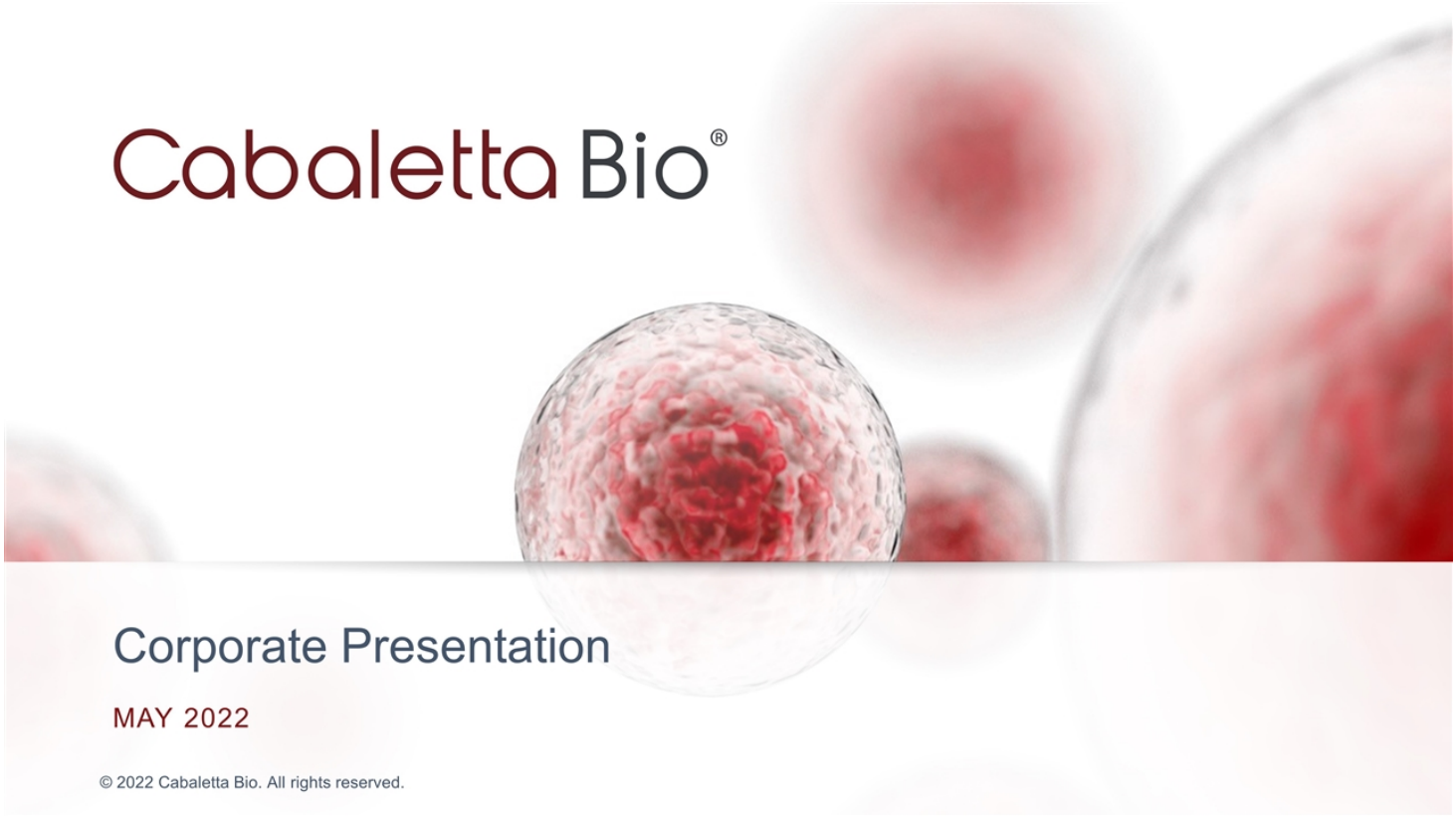

Corporate Presentation

MAY 2022

Cabaletta Bio®

Cabaletta Bio Presents Updated Interim DesCAARTes™
Trial Phase 1 Data at the ASGCT 25th Annual Meeting

PHILADELPHIA, May 18, 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 A3, safety data through 3 months and persistence data through 1 month offollow-up in cohorts A1 through A4 from the DesCAARTes™ trial at the American Society of Gene & Cell Therapy (ASGCT) 25th Annual Meeting being held in Washington, D.C. from May16-19, 2022.

"At ASGCT, we presented updated interim data showing that DSG3-CAART has had a favorable safety profile with no dose limiting toxicities or cytokine release syndrome of any grade through cohort A4, which was a dose of 2.5 billion DSG3-CAART cells. In addition, we have observed a dose dependent increase in DSG3-CAART persistence, which at cohort A4 approached the lower end of the range that is observed in anti-CD19 CART oncology studies in combination with lymphodepletion," said David Chang, M.D., Chief Medical Officer of Cabaletta. "These data continue to support the planned dose escalation in this trial and our conviction in the potential of this program. As we progress through additional cohorts of the study, we look forward to evaluating the relationship between DSG3-CAART persistence and potential clinical responses in patients with mPV along with the opportunity to explore higher doses and an enhanced manufacturing process to meet our goal of reaching deep, durable and potentially curative responses for these patients."

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 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). The trial is currently in cohort A5 (5.0 to 7.5 billion cells) and is being conducted across multiple clinical sites throughout the United States. The Company plans to include two new additional dose cohorts – A5e (enhanced manufacturing process at 5.0 to 7.5 billion cells) and A6m (multi-dose regimen at 10 to 15 billion cells). The prioritization of cohorts following cohort A5 (e.g. A5e or A6m) is subject to evaluation of emerging data and discussions with the FDA, as applicable.

The updated interim DesCAARTes™ trial Phase 1 data included 12 treated subjects, four cohorts with three patients per cohort; nine having completed six months follow up after DSG3-CAART infusion. The posters as presented at ASGCT are available at https://www.cabalettabio.com/technology/posters-publications. The data show:

- No DLTs, CRS of any grade, or related serious AEs were observed in any subject within three months of DSG3-CAART infusion through cohort A4 (2.5 billion cells).

- There was a dose dependent increase in DSG3-CAART persistence through day 29 in cohorts A1 to A4, indicating that DSG3-CAART cells were not eliminated through immune-mediated rejection.
    - Persistence (AUC_{d29} and C_{max}) in cohort A4 approached the lower end of the range that is observed in clinical trials of anti-CD19 CART combined with lymphodepletion in B-cell malignancies
- In cohorts A1 to A3:
    - Disease activity was clear or almost clear (PDAI 0-1) in 0/9 subjects at screening, 1/9 at pre-infusion, 2/9 at month one, 5/9 at month two, 3/9 at month three, 2/9 at month four, 3/9 at month five and 1/9 at month six after treatment.
    - Through six months post DSG3-CAART infusion, no clear pattern was observed in changes in anti-DSG3 Ab levels (ELISA) or disease activity (PDAI) in the low dose cohorts where the A3 dose (500 million cells) represents 6.7 to 10% of the ongoing cohort A5 dose (5.0 to 7.5 billion cells).
- One subject from cohort A1 was retreated with 500 million cells (the cohort A3 dose) and persistence in the subject was similar to the three subjects who were originally administered the cohort A3 dose, suggesting that there was not immune-mediated clearance of DSG3-CAART cells after retreatment and repeat dosing of patients is possible, if indicated.

Data presented on the company's manufacturing process were as follows:

- In cohorts A1-A4, the manufacturing success rate was 100% with functional DSG3-CAART cells manufactured successfully from mPV patient apheresis material.
- Infused DSG3-CAART cells exhibited a stem cell or central memory phenotype with a strong positive correlation between the dose of gene modified T cells and post-infusion persistence to day 29.
- These data suggest that DSG3-CAART cells are not being eliminated by the pre-existing anti-DSG3 immunity present in mPV.

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.

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 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 from cohorts A1 through A3 of the DesCAARTes™ trial, including 3-month safety and 1-month persistence data in cohorts A1 through A4, described herein; the expected timing and significance of the announcement of 28-day safety for cohort A5 and clinical and translational data for cohort A4 in mid-2022; the expectation that Cabaletta may improve outcomes for patients suffering from mPV; Cabaletta's ability to continue progressing in cohort A5, including the planned addition of an enhanced manufacturing process; Cabaletta's ability to escalate dosing as high as 10 to 15 billion cells in a planned future cohort or otherwise; 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; Cabaletta's ability to safely retreat additional patients and whether Cabaletta will continue to observe a lack of immune-mediated clearance of DSG3-CAART cells after retreatment and repeat dosing of patients; the expectation that Cabaletta Bio may improve outcomes for patients suffering from MuSK MG; 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; Cabaletta's plans to advance development of its preclinical pipeline; presentation of additional data at upcoming scientific conferences, and other preclinical data; 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.

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 and clinical trials of DSG3-CAART; 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, such as the ongoing COVID-19 pandemic, affecting countries or regions in which we have operations or do business; Cabaletta's ability to retain and recognize the intended incentives conferred by Orphan Drug Designation and Fast Track Designation for DSG3-CAART for improving healing of mucosal blisters in patients with mucosal pemphigus vulgaris; Cabaletta's ability to demonstrate sufficient evidence of safety, efficacy and tolerability in its preclinical and clinical trials of DSG3-CAART; 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 initial or interim results of preclinical studies or clinical studies will not be predictive of future results in connection with future studies. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause Cabaletta's actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in Cabaletta's most recent annual report on Form 10-K as well as discussions of potential risks, uncertainties, and other important factors in Cabaletta's other filings with the Securities and Exchange Commission. All information in this press release is as of the date of the release, and Cabaletta undertakes no duty to update this information unless required by law.

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