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

August 18, 2021
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 August 18, 2021, 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 August 18, 2021, the Company issued a press release announcing clinical data from the second dose cohort in its ongoing DesCAARTes™ Phase 1 clinical trial of DSG3-CAART for the treatment of patients with mucosal-dominant pemphigus vulgaris. 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 August 18, 2021, furnished herewith.
99.2	Press Release issued by the registrant on August 18, 2021.
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.

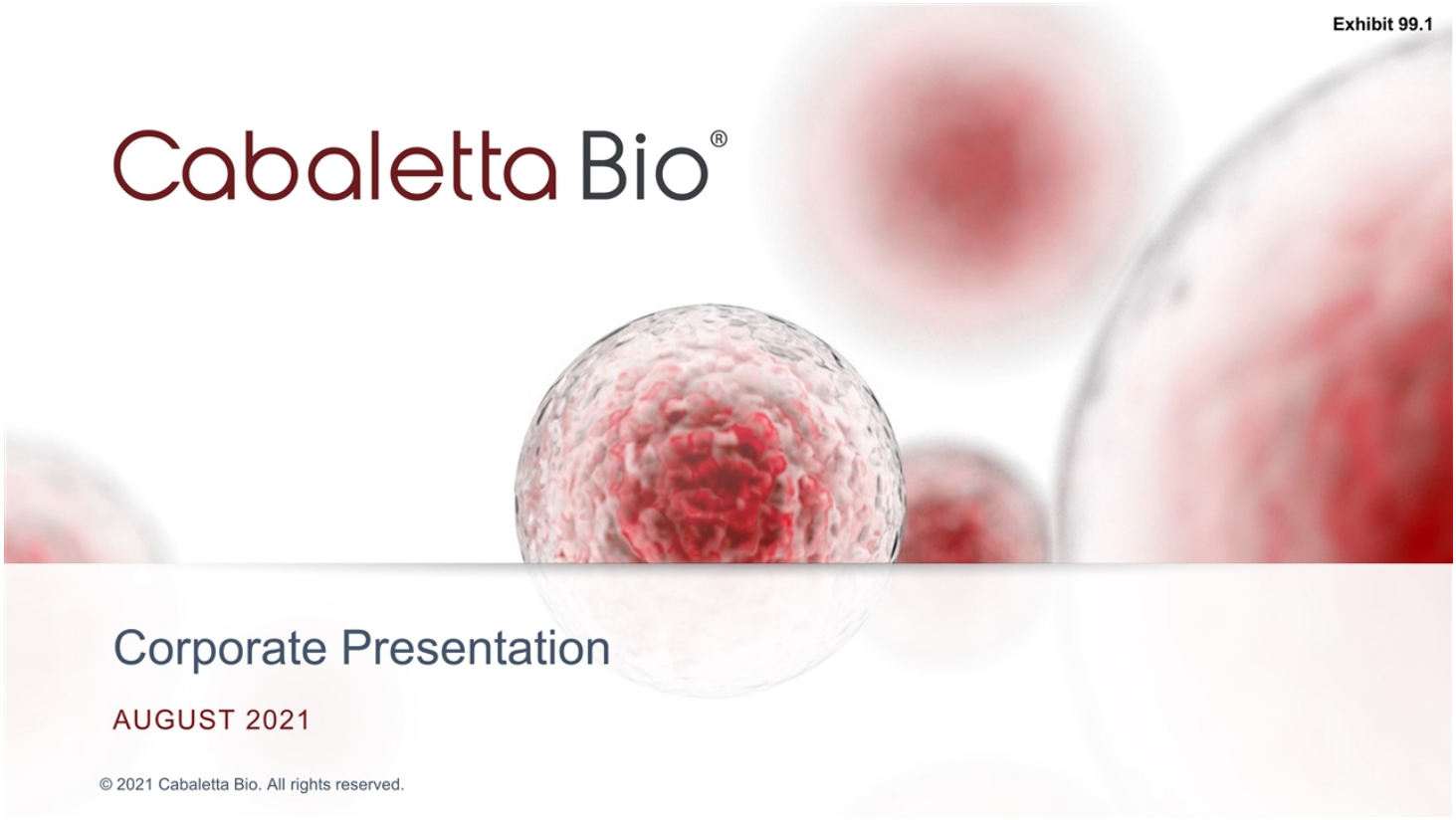
CABALETTA BIO, INC.

Date: August 18, 2021

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

Exhibit 99.1

Cabaletta Bio®



Corporate Presentation

AUGUST 2021

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 CAR T technology and CABA platform; the therapeutic potential and clinical benefits of our product candidates; our ability to successfully complete our preclinical and clinical studies for our product candidates, including our ongoing Phase 1 DesCAARTes™ trial, MuSK-CAART study and other discovery programs; our ability to obtain and maintain regulatory approval of our product candidates, including our planned IND submission for our MuSK-CAART program; 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 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 during 2021; and our ability to fund operations for at least the next 12 months. 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 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, 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 productive 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 2020 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

- Where there is a biologic opportunity for deep and durable, perhaps curative, responses
- Leveraging a clinically validated CAR T product design and manufacturing process through Penn alliance

DesCAARTes™ trial enrolling patients with mucosal pemphigus vulgaris (mPV) at 500M cell dose

- No DLTs or clinically relevant AEs observed to date[1] in all 6 patients following completion of first 2 dose cohorts (20M & 100M cells)
- DSG3-CAART persistence observed via qPCR in all 6 patients within the first 2 dose cohorts during the first 28 days following infusion
  - Without lymphodepletion and in presence of circulating anti-DSG3 antibodies
- Potential to report biologic activity data (20M & 100M) and safety data (500M cells) this year[2]

Preclinical pipeline led by MuSK-CAART for myasthenia gravis – IND filing planned in 2H21

- PLA2R-CAART pre-IND interaction with FDA anticipated in 2H21 for PLA2R positive primary membranous nephropathy patients
- Product portfolio[3] currently targeting diseases that affect over 80,000 patients in the US

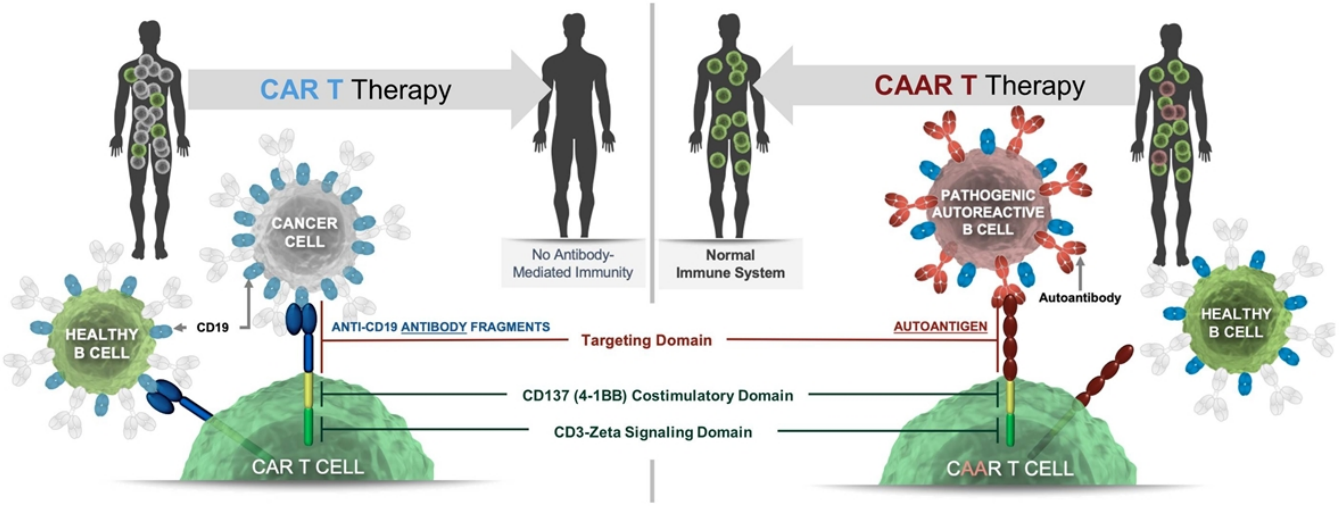
Cash runway through at least 4Q22 with $103M in cash and investments as of June 30, 2021

** 20M, 100M & 500M refers to the number of DSG3-CAART cells infused for patients in dosing cohorts 1-3, in millions.*

1. As of August 17, 2021.
2. Assumes no dose-limiting toxicities are observed during cohort and uninterrupted enrollment occurs in the trial.
3. 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

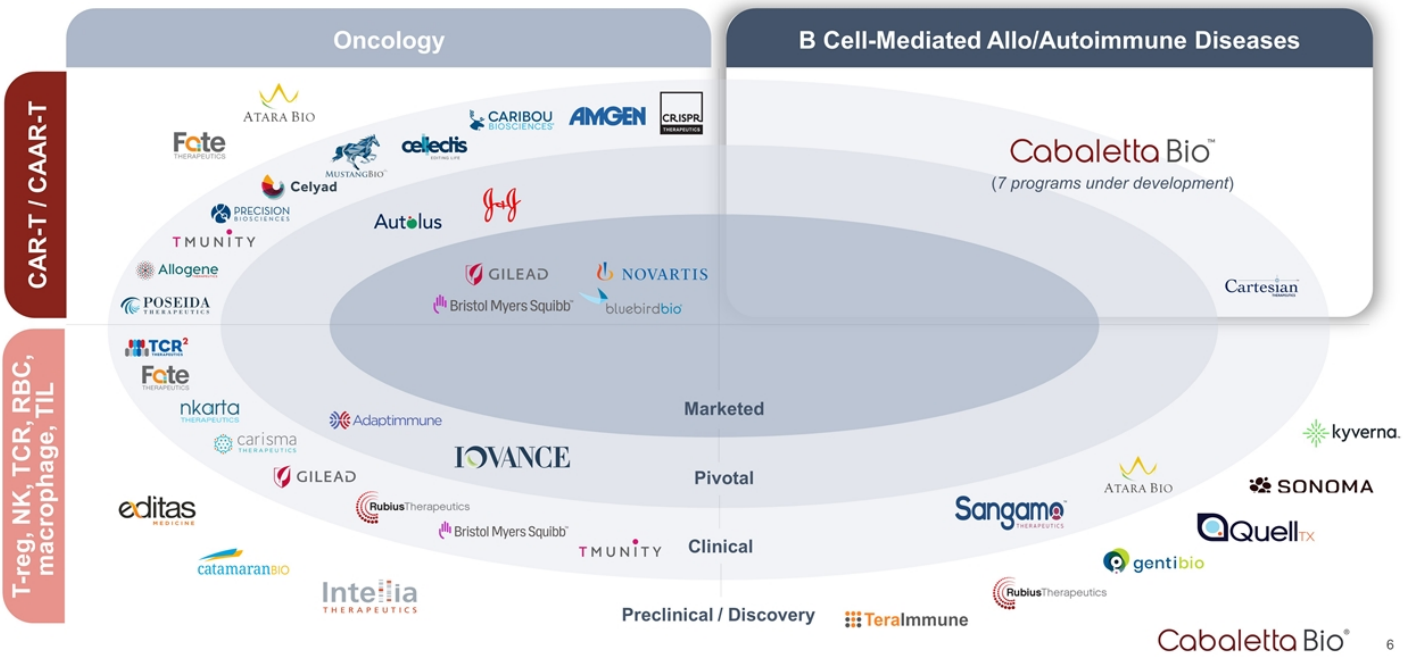
Kymriah

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



CABA platform may apply across a range of autoimmune diseases

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

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

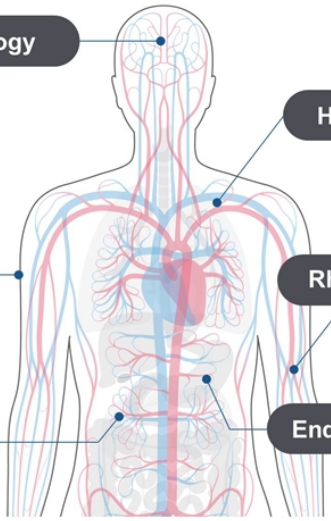
Hematology
- Immune Thrombocytopenic Purpura[3]
- Thrombotic Thrombocytopenic Purpura[1,2,3]
- Antiphospholipid Syndrome[4,5]
- Autoimmune Hemolytic Anemia[3]

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

Rheumatology
- Rheumatoid Arthritis[2,3,4]
- Systemic lupus erythematosus[3,4,5]
- ANCA-Associated Vasculitis[3,4,5]
- Myositis[5]

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

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



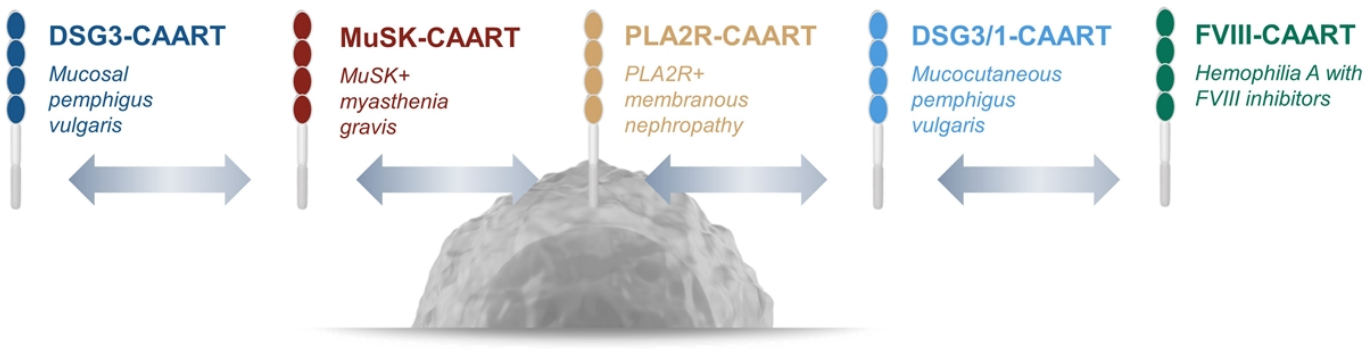
** Illustrative list of diseases where biologic opportunity for cure or treatment may be possible.*

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

Modular platform with “plug-and-play” architecture

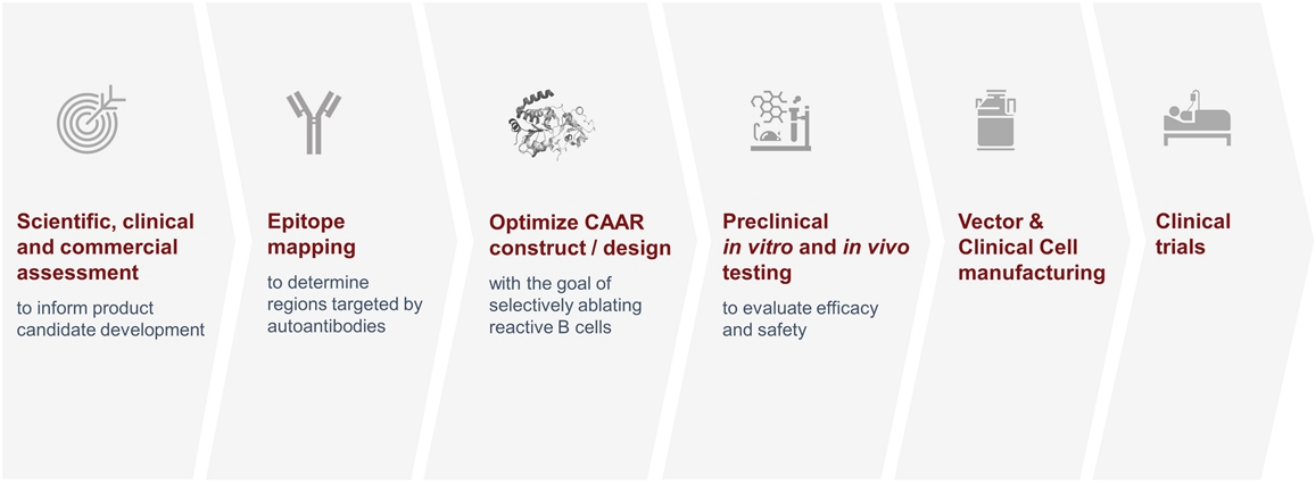
Technology foundation designed to enable a portfolio of programs targeting B cell-mediated diseases

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

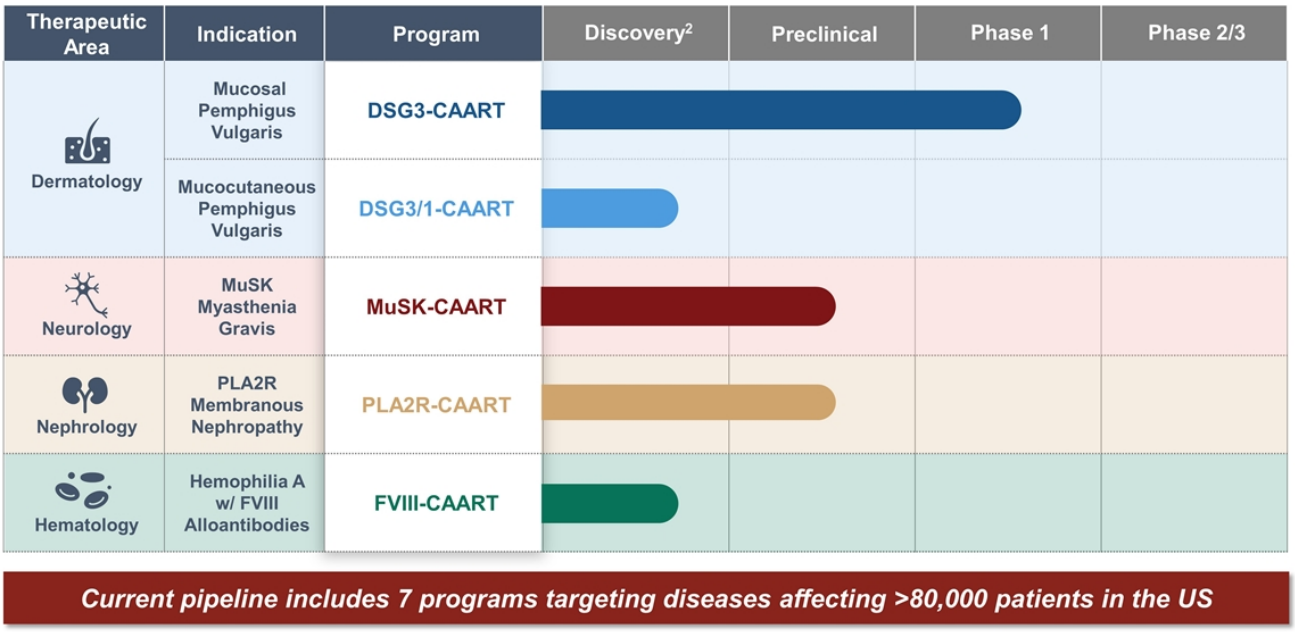


Clinically validated engineered T cell platform is the foundational technology

CABA (Cabaletta Approach for Selective B cell Ablation) platform



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



Current pipeline includes 7 programs targeting diseases affecting >80,000 patients in the US

1. Two additional undisclosed disease targets added to our pipeline portfolio through expansion of our Sponsored Research Agreement with the University of Pennsylvania are not shown.
2. In our discovery stage, we perform epitope mapping and optimize CAAR construct and design.

Data from the DesCAARTes™ trial provides read-through to pipeline

Manufacturing

- Strong operating partnership with Penn CVPF manufacturing organization
- Use of validated process from CAR T experience at Penn helps mitigate risk
- 100% success rate for DesCAARTes™ trial manufacturing to date[1]

Clinical data

- No DLTs or any clinically relevant toxicities observed to date[1] in all 6 patients
  - DSG3-CAART persistence via qPCR in all patients during 28 days post infusion
  - Without lymphodepletion, but in presence of circulating anti-DSG3 antibodies
- Potential to report biologic activity (20M & 100M) and 28-day safety data (500M) in 4Q21

Biologic Activity Indicators

- We are evaluating:
  - Persistence of DSG3-CAART detected via qPCR
  - Change in level of DSG3 antibodies (targeting persistent reduction)
  - Reduced mPV therapy and absence of new systemic rescue therapy
  - Change in disease activity based on clinically validated scales (e.g. PDAI, ODSS)

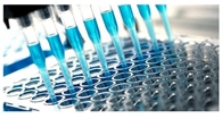
1. As of August 17, 2021.
2. Data expected within 6 months of completion for each cohort

Cabaletta Bio®

PV is an optimal lead indication for CAAR T therapy

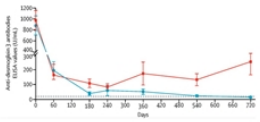
DSG3 antibodies are widely considered to be necessary and sufficient to cause PV[1]

1



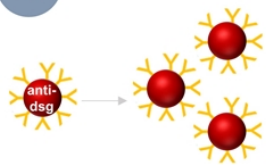
Serum anti-DSG3 **antibodies are 98 - 100% sensitive *and* specific**[2]

2



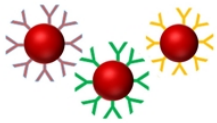
Depletion of B cells by rituximab[3] or antibody by plasmapheresis **transiently improves clinical disease**

3



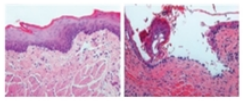
Incomplete B cell depletion by rituximab leads to PV recurrences, with **identical disease-causing B cell clones**[4,5]

4



The B cell repertoire and **antigenic epitopes** on DSG1/3 **are well understood**[6], and formed the basis for DSG3 and DSG1 CAAR designs

5

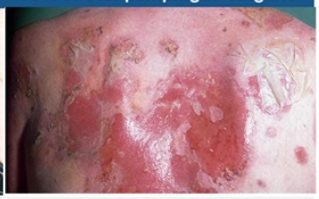


The DSG3 CAAR has **published animal model** proof-of-concept validation[7]

1. Spindler, Volker, et al. "Mechanisms causing loss of keratinocyte cohesion in pemphigus." Journal of Investigative Dermatology 138.1 (2018): 32-37.
2. Schmidt, Enno, et al. "Novel ELISA systems for antibodies to desmoglein 1 and 3." Experimental dermatology 19.5 (2010): 458-463.
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. Mouquet, Hugo, et al. "B-cell depletion immunotherapy in pemphigus: effects on cellular and humoral immune responses." Journal of Investigative Dermatology 128.12 (2008): 2859-2869.
5. Hammers, Christoph M., et al. "Persistence of anti-desmoglein 3 IgG+ B-cell clones in pemphigus patients over years." Journal of Investigative Dermatology 135.3 (2015): 742-749.
6. 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.
7. Ellebrecht, Christoph T., et al. "Reengineering chimeric antigen receptor T cells for targeted therapy of autoimmune disease." Science 353.6295 (2016): 179-184.

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]

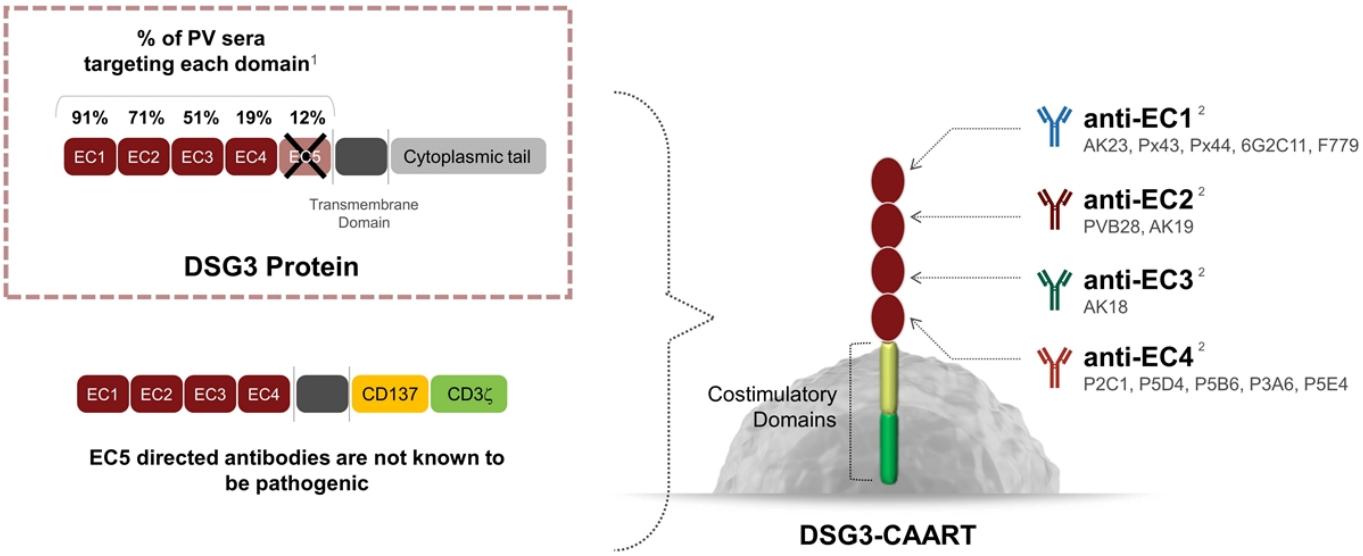
- Response: ~40% of patients achieved a 16-week period with no lesions or medicines during 1 yr[4,5]
- 22% annual serious adverse event (SAE) rate[4]
  - 4-9%[3,4,5] annual risk of severe infection in PV
- Real world data indicate:
  - *Transient* remission ~ 70% CROT[6]:
    - ~30% relapse in 1 year[6]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

DSG3-CAART preclinical data[1,2]

No evidence of toxicity at clinically relevant doses with selective and specific target engagement

	INDICATOR	RESULTS
Tolerability	***In vitro* off-target toxicity**	No specific cytotoxicity at clinically relevant cell numbers vs FcγR-expressing cells No confirmed interactions with human membrane proteins
	***In vivo* off-target toxicity**	No off-target effects detected at clinically relevant doses
Target Engagement	**Anti-DSG3 autoantibody titer**	Serologic 'remission' – dose-dependent elimination of anti-DSG3 B cells and antibodies
	CAAR T cell engraftment	Dose-dependent increase in CAAR-positive cells observed via flow cytometry
	Tissue blistering	Histologic 'remission' – no blistering of oral mucosa
	Anti-DSG3 hybridoma outgrowth	Significantly delayed outgrowth despite soluble anti-DSG antibodies

1. Ellebrecht, Christoph T., et al. "Reengineering chimeric antigen receptor T cells for targeted therapy of autoimmune disease." Science 353.6295 (2016): 179-184.
2. Lee, Jinmin, et al. "Antigen-specific B-cell depletion for precision therapy of mucosal pemphigus vulgaris." The Journal of Clinical Investigation (2020).

DesCAARTes™:

Phase 1 clinical trial in mucosal-dominant PV (mPV) patients

Open-label study to determine the maximum tolerated dose & fractionation of DSG3-CAART

Major Inclusion Criteria

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

Major Exclusion Criteria

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

SCREENING → MANUFACTURING → TREATMENT (~1 WEEK) → MONITORING (2-4 WEEKS) → Next Patient

Part	Cohort	# Subjects
A – Dose Escalation Fractionated infusion at increasing dose levels	A1-A4	3 (+3) per cohort
B – Dose Consolidation Consolidating selected dose fractions into a single infusion	B1-B2	3 (+3) per cohort
C – Expansion[1] Expanded subject enrollment at final selected dose	C	~12
	Total	**~30 (+18)**

Study Endpoint & Objectives

Primary Endpoint: Adverse Events, including Dose Limiting Toxicity (DLT)

- 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

Secondary Objectives: DSG3 ELISA titer changes, CAAR T expansion/persistence, change in PDAI, rate of/time to/duration of remission, manufacturing success rate

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.

DesCAARTes™ clinical trial assessments and timeframes

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

Day 28 safety data

Infusion of DSG3-CAART in context of circulating soluble Ab

Other safety measures

- CRS / neurotoxicity
- Other adverse events

Primary safety endpoint at 3 months

Potential for disease flare during planned steroid taper

Early evaluations of efficacy includes[1]:

- Persistence of DSG3-CAART detected via qPCR
- Change in level of DSG3 antibodies (targeting persistent reduction)
- Reduced mPV therapy and absence of new systemic rescue therapy
- Change in disease activity based on clinically validated scales
  - e.g. PDAI, ODSS

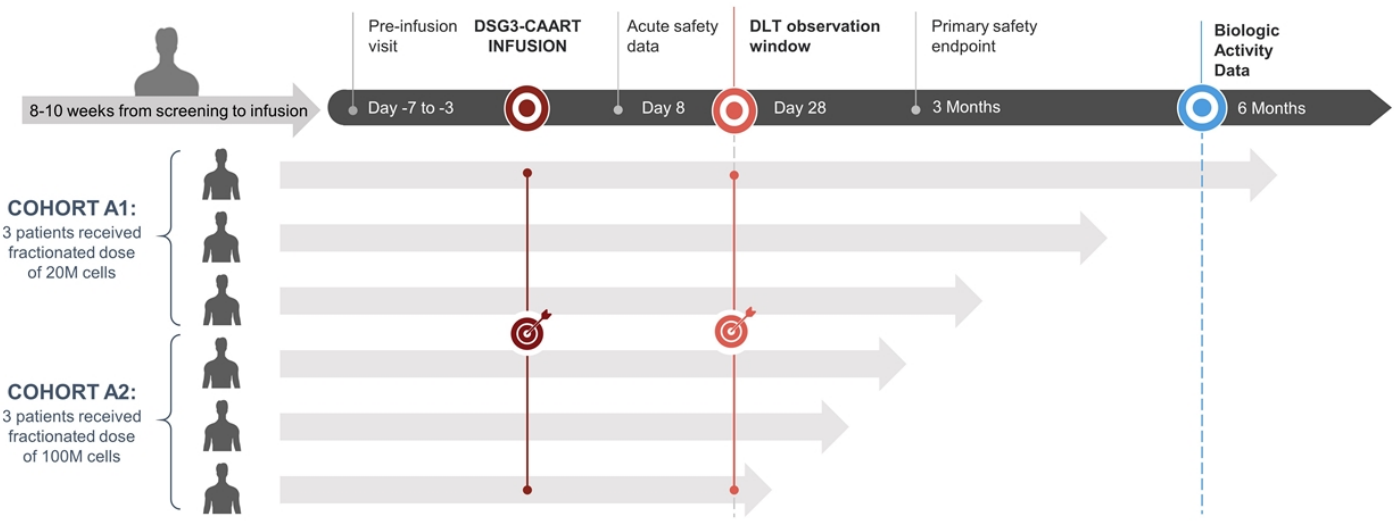
Data expected within 6 months of completion for each cohort

** Clearance of 28-day observation window without DLTs required to initiate next dosing cohort.*

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 1st or 2nd cohorts of DesCAARTes™ trial

DSG3-CAART persistence observed via qPCR across cohorts

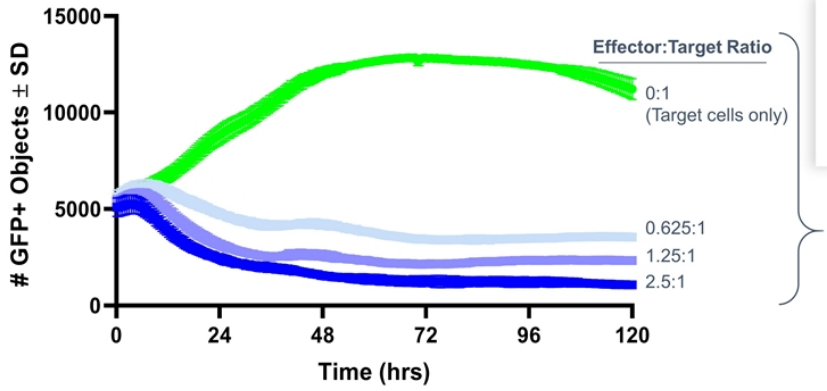


No clinically meaningful adverse events in any subject to date[1], enabling progression to cohort A3 with dose of 500M cells

1. As of August 17, 2021.

Manufactured DSG3-CAART cells exhibit target elimination *in vitro*

100% success rate for manufacturing of DSG3-CAART cells in DesCAARTes™ trial to date[1]



DSG3-CAART cells successfully engage & eliminate DSG3 antibody expressing target cells *in vitro*

Samples run in triplicate

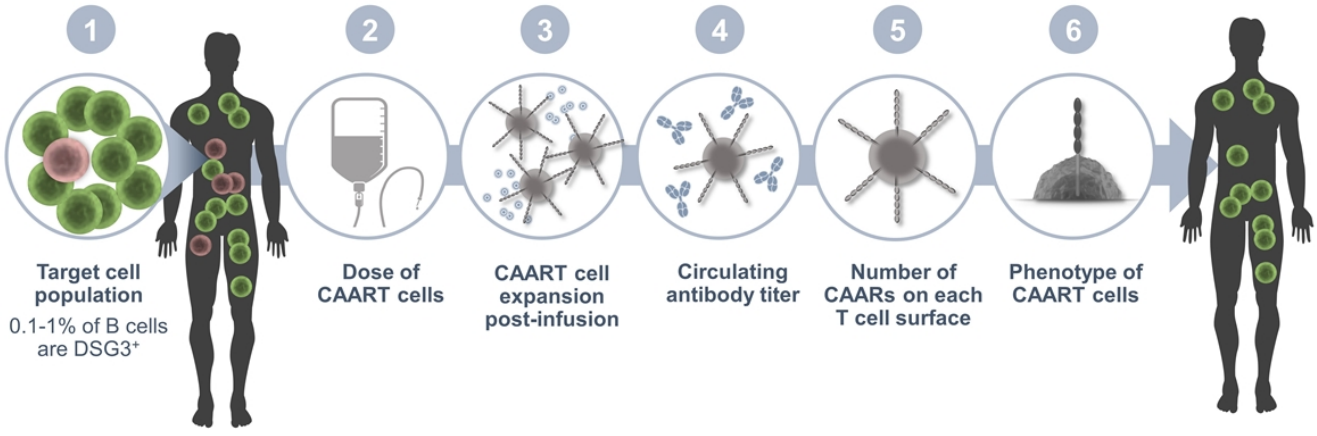
1 × 10^5 target cells per well

Manufacturing partnership with Penn is delivering necessary quality & capacity for the clinical trial requirements

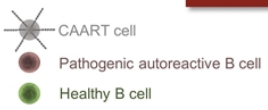
1. As of August 17, 2021.

Potential drivers of biologic activity in autoimmune disease

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



Many options exist to optimize product and patient profiles



Accelerating timelines for DesCAARTes™ trial

Rapid cadence of trial recruitment may enable enrollment & dosing of first 4 cohorts by end of 2021[1]

Growing clinical site network with high investigator engagement

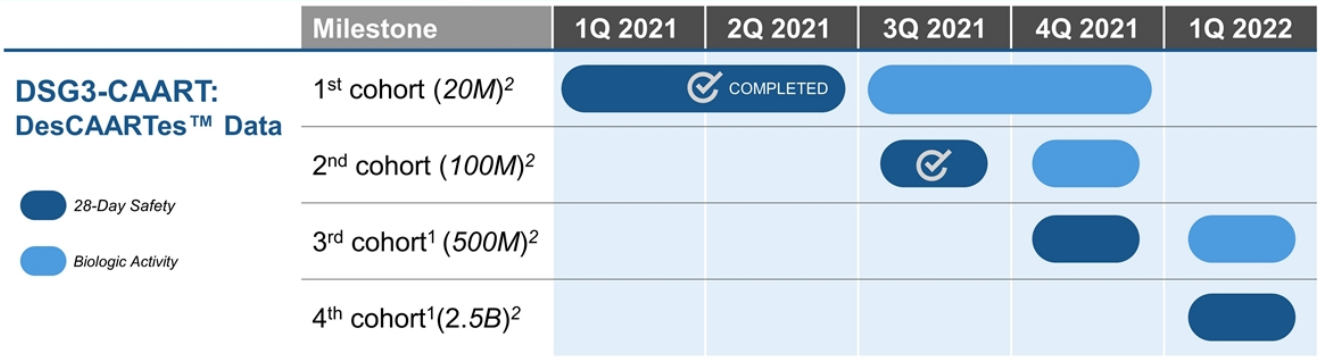
Penn · Stanford Medicine · UC Davis University of California

Expanding relationships with patient advocacy organizations

ippf · NORD National Organization for Rare Disorders · mg

Opportunities to accelerate development

ORPHAN DRUG · FAST TRACK



Accelerating development & learnings from DesCAARTes™ trial to inform MuSK-CAART & future programs

1. Assumes no dose-limiting toxicities are observed during cohort and uninterrupted enrollment occurs in the trial.
2. Number of transduced cells.

DSG3/1 CAART for mucocutaneous PV (mcPV)

Plan to submit an IND after review of DSG3-CAART safety and biologic activity data with FDA

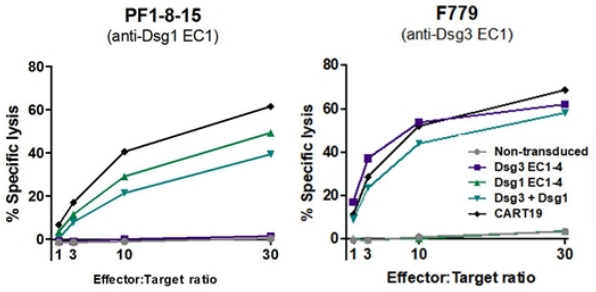
DSG3/1 CAARs designed for mcPV

- DSG3 and DSG1 autoantibodies
- Most severe and common form of PV (~75%)
- Mucosal blistering, plus skin erosion and blistering
- Managed with immune suppression, similar to mPV
  - High risk of relapse
  - Potential for hospitalizations and fatal infections

% of PV sera targeting each domain[1]

DSG1-CAART and DSG3-CAART both demonstrated specific cytotoxicity *in vitro*[2]

- Together, DSG1-CAART and DSG3-CAART demonstrated cytotoxicity towards anti-DSG3 and anti-DSG1 B cells



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. As presented at the 2018 International Investigative Dermatology conference.

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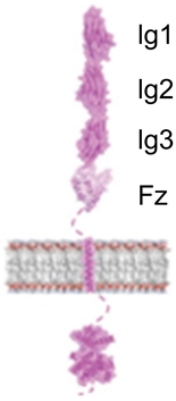
High unmet need in MuSK myasthenia gravis; a valuable CAAR target

All known extracellular domains can be included in the CAAR design

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

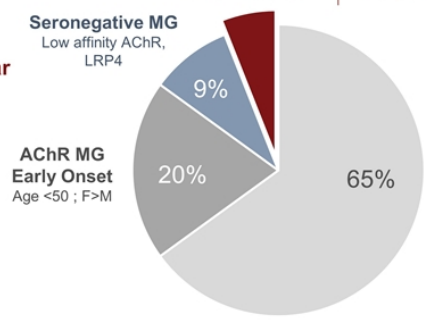
1. Autoantibody titers drop after rituximab[1,2]
2. Pathogenic B cells are incompletely eliminated by rituximab and persist during relapse[3]



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

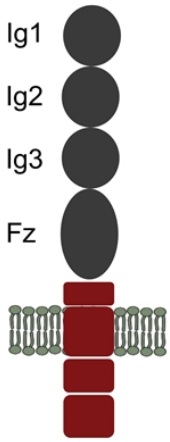


Total US MG Prevalence: 50,000 to 80,000 patients

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).

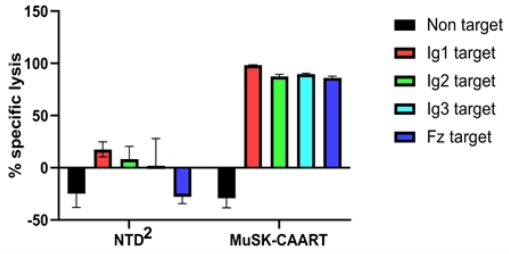
MuSK-CAART showed *in vitro* selective & specific target engagement[1]

Additional *in vitro* studies demonstrated no confirmed off-target toxicity observed with MuSK-CAART to date

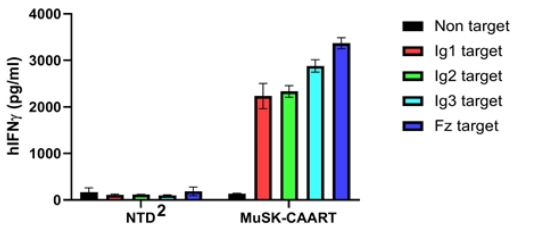


MuSK-CAART

MuSK-CAART cytotoxicity vs all epitopes tested[3]



Pro-inflammatory cytokine production[3]



MuSK-CAART observed to be specific for anti-MuSK antibody expressing cells *in vitro*

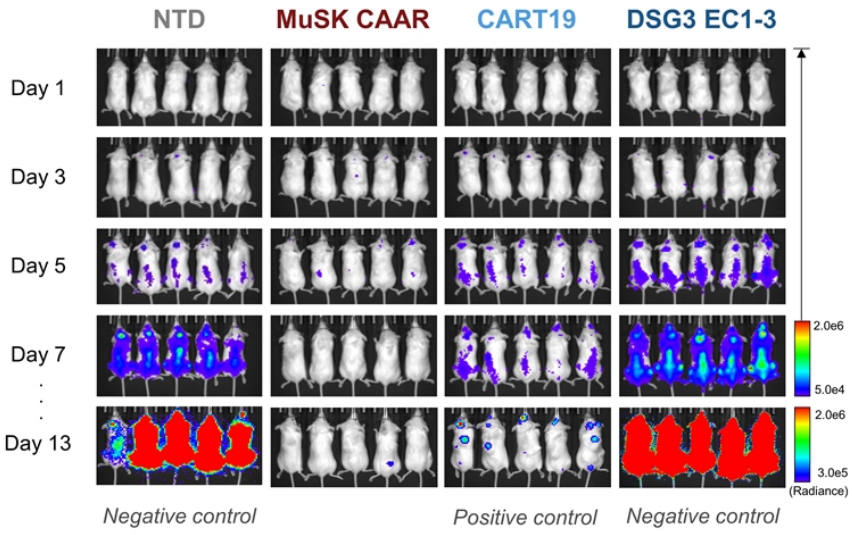
- No off-target toxicity observed *in vitro*
  - ~6,000 human membrane proteins evaluated
- No on-target toxicity observed *in vitro*
  - Cellular assays to evaluate cytotoxicity against native ligand LRP4

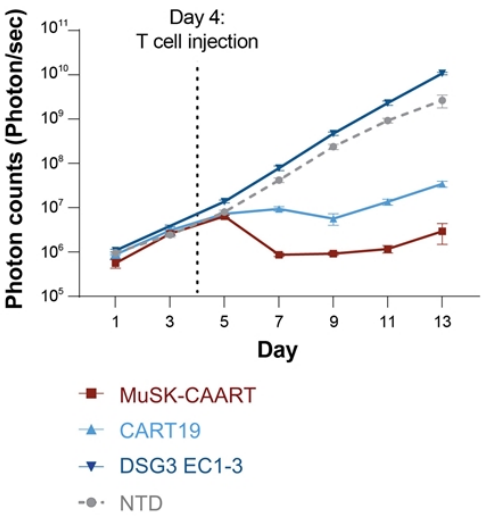
MuSK-CAART program on track for IND filing in 2H 2021

1. https://cabalettabio.com/technology/posters-publications.
2. NTD = non transduced T cell control against the same target cells
3. Target cells are the pre B cell line, Nalm-6, genetically modified to express anti-MuSK antibodies specific for one of the MuSK domains, Ig1, Ig2, Ig3, or Fz

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





1. https://cabalettabio.com/technology/posters-publications.
2. Target cells represent a B cell tumor line (CD19 positive) that has been modified to express the anti-MuSK antibody.

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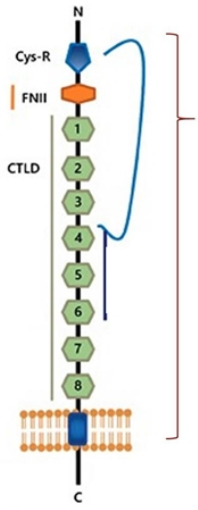
Preclinical stage CAART program in membranous nephropathy

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

Membranous nephropathy (MN) is a type of glomerular disease that causes nephrotic syndrome and may lead to kidney failure

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 precede and 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

- Single pass transmembrane protein with distinct immunogenic regions
- Epitopes are well-defined
- IgG4-dominant disease, similar to PV and MuSK MG

Request for pre-IND interaction submitted to FDA; anticipate interaction to be conducted in 2H21

Changing treatment paradigm highlights the role of B cells in disease

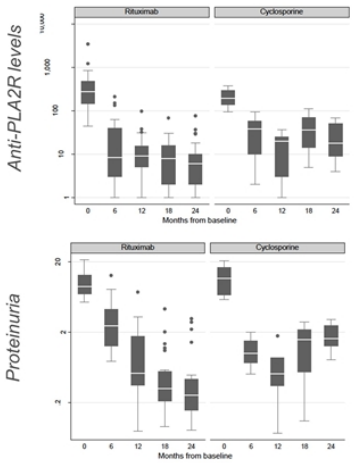
Opportunity to develop antigen-targeted therapy to address significant unmet need

High unmet need despite B cell-depleting therapies

- Rituximab increasing 1st line for medium to high-risk pts
  - 1/3 cure; 1/3 relapse; 1/3 fail[1]
  - Relapse of nephrotic syndrome occurs within 2-4 years
  - Preceded by return of B cells & PLA2R autoantibodies
- Patients with higher anti-PLA2R levels at baseline and with epitope spreading less likely to respond to rituximab
- Up to 30% of diagnosed patients develop ESRD

MENTOR trial results:

Antibody levels & proteinuria by group in patients with complete or partial remission at month 24

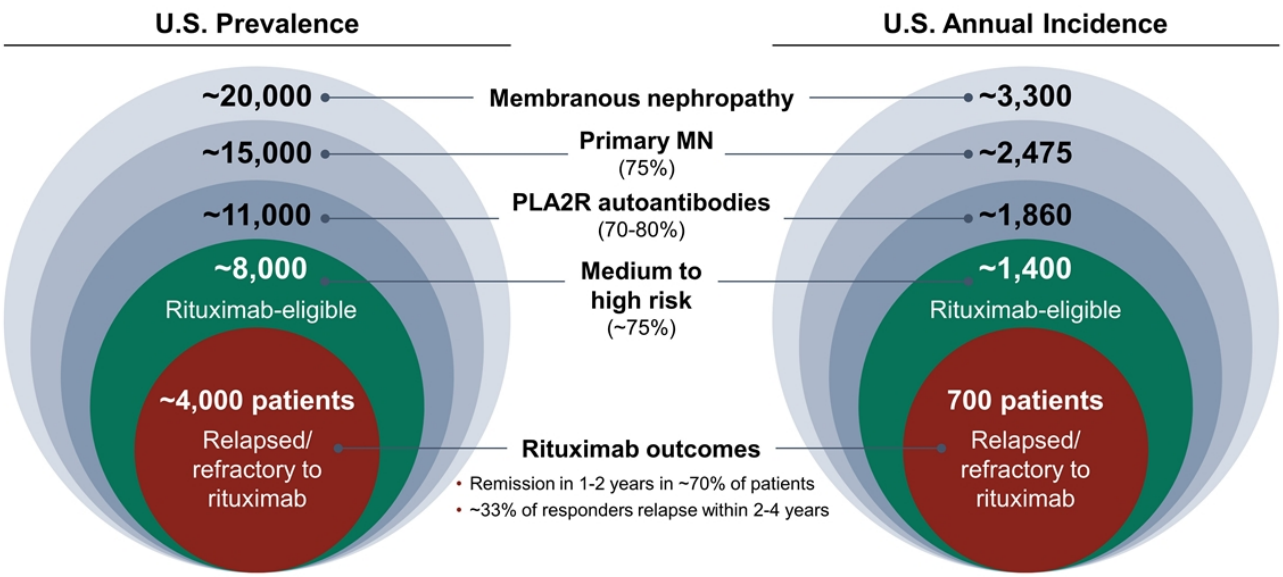


PLA2R antibody levels correlate with proteinuria, a commonly used surrogate endpoint

1. Accelerated rituximab clearance secondary to renal damage in patients with MN thought to be a major driver of limited drug effect.

Potential addressable market for PLA2R-CAART

Eligible population prevalence of ~4,000 to 8,000 patients & annual incidence of ~700 to 1,400 patients



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Manufacturing strategy

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

Stage 1: Penn DSG3-CAART Phase 1[1]	**Stage 2:** CDMOs & CABA Process MuSK-CAART Phase 1	**Stage 3:** Cabaletta Facility Commercialization & Scale-Up
2019 –	2021 –	Data-gated 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 and build out 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.

Parallel steps in manufacturing process[1] for CAR T vs CAAR T

Vector production and cell processing are key risks mitigated by strategy, partnership, process and people

Utilizing a clinically validated CART19 cell manufacturing process mitigates risks

- Cross referenced Penn CART19 IND including CMC process[1]
- Penn process, not Novartis process, avoiding Kymriah release challenges[2]
- Engineering runs have demonstrated efficient manufacture of DSG3-CAART cells from PV patients[3]

Multiple runs contractually secured each month at Penn

- Subject to future COVID-19 impact

DSG3 vector supply validated and secured

1. Penn-sponsored CD19 CAR IND CMC data has been cross-referenced in DSG3-CAART IND to provide additional data.
2. Manufacturing challenges were due to release specifications: https://www.biopharmadive.com/news/novartis-hits-car-t-manufacturing-snag-as-kymriah-sales-disappoint/528202/.
3. T cells isolated from patients with a range of treatment regimens of low to high intensity were tested; the highest intensity regimen and patients with ALC<1000 cells/uL expanded less well and will be excluded from the trial design.

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Leadership team

LEADERSHIP TEAM

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

MERCK tengion Penn

Gwendolyn Binder, Ph.D.
EVP Science & Technology

Adaptimmune Penn

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

AstraZeneca Penn

Anup Marda
Chief Financial Officer

Bristol-Myers Squibb

Arun Das, M.D.
Executive Director BD

Goldman Sachs Children's Hospital of Philadelphia

Martha O'Connor
Chief HR Officer

Bristol-Myers Squibb accentureconsulting

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Carl June, M.D.

Penn

Jay Siegel, M.D.

janssen FDA

Iain McInnes, PhD, FRCP, FRSE, FMedSci

University of Glasgow

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Cabaletta today

Leveraging a clinically validated CAR T platform as a novel approach to treating autoimmune diseases aiming to provide:

- **Deep and durable responses**, potentially cures, for autoimmune patients and
- **An exceptional safety profile,** based on
- **Highly specific, targeted therapy** designed to eliminate only pathogenic B cells

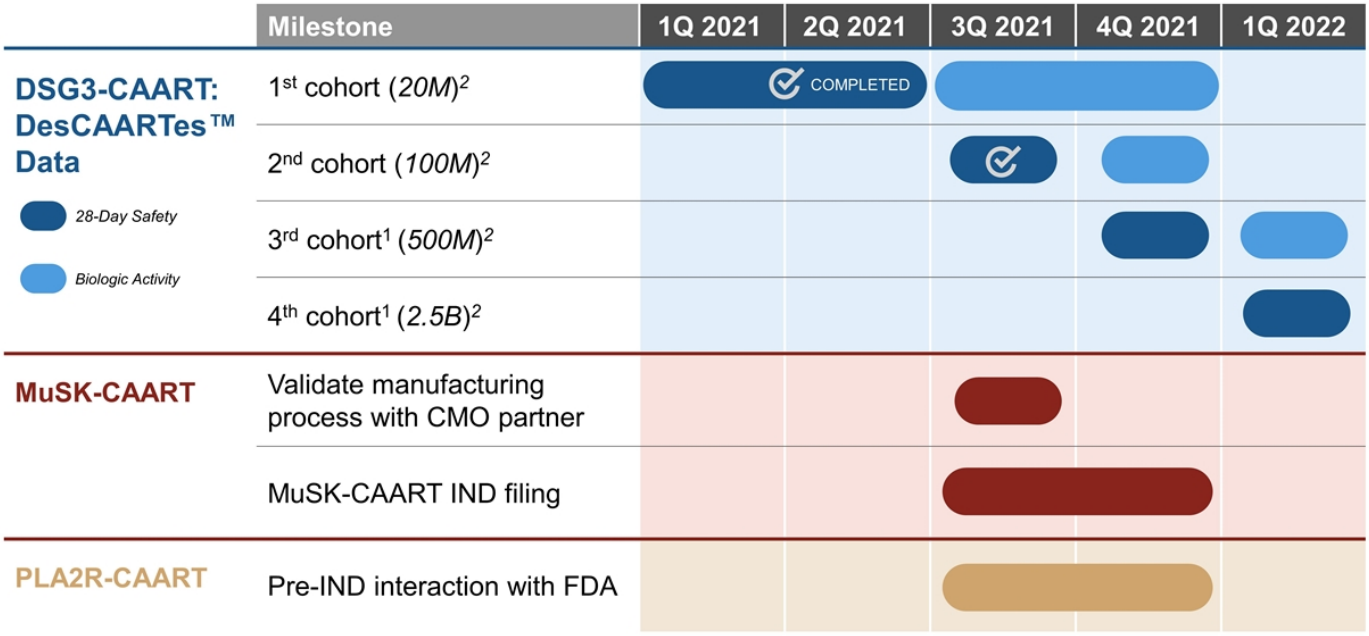
Multiple potential near-term clinical data catalysts with potential pipeline read-through

- **Safety, biologic activity data, clinical responses**

Expanding network of academic & industry partners to enhance platform

WuXi AppTec · B-MoGen Biotechnologies Inc. · ARTISANBIO · Penn · Children's Hospital of Philadelphia · Yale · UCDAVIS University of California

Anticipated near-term milestones



1. Assumes no dose-limiting toxicities are observed during cohort and uninterrupted enrollment occurs in the trial.
2. Number of transduced cells.

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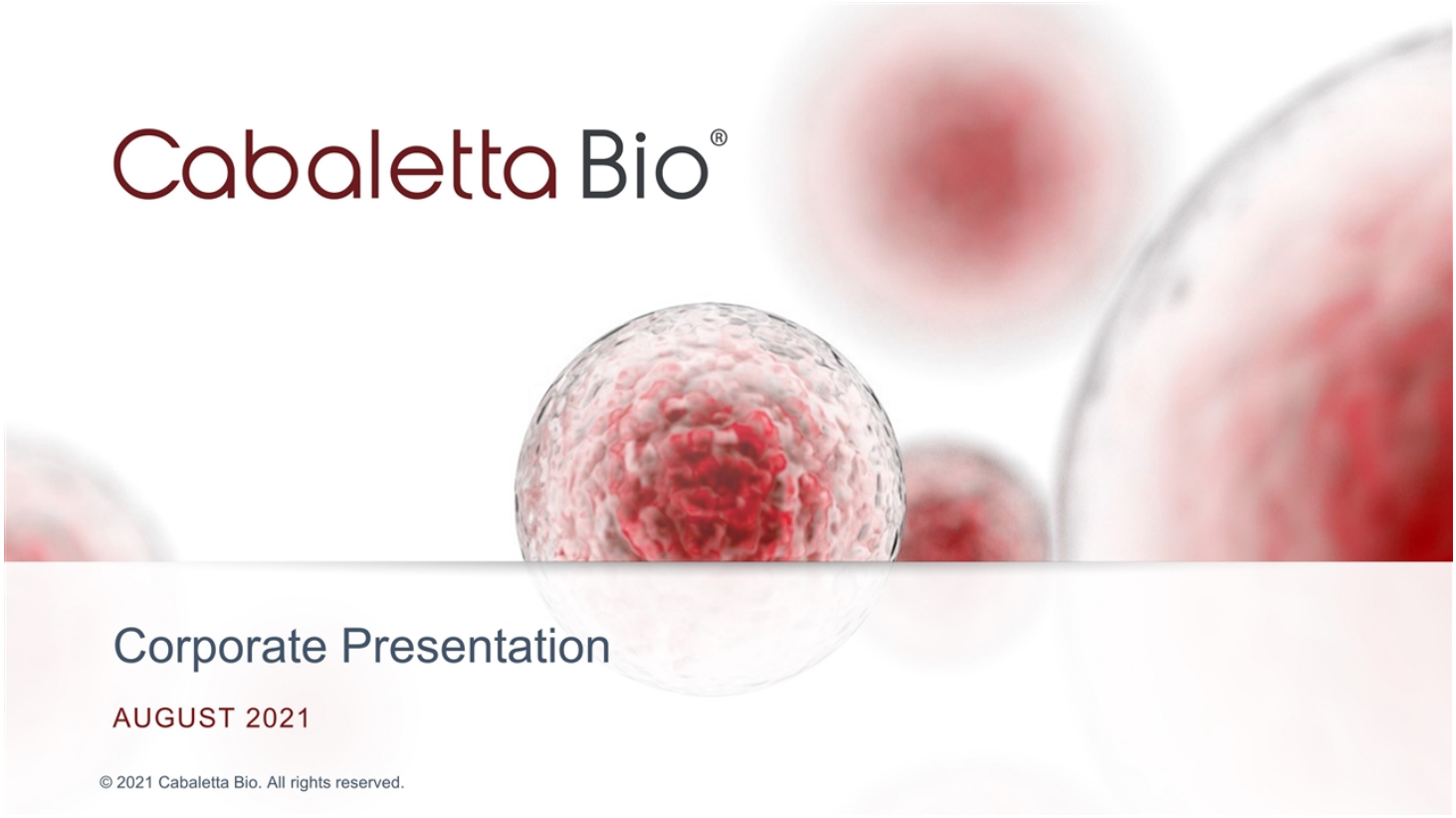

Corporate Presentation

AUGUST 2021

Cabaletta Bio™

Cabaletta Bio Reports Clinical Data from the Second Dose Cohort in DesCAARTes™ Trial in Patients with mPV

- *No dose-limiting toxicities (DLTs) or clinically relevant adverse events observed as of August17 using 100 million cells in the second dose cohort*
- *DSG3-CAART persistence observed in all three patients in the second dose cohort during the 28 days following infusion*
- *Dosing initiated in third cohort at 500 million cells, with biologic activity data from the first two dosing cohorts and third cohort safety data anticipated in 4Q21*

PHILADELPHIA, Aug 18, 2021 — Cabaletta Bio, Inc. (Nasdaq: CABA), a clinical-stage biotechnology company focused on the discovery and development of engineered T cell therapies for patients with B cell-mediated autoimmune diseases, today announced 28-day data from the second dose cohort, at the 100 million cell dose level, in the DesCAARTes™ Phase 1 clinical trial of DSG3-CAART for the treatment of patients with mucosal-dominant pemphigus vulgaris (mPV).

"We continue to be encouraged by the safety profile of DSG3-CAART in all patients dosed to date. In the second cohort, with patients receiving 100 million DSG3-CAART cells – a five-fold higher dose than the initial cohort – there were no clinically relevant adverse events or DLTs observed either acutely or in the 28-day DLT monitoring period following infusion," said David J. Chang, M.D., Chief Medical Officer of Cabaletta. "Similar to the first cohort, this safety profile was observed in the presence of circulating anti-DSG3 antibodies. In the absence of preconditioning, DSG3-CAART persistence was observed via quantitative polymerase chain reaction in peripheral blood samples of all three patients in the second dose cohort during the 28 days following infusion."

In addition to assessing the safety and tolerability of DSG3-CAART, the trial is designed to evaluate early signs of efficacy through clinical outcomes, such as persistent decline in disease activity, reduction or discontinuation of immunosuppressive therapies and systemic corticosteroids, and absence of systemic rescue medication, as well as other biologic activity measures, including a persistent decline in anti-DSG3 antibody titers, indicating target engagement. "The persistence of DSG3-CAART post-infusion is also being evaluated as it may be an important indicator. We look forward to generating data on potential biologic activity, with the goal of providing a targeted and highly effective, and perhaps curative, therapy without generalized immunosuppression," continued Dr. Chang.

The DesCAARTes™ trial has initiated dosing of patients in the third cohort at a treatment dose of 500 million DSG3-CAART cells. Cabaletta expects to announce top-line data on biologic activity from the first two cohorts as well as safety data from the 500 million dose cohort in the fourth quarter of 2021. Absent DLTs in the third cohort, a fourth dose cohort using 2.5 billion cells is also anticipated to initiate dosing this year. Cabaletta will continue to provide additional data on a cohort-by-cohort basis for the DesCAARTes™ trial as they become available.

About the DesCAARTes™ Clinical Trial

Cabaletta's DesCAARTes™ Phase 1 trial is an open-label, multi-center study of DSG3-CAART in adults with mucosal-dominant pemphigus vulgaris (mPV). The trial is designed to evaluate the safety and tolerability of DSG3-CAART as well as to identify evidence of target engagement and early signs of efficacy. The study consists of three parts: 1) dose escalation, 2) dose consolidation, and 3) expansion at the final selected dose and schedule. The trial is expected to enroll approximately 30 patients across multiple clinical sites throughout the United States. Visit our website (DesCAARTes™ Phase 1 Trial) for more information.

About Pemphigus Vulgaris

mPV is a rare autoimmune blistering disease that is characterized by the loss of adhesion between cells of the skin or mucous membranes. mPV is caused by the production of autoantibodies that disrupt structural proteins within the skin and/or mucosa that connect with other proteins to enable the skin and/or mucosal cells to connect with each other. The autoantibodies can target DSG3 and/or desmoglein 1 (DSG1), which are primarily expressed in the mucosal membranes and skin, respectively. mPV is characterized by autoantibodies against DSG3 only whereas mucocutaneous PV (mcPV) is characterized by autoantibodies against DSG3 and DSG1.

About CAAR T Cell Therapy

Chimeric AutoAntibody Receptor (CAAR) T cells are designed to selectively bind and eliminate only disease-causing B cells, while sparing the normal B cells that are essential for human health. CAAR T cells are based on the chimeric antigen receptor (CAR) T cell technology. While CAR T cells typically contain a CD19-targeting molecule, CAAR T cells express an autoantibody-targeted antigen on their surface. The co-stimulatory domain and the signaling domain of both a CAR T cell and a CAAR T cell carry out the same activation and cytotoxic functions. Thus, Cabaletta's CAARs are designed to direct the patient's T cells to kill only the pathogenic cells that express disease-causing autoantibodies on their surface, potentially leading to complete and durable remission of disease while sparing all other B cell populations that provide beneficial immunity from infection.

About Cabaletta Bio

Cabaletta Bio is a clinical-stage biotechnology company focused on the discovery and development of engineered T cell therapies, and exploring their potential to provide a deep and durable, perhaps curative, treatment, for patients with B cell-mediated autoimmune diseases. The Cabaletta Approach to selective B cell Ablation (CABA™) platform, in combination with Cabaletta's proprietary technology, utilizes CAAR T cells that are designed to selectively bind and eliminate only specific autoantibody-producing B cells while sparing normal antibody-producing B cells, which are essential for human health. The Company's lead product candidate, DSG3-CAART, is being evaluated in the DesCAARTes™ phase 1 clinical trial as a potential treatment for patients with mucosal pemphigus vulgaris, a prototypical B cell-mediated autoimmune disease. The FDA granted Fast Track Designation for DSG3-CAART in May 2020. For more information about the DesCAARTes™ Phase 1 clinical trial, please visit our website (DesCAARTes™ Phase 1 Trial). The Company's lead preclinical product candidate, MuSK-CAART, is in IND-enabling studies and is designed as a potential treatment for patients with MuSK-associated myasthenia gravis. For more information, visit www.cabalettabio.com.

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 progress and results of its DesCAARTes™ Phase 1 trial, including Cabaletta Bio's ability to enroll the requisite number of patients and dose each dosing cohort in the intended manner; the expectation that Cabaletta Bio may improve outcomes for patients suffering from mPV; the effectiveness and timing of product candidates that Cabaletta may develop, including in collaboration with academic partners; the safety, efficacy and tolerability of DSG3-CAART for the treatment of mPV; the impact of COVID-19 on the timing, progress, interpretability of data, and results of ongoing or planned clinical trials; the significance of data Cabaletta may announce regarding certain efficacy outcomes assessed in the DesCAARTes™ trial; the impact of preclinical data on the future development of CAAR T therapies in our pipeline portfolio expectations of the potential impact of COVID-19 on strategy, future operations, and the timing of its clinical trials, including the potential impacts on conduct of its DesCAARTes™ Phase 1 trial; and statements regarding 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 may not inform long-term results; Cabaletta Bio's ability to demonstrate sufficient evidence of safety, efficacy and tolerability in its preclinical and clinical trials of DSG3-CAART; 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 we have operations or do 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 PV; 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; 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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