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

Date of Report (Date of earliest event reported): June 1, 2021

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 5.07 Submission of Matters to a Vote of Security Holders.

Cabaletta Bio, Inc., a Delaware corporation (the "Company") held its Annual Meeting of Stockholders (the "Annual Meeting") on June 1, 2021. As of April 9, 2021, the record date for the Annual Meeting, there were 20,144,464 outstanding shares of the Company's common stock. The Company's stockholders voted on the following matters, which are described in detail in the Company's Definitive Proxy Statement filed with the U.S. Securities and Exchange Commission on April 21, 2021: (i) to elect two directors, Catherine Bollard, MBChB, M.D. and Richard Henriques, MBA, as Class II directors of the Company to serve for a three-year term expiring at the Company's 2024 annual meeting of stockholders and until their successor has been duly elected and qualified, subject to their earlier death, resignation or removal ("Proposal 1") and (ii) to ratify the appointment of Ernst & Young as the Company's independent registered public accounting firm for the fiscal year ending December 31, 2021 ("Proposal 2").

The Company's stockholders approved the Class II director nominees, Catherine Bollard, MBChB, M.D. and Richard Henriques, MBA, recommended for election in Proposal 1 at the Annual Meeting. The votes cast at the Annual Meeting were as follows:

	For	Withheld	Broker Non-Votes
Catherine Bollard, MBChB, M.D.	13,507,815	460,898	2,424,484
Richard Henriques, MBA	13,426,897	541,816	2,424,484

The Company's stockholders ratified the appointment of Ernst & Young as the Company's independent registered public accounting firm for the fiscal year ending December 31, 2021, recommended for ratification in Proposal 2 at the Annual Meeting. The votes cast at the Annual Meeting were as follows:

For	Against	Abstain	Broker Non-Votes
16,382,222	4,385	6,590	0

No other matters were submitted to or voted on by the Company's stockholders at the Annual Meeting.

Item 7.01 Regulation FD Disclosure.

On June 3, 2021, 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 9.01 Financial Statements and Exhibits.

(d) Exhibits

99.1 Cabaletta Bio, Inc. Corporate Presentation, dated June 3, 2021.

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, hereunto duly authorized.

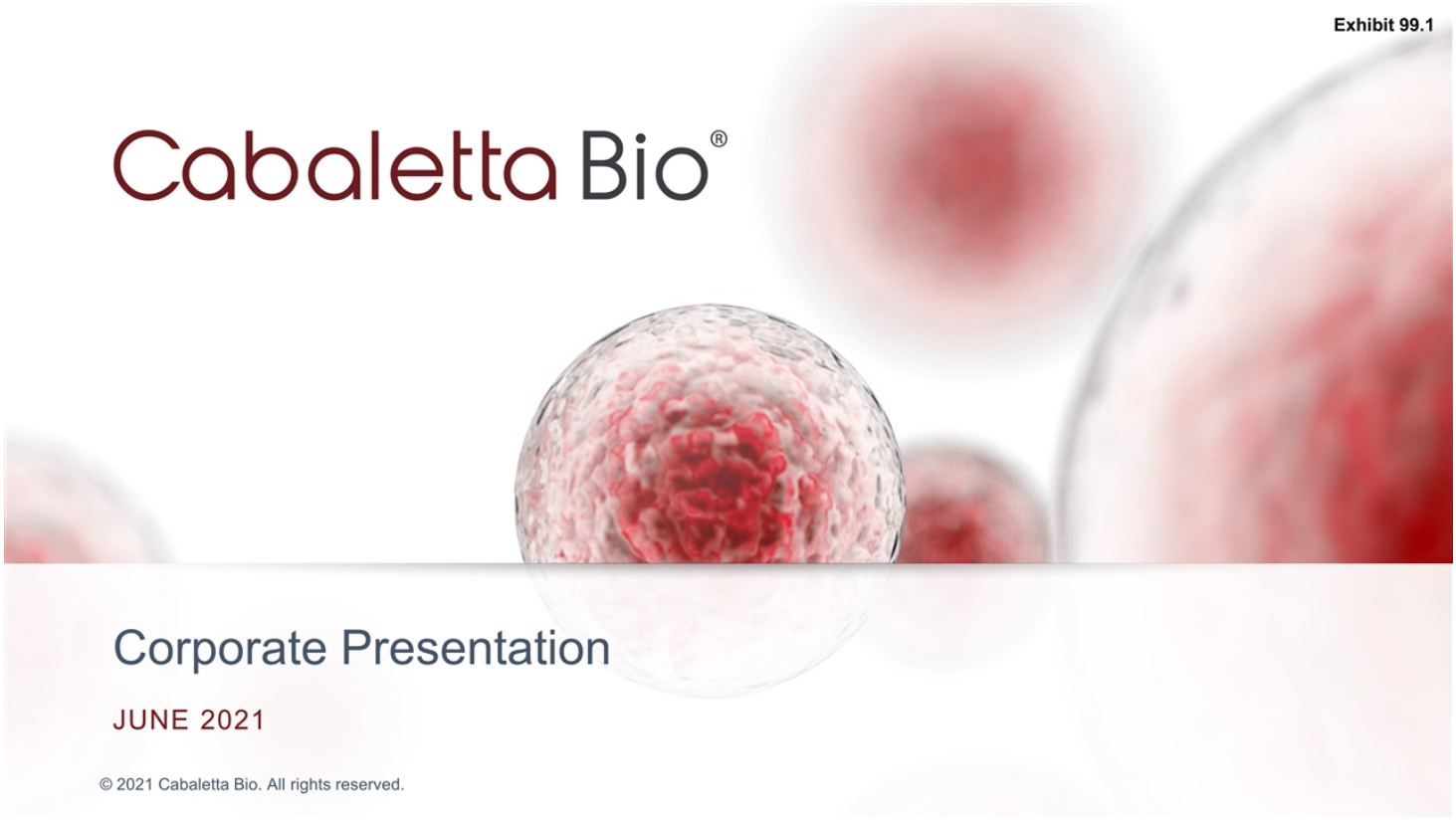
CABALETTA BIO, INC.

Date: June 3, 2021

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

Exhibit 99.1

Cabaletta Bio®



Corporate Presentation

JUNE 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 and does not constitute an offer to sell or a solicitation of an offer to buy securities, nor shall there be any sale of any securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction. 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 neither this Presentation, nor any sale of securities, shall 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" relating to our business, operations, and financial conditions, including, but not limited to, current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our development plans, our preclinical and clinical results and other future conditions. 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. Factors which could cause actual results to differ materially from those in the forward-looking statements include, among others, the success, cost, and timing of our product candidate development activities and preclinical studies and clinical trials, our ability to obtain and maintain regulatory approval for our product candidates, our ability to commercialize our product candidates, future agreements with third parties in connection with the development or commercialization of our product candidates, the size and growth potential of the market for our product candidates, our ability to contract with third-party suppliers and manufacturers and our ability to develop internal manufacturing capabilities and facilities, the accuracy of our estimates regarding expenses, future revenue, capital requirements, and needs for additional financing, and our ability to obtain and maintain intellectual property protection for our product candidates. 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, uncertainties caused by adverse economic conditions, including, without limitation, 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

Phase 1 DesCAARTes™ trial ongoing for patients with mucosal pemphigus vulgaris (mPV)

- No DLTs or any clinically relevant toxicities observed in the 1st 28 days following infusion for all 3 patients in the 1st cohort
  - DSG3-CAART cells were detected at low levels via qPCR in both patients evaluated to date
  - 20M cell dose without lymphodepletion and in the presence of circulating anti-DSG3 antibodies within patients
- Target engagement data from cohort 1, and acute safety data from the 1st 3 cohorts anticipated this year[1]

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

- PLA2R-CAART pre-IND meeting with FDA anticipated in 2H21 for PLA2R positive 1^0 membranous nephropathy patients
- Product portfolio[2] currently targeting diseases that affect over 80,000 patients in the US

Issued U.S. patent on lead clinical program with emerging differentiated IP portfolio

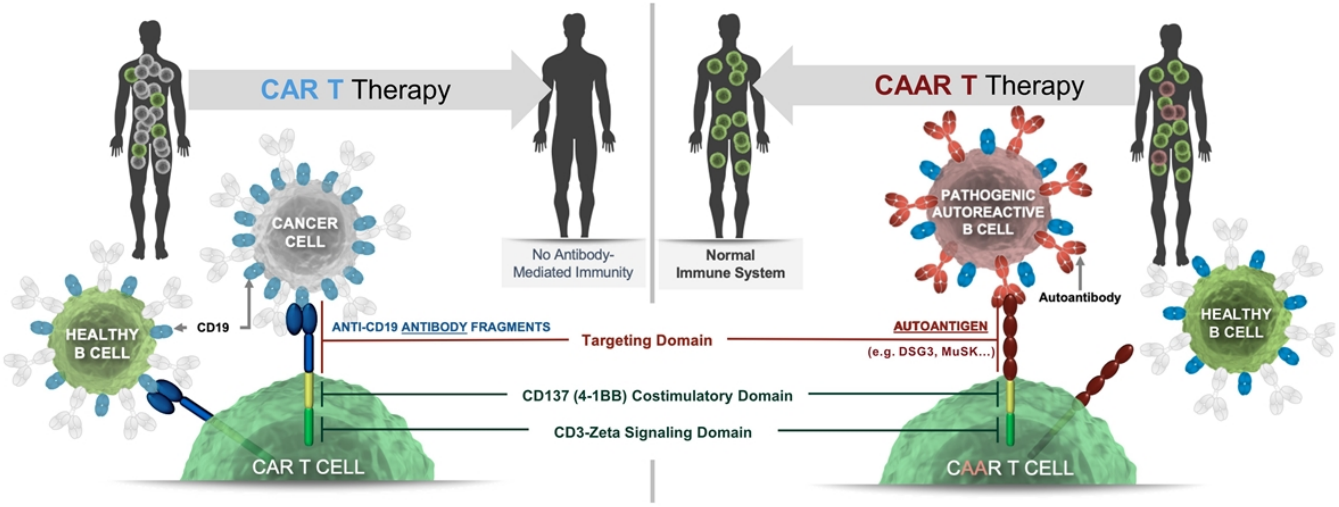
- First issued CAAR T product patent covers all or any part of the relevant human antigens (DSG3 and DSG1)

Cash runway through at least 4Q22 with $102M in cash and investments as of March 31, 2021

1. Assumes no dose-limiting toxicities are observed during cohort and uninterrupted enrollment occurs in the trial.
2. Includes five disclosed product candidates and two undisclosed pipeline disease targets in our pipeline through expansion of our Sponsored Research Agreement with the University of Pennsylvania.

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

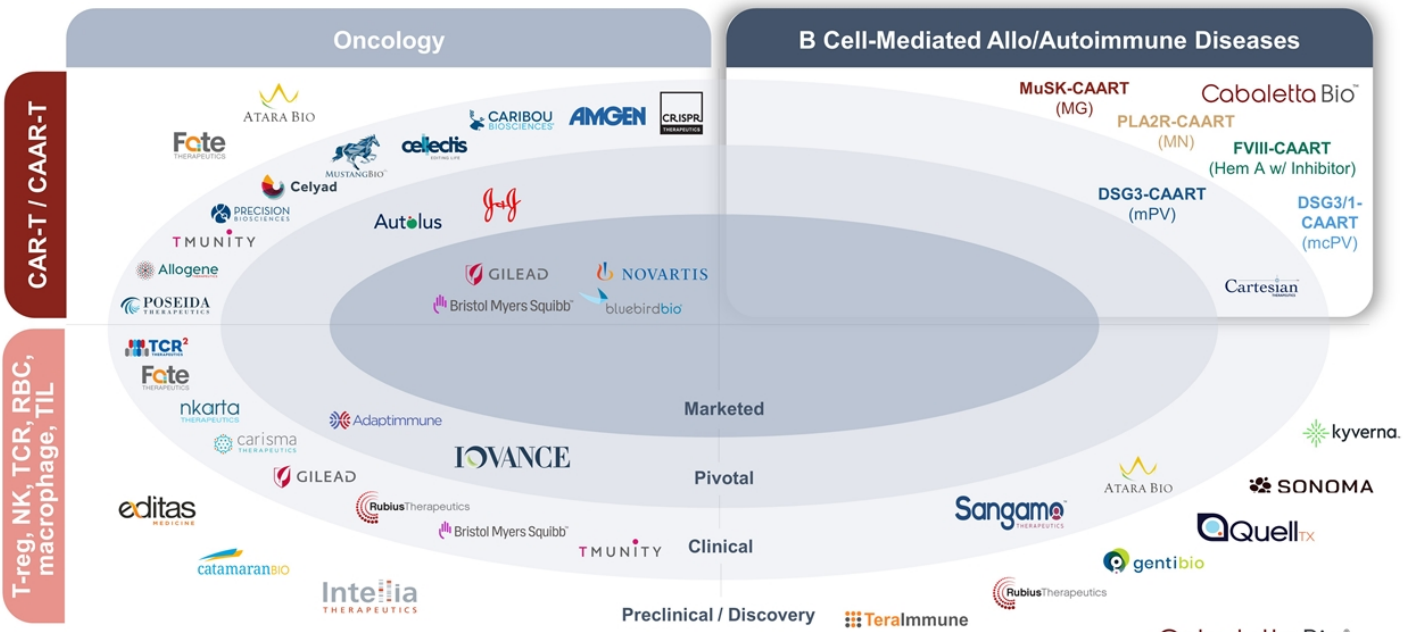
Kymriah

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]

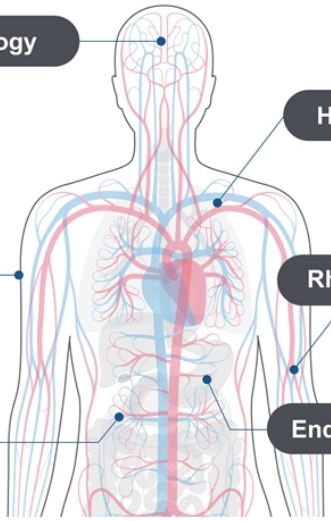
Hematology
- Immune Thrombocytopenic Purpura[3]
- Thrombotic Thrombocytopenic Purpura[1,2,3]
- Antiphospholipid Syndrome[4,5]
- Autoimmune Hemolytic Anemia[3]

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]



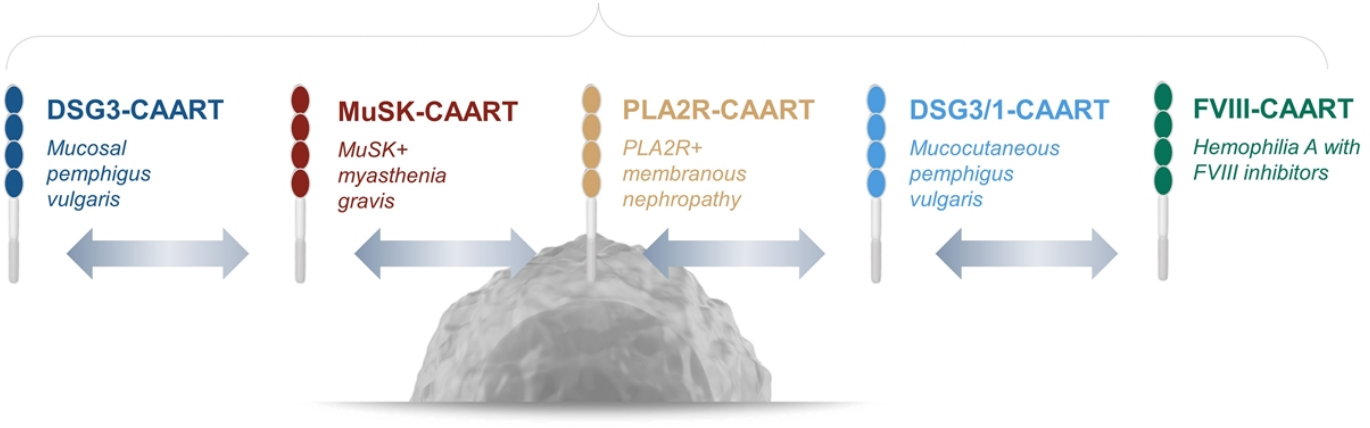
** Illustrative list of diseases where biologic opportunity for cure or treatment may be possible.*

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

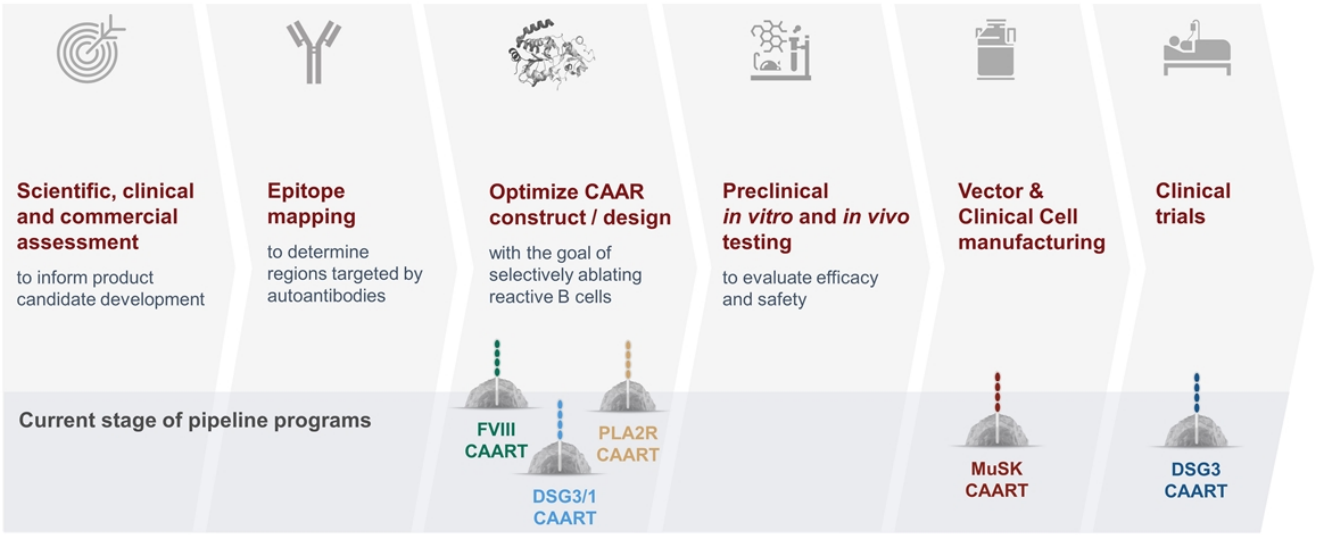
Technology foundation designed to enable a portfolio of programs targeting B cell-mediated diseases

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



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

We believe the initial DesCAARTes™ data begins to de-risk the platform

Manufacturing success in clinical trial

- 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 through June 1, 2021

Acute safety in patients with mPV

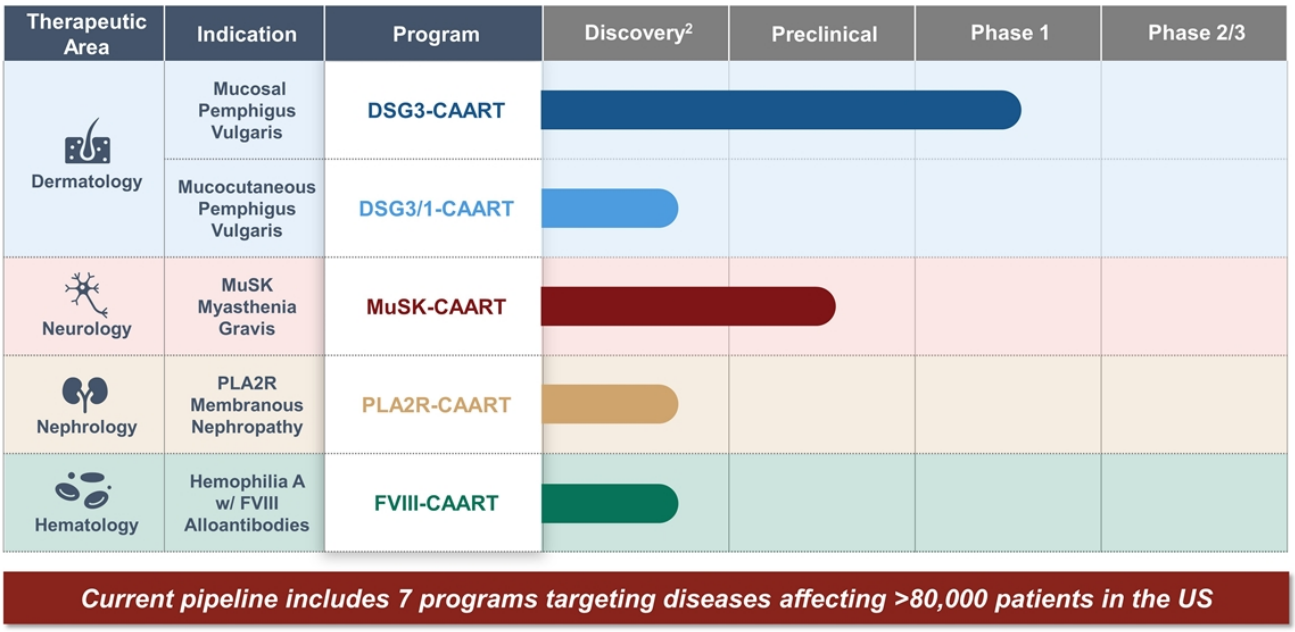
- No DLTs or any clinically relevant toxicities observed in initial cohort through 28 days
  - DSG3-CAART was detected at low levels via qPCR in both patients evaluated to date
  - 20M DSG3-CAART cell dose administered without lymphodepletion
  - In patients with soluble circulating anti-DSG3 antibodies
- Second dosing cohort is at 100M DSG3-CAART cells
  - Two cohorts higher than 100M cells are currently planned as well, if necessary

Future Data: Target engagement

- We believe biologic activity is present if DSG3 Ab titers consistently reduced by >20%
- More robust anti-DSG3 titer decline expected with greater target engagement
- Many variables to modify and strategies to maximize target engagement

1. As of June 1, 2021.

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



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

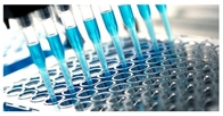
1. Two additional undisclosed disease targets added to our pipeline portfolio through expansion of our Sponsored Research Agreement with the University of Pennsylvania are not shown.
2. In our discovery stage, we perform epitope mapping and optimize CAAR construct and design.

Cabaletta Bio®

PV is an optimal lead indication for CAAR T therapy

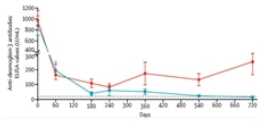
DSG3 antibodies are widely considered to be necessary and sufficient to cause PV[1]

1



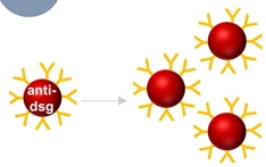
Serum anti-DSG3 **antibodies are 98 - 100% sensitive *and* specific**[2]

2



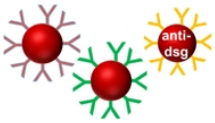
Depletion of B cells by rituximab[3] or antibody by plasmapheresis **transiently improves clinical disease**

3



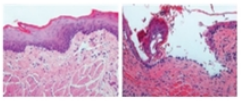
Incomplete B cell depletion by rituximab leads to PV recurrences, with **identical disease-causing B cell clones**[4,5]

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

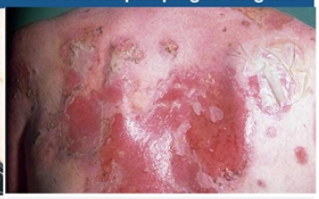


The DSG3 CAAR has **published animal model** proof-of-concept validation[7]

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]

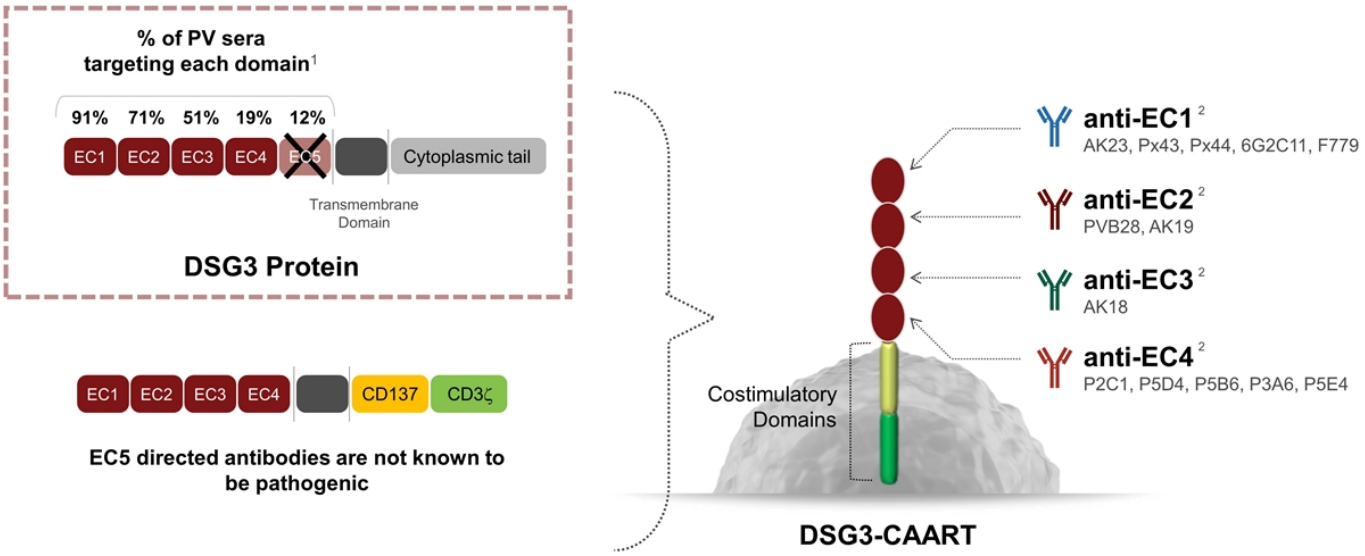
- Response: ~40% of patients achieved a 16-week period with no lesions or medicines during 1 yr[4,5]
- 22% annual serious adverse event (SAE) rate[4]
  - 4-9%[3,4,5] annual risk of severe infection in PV
- Real world data indicate:
  - *Transient* remission ~ 70% CROT[6]:
    - ~30% relapse in 1 year[6]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

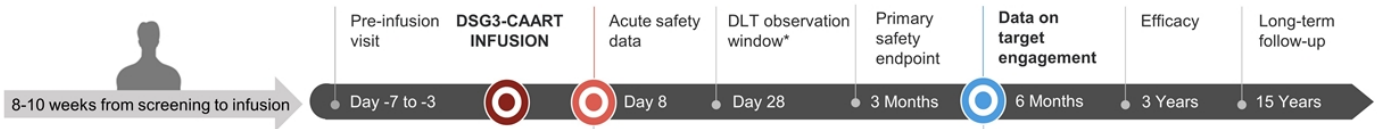
- DLTs include any grade 3 or 4 CRS or neurotoxicity, or any grade 2 CRS or neurotoxicity that failed to improve to ≤ Grade 1 or baseline within 7 days

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

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 (Day 8) and at 3 months, with data on potential target engagement by 6 months



Day 8 acute safety data

Monitors for key risks:

- CRS / neurotoxicity
- Impact of soluble antibody
- Other adverse events

Primary safety endpoint at 3 months

Potential for disease flare during planned steroid taper

Target engagement to be assessed by declining anti-DSG3 titers[1,2]

- We believe initial signal would be evidenced by a consistent reduction in anti-DSG3 titers ≥20% within a patient. More robust decline expected with greater target engagement
- Translational program evaluating potential for *in vivo* expansion and threshold dose effect[3,4]

Other key potential efficacy measures[2]

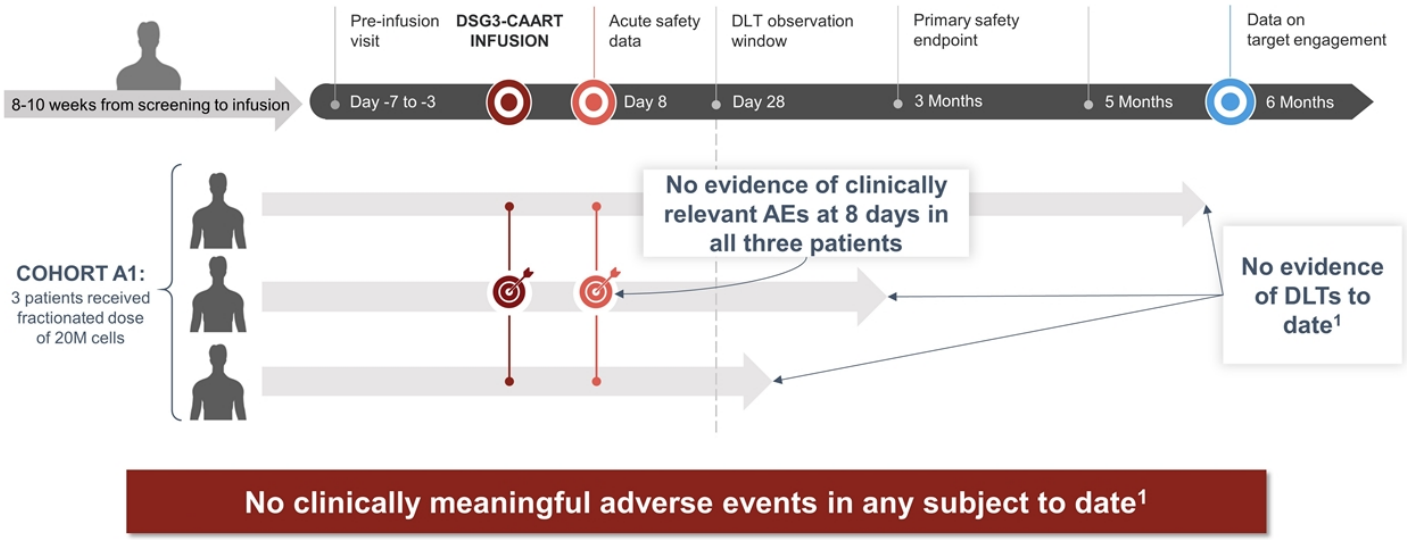
- Disease activity (clinical)
- Steroid / immunosuppressive use

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

1. Spindler, Volker, et al. "Mechanisms causing loss of keratinocyte cohesion in pemphigus." Journal of Investigative Dermatology 138.1 (2018): 32-37.
2. This information represents data that we believe can be used to inform potential efficacy endpoints in future clinical development.
3. Dasyam, Nathaniel, Philip George, and Robert Weinkove. "Chimeric antigen receptor T-cell therapies: Optimising the dose." British journal of clinical pharmacology 86.9 (2020): 1678-1689.
4. Raje, Noopur, et al. "Anti-BCMA CAR T-cell therapy bb2121 in relapsed or refractory multiple myeloma." New England Journal of Medicine 380.18 (2019): 1726-1737.

No DLTs observed to date in 1st cohort of DesCAARTes™ trial

Promising initial safety profile for all 3 patients dosed with DSG3-CAART in the 1st trial cohort

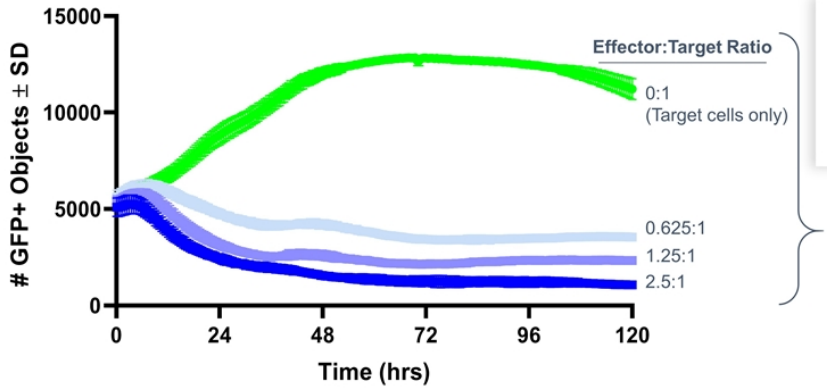


No clinically meaningful adverse events in any subject to date[1]

1. As of June 1, 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 June 1, 2021.

Initial clinical safety profile in 1st cohort informed by several factors

No DLTs or clinically relevant toxicities in 1st three patients to date[1]

- At a 20 million cell dose, in the absence of lymphodepletion
- Circulating anti-DSG3 antibodies present in all patients at infusion
- All patients in the 1st cohort have completed the 28-day DLT monitoring period
  - DSG3-CAART was observed at low levels via qPCR in patients 1 and 2
  - DSG3-CAART evaluation has not yet occurred in patient 3

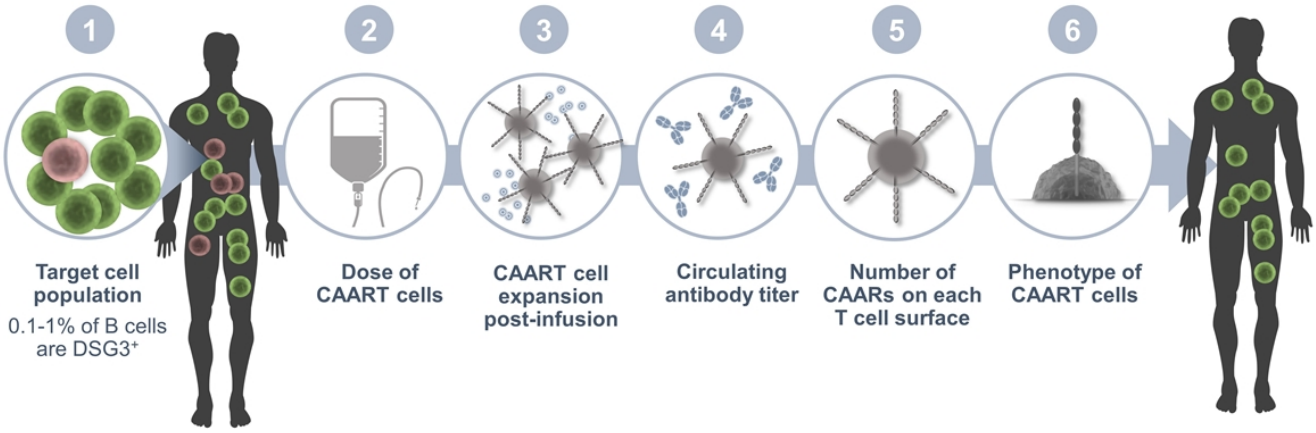
Future topline target engagement data to be disclosed on a cohort-by-cohort basis

- Target engagement in the 1st cohort possible, but not expected
- Topline target engagement data on 1st cohort to be reported in 2H21

1. As of June 1, 2021.

Potential drivers of target engagement in autoimmune disease

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



Many options exist to enhance signals of target engagement

CAART cell

Pathogenic autoreactive B cell

Healthy B cell

Accelerating timelines for DesCAARTes™ trial

Strong interest by study sites, with three sites actively enrolling and many more working to open

Growing clinical site network with high investigator engagement

Penn · Stanford Medicine · UC Davis University of California

Expanding relationships with patient advocacy organizations

ippf Pemphigus & Pemphigoid · NORD National Organization for Rare Disorders · mg Myasthenia Gravis Foundation of America

Opportunities to accelerate development

ORPHAN DRUG · FAST TRACK

DSG3-CAART: Data from DesCAARTes™ Trial

- *Acute Safety*
- *Target Engagement*

Milestone	1Q 2021	2Q 2021	3Q 2021	4Q 2021
1st cohort[1]	COMPLETED			
2nd cohort[1]				[2]
3rd cohort[1]				

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. Expect to report in 4Q21 or 1Q22.

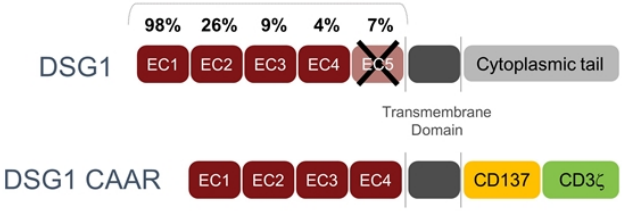
DSG3/1 CAART for mucocutaneous PV (mcPV)

Plan to potentially submit an IND after review of safety and target engagement data from DSG3-CAART

DSG3/1 CAARs designed for mcPV

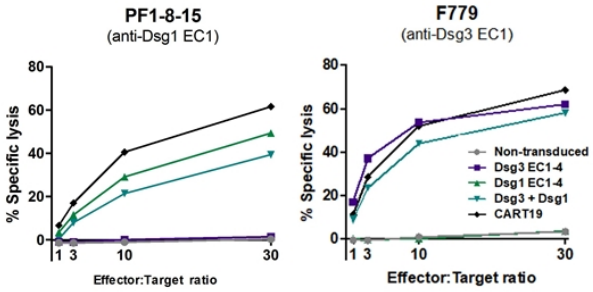
- DSG3 and DSG1 autoantibodies
- Most severe and common form of PV (~75%)
- Mucosal blistering, plus skin erosion and blistering
- Managed with immune suppression, similar to mPV
  - High risk of relapse
  - Potential for hospitalizations and fatal infections

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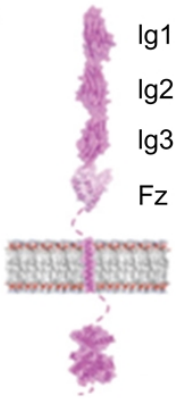
High unmet need in MuSK myasthenia gravis; a valuable CAAR target

All known extracellular domains can be included in the CAAR design

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

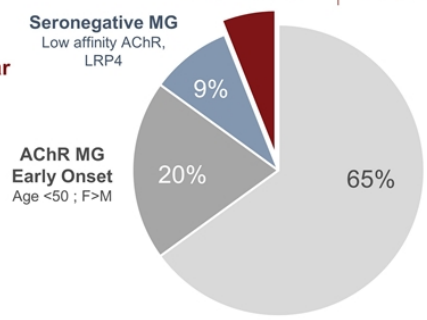
1. Autoantibody titers drop after rituximab[1,2]
2. Pathogenic B cells are incompletely eliminated by rituximab and persist during relapse[3]



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

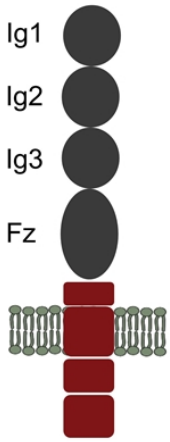


Total US MG Prevalence: 50,000 to 80,000 patients

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).

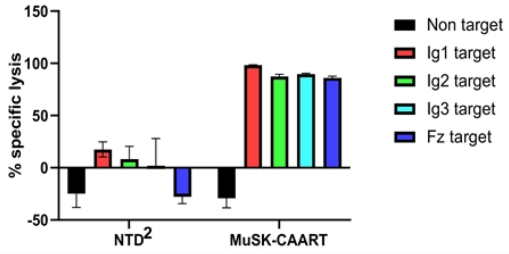
MuSK-CAART showed *in vitro* selective & specific target engagement[1]

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

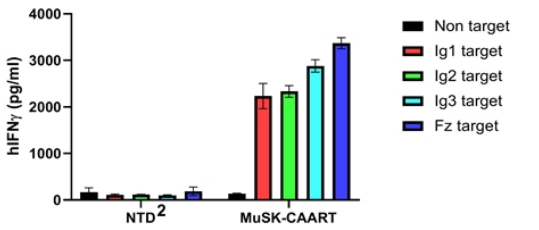


MuSK-CAART

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*

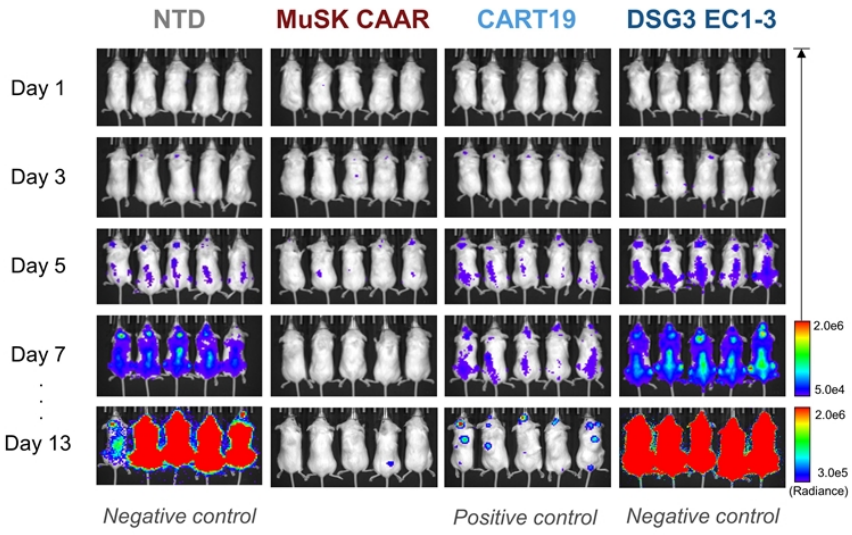
- No off-target toxicity observed *in vitro*
  - ~6,000 human membrane proteins evaluated
- No on-target toxicity observed *in vitro*
  - Cellular assays to evaluate cytotoxicity against native ligand LRP4

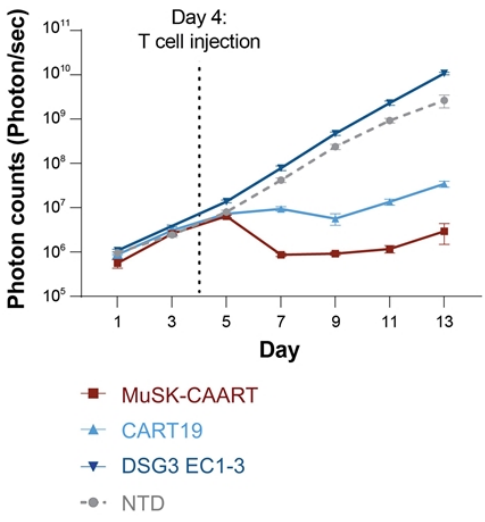
MuSK-CAART program on track for IND filing in 2H 2021

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

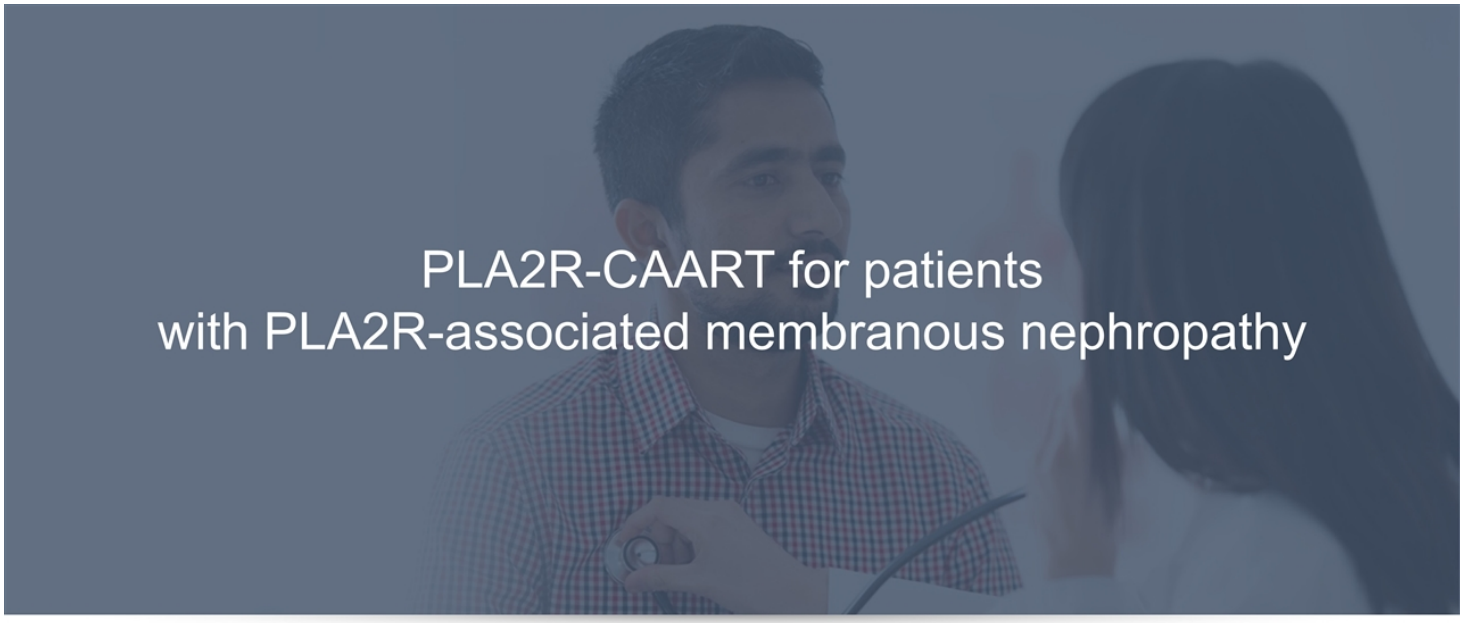
MuSK-CAART demonstrated specific *in vivo* target engagement[1]

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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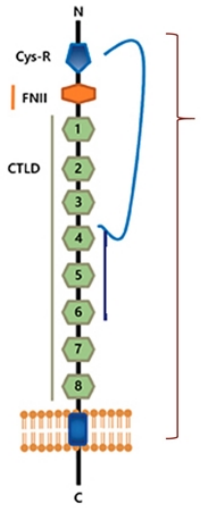
Discovery-stage CAART program in membranous nephropathy

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

Multiple lead candidates containing the main immunogenic epitopes demonstrate specific target engagement and cytolytic activity; lead product candidate being confirmed

Changing treatment paradigm highlights the role of B cells in disease

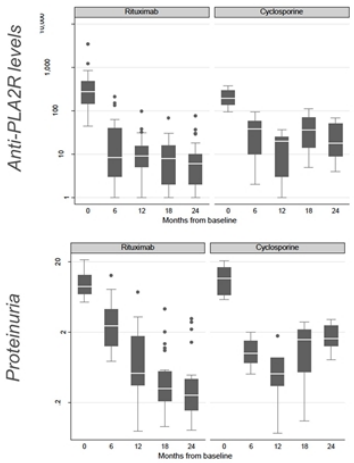
Opportunity to develop antigen-targeted therapy to address significant unmet need

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

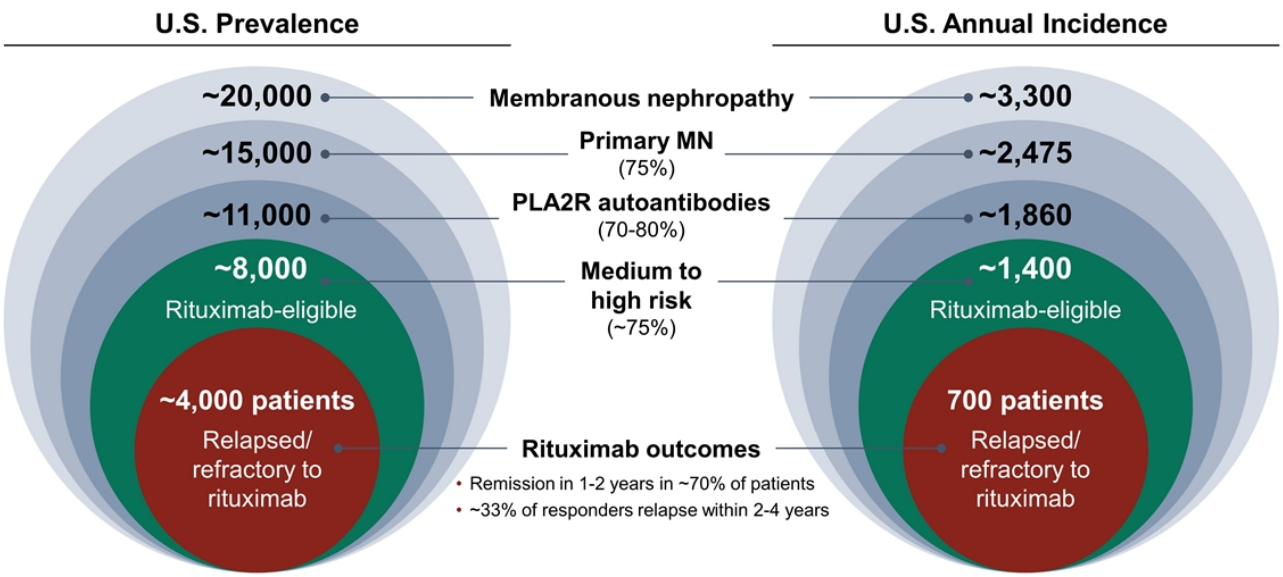


PLA2R antibody levels correlate with proteinuria, a commonly used surrogate endpoint

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

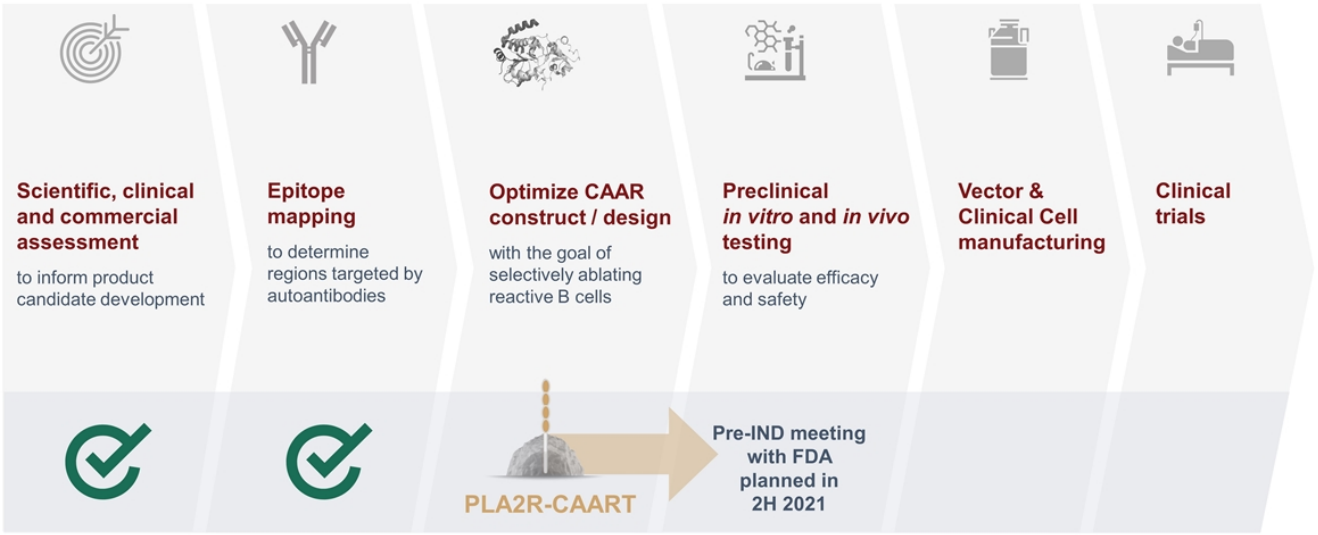
Potential addressable market for PLA2R-CAART

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



Consistent progress on PLA2R-CAART program

Rapid advancement through CABA development engine with near-term planned interactions with FDA



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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
• 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	• 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

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Bristol-Myers Squibb accentureconsulting

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janssen FDA

Iain McInnes, PhD, FRCP, FRSE, FMedSci

University of Glasgow

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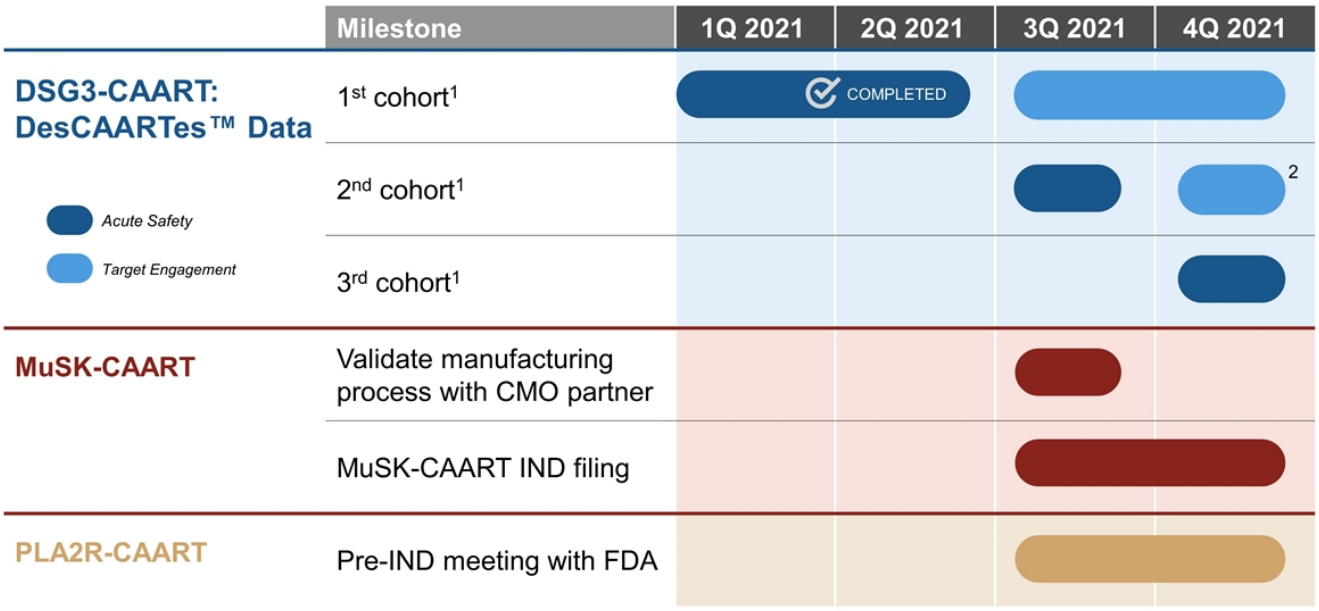
Updated 2021 anticipated milestones



1. Assumes no dose-limiting toxicities are observed during cohort and uninterrupted enrollment occurs in the trial.
2. Expect to report in 4Q21 or 1Q22.

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
- **Highly specific, targeted therapy** designed to eliminate only pathogenic B cells
- **Target engagement** based on strength of biological rationale, deep understanding of translational data and many ways to deliver on the promise for patients

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

- **Acute safety, target engagement, clinical responses**

Expanding network of academic & industry partners to enhance platform

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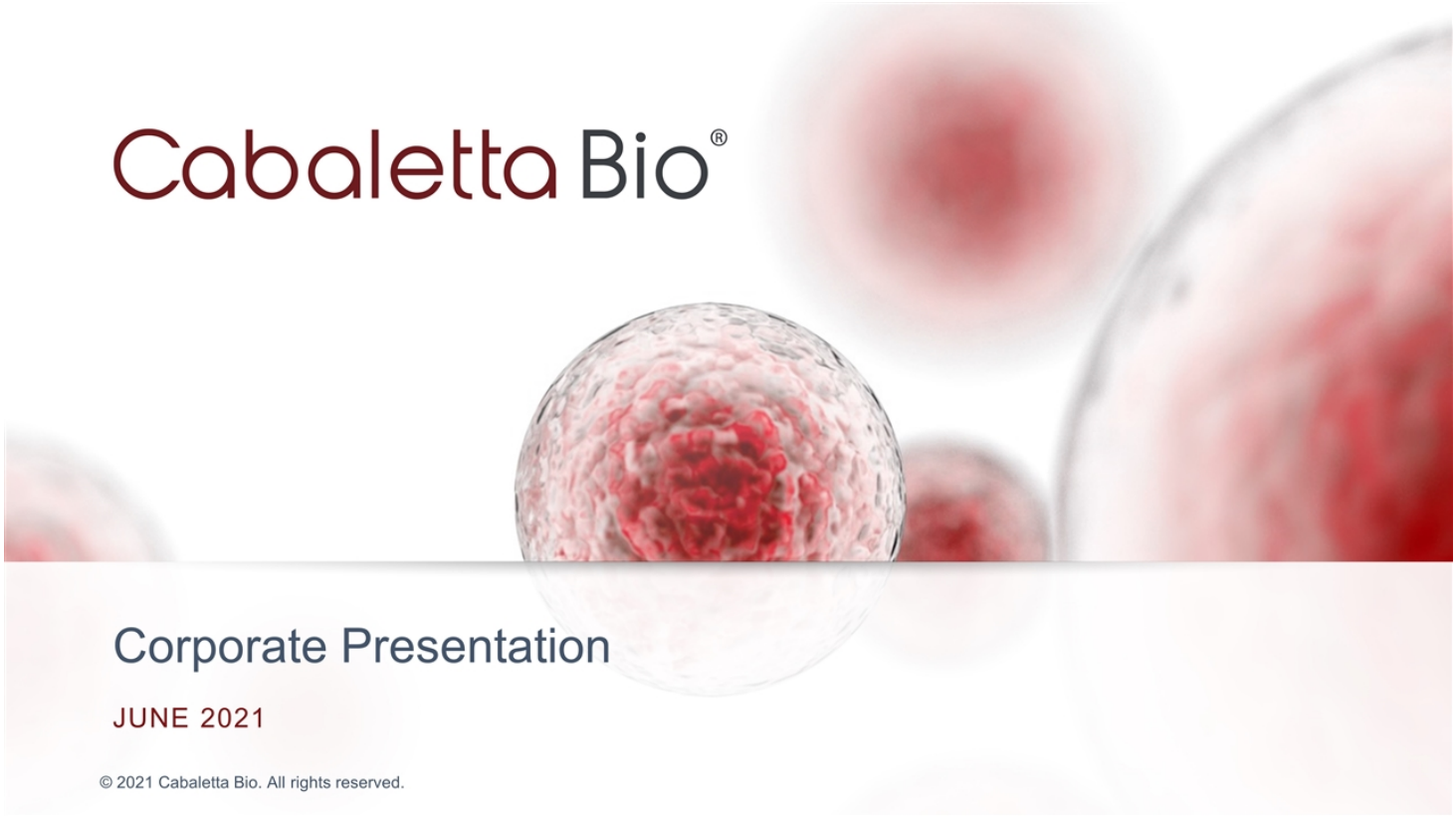

Corporate Presentation

JUNE 2021