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) February 20, 2020

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 February 20, 2020, Cabaletta Bio, Inc., a Delaware corporation (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 (the "Corporate Presentation"). A copy of the Corporate Presentation is attached hereto as Exhibit 99.1 and is incorporated by reference into this Item 7.01 of this Current Report on Form 8-K.

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

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

99.1 Cabaletta Bio, Inc. Corporate Presentation, dated February 20, 2020.

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: February 20, 2020

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

Exhibit 99.1

Cabaletta Bio™

Selective B cell ablation for autoimmune disease

February 2020

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. The 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. 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.
- 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.

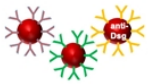
Our vision

Develop and launch the first curative targeted cellular therapies for patients with autoimmune diseases

Key messages

Leveraging CAR T experience to specifically target B cell-mediated **autoimmune diseases**

- Developing CAAR T products (Chimeric AutoAntibody Receptor T)
  - where there is a biologic opportunity for cure (over two dozen potential targets identified)
  - by designing CAARs to selectively eliminate ONLY pathogenic B cells displaying targeted antibody
  - while leveraging CART19 design and manufacturing experience from Penn



- DesCAARTes Phase 1 trial – DSG3-CAART in mucosal pemphigus vulgaris (PV) patients
  - progressing to support expected timelines
  - Orphan Drug Designation granted by the FDA in January 2020 for the treatment of PV
  - CABA Labs leading evaluation and development of risk mitigating approaches
- Expanding product pipeline with our CABA platform (Cabaletta Approach for selective B cell Ablation)
  - preclinical data published on PV, myasthenia gravis, and hemophilia A inhibitor
  - robust IP portfolio emerging with first US patent issued on lead program
- Planned catalysts in 2020
  - **DesCAARTes trial** – Report clinical acute tolerability (8 day) data from initial cohort
  - **MuSK-CAART** – Confirm *in vivo* target engagement and initiate IND-enabling studies
  - **Manufacturing independence** – Initiate validation of manufacturing for clinical trials with CMO[1]

1. Contract Manufacturing Organization

Leadership

Diversified with long-standing history of professional collaborations among team and with co-founders

Scientific Advisory Board

Aimee Payne, MD PhD
Co-chair, Co-founder
Penn

Jay Siegel, MD
janssen
FDA Center for Biologics Evaluation and Research

Michael Milone, MD PhD
Co-chair, Co-founder
Penn

Steven Nichtberger, MD
President, CEO & Chairman
MERCK tengion Penn

Board of Directors

Catherine Bollard, MD PhD
The George Washington University Hospital

Mark Simon
Torreya Partners

Brian Daniels, MD
5AM Ventures Bristol-Myers Squibb

Richard Henriques
Bill & Melinda Gates foundation MERCK

Anup Marda
Chief Financial Officer
Bristol-Myers Squibb

Arun Das, MD
Senior Director BD
Goldman Sachs Children's Hospital of Philadelphia

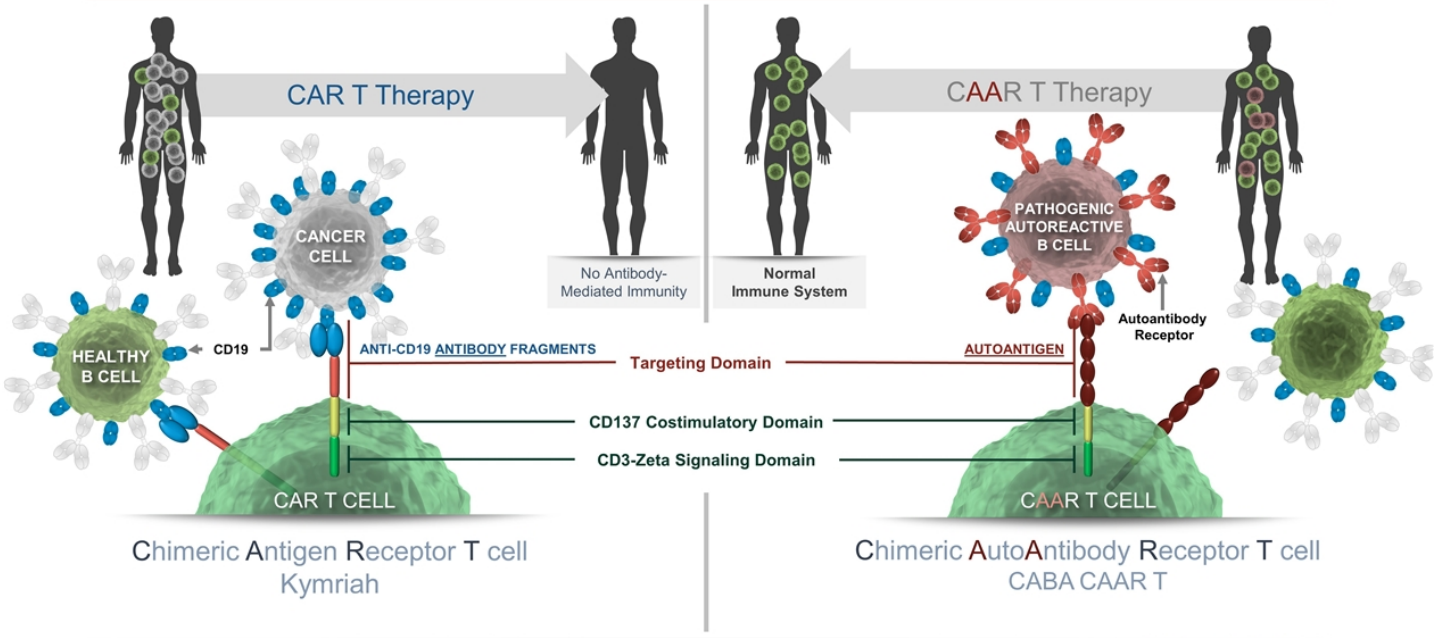
Gwendolyn Binder, PhD
EVP Science & Technology
Penn Adaptimmune

David Chang, MD
Chief Medical Officer
AstraZeneca Penn

Brian Stalter
General Counsel
MEDAREX Bristol-Myers Squibb

Martha O'Connor
Chief HR Officer
Bristol-Myers Squibb accentureconsulting

Scientific platform and strategy



Chimeric Antigen Receptor T cell
Kymriah

Chimeric AutoAntibody Receptor T cell
CABA CAAR T

Our CABA (Cabaletta Approach for Selective B cell Ablation) Platform

Proven ability to identify multiple product candidates

Scientific, clinical and commercial assessment | Epitope mapping | CAAR construct / design | *In vitro* studies | *In vivo* studies | GMP manufacturing | Clinical trial development

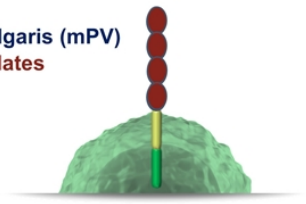
Scientific, clinical and commercial assessment to inform product candidate development

Epitope mapping to determine regions targeted by autoantibodies

Optimizing CAAR construct / design with the goal of selectively ablating reactive B cells

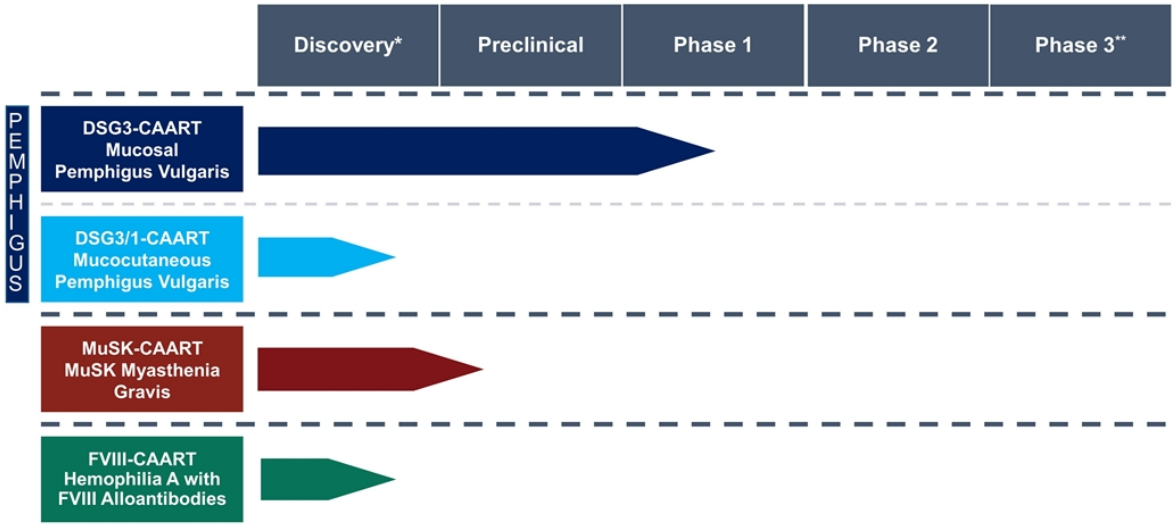
Preclinical *in vitro* and *in vivo* testing to evaluate efficacy and safety

- **Mucosal pemphigus vulgaris (mPV)**
- **Multiple product candidates**



Cabaletta Pipeline

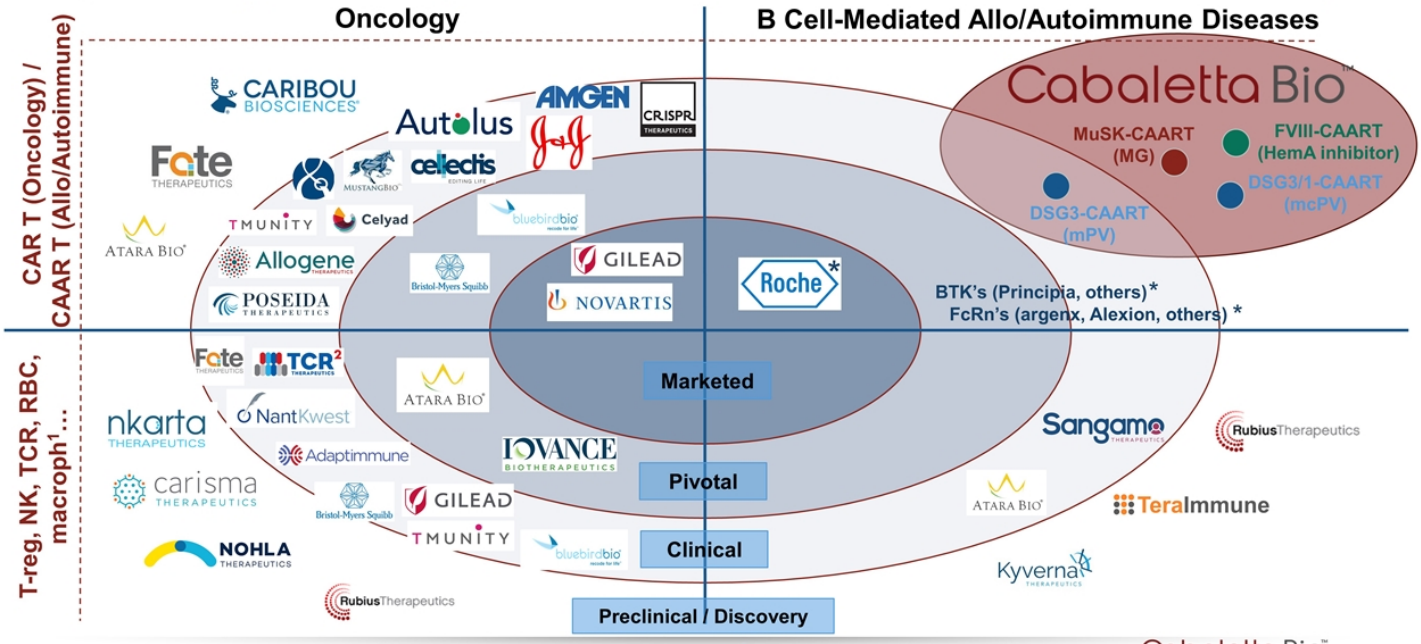
Multiple disease targets with preclinical evidence of selective and specific target engagement



* In our discovery stage, we perform epitope mapping and optimize CAAR construct and design.
** May not be required if Phase 2 is a registrational clinical trial.

Cabaletta product candidates are filling an adjacent white space

CAR T therapy products are approved for B cell cancers



1. T-reg = T-regulatory, NK = Natural Killer, RBC = Red Blood Cell, Macroph = Macrophage

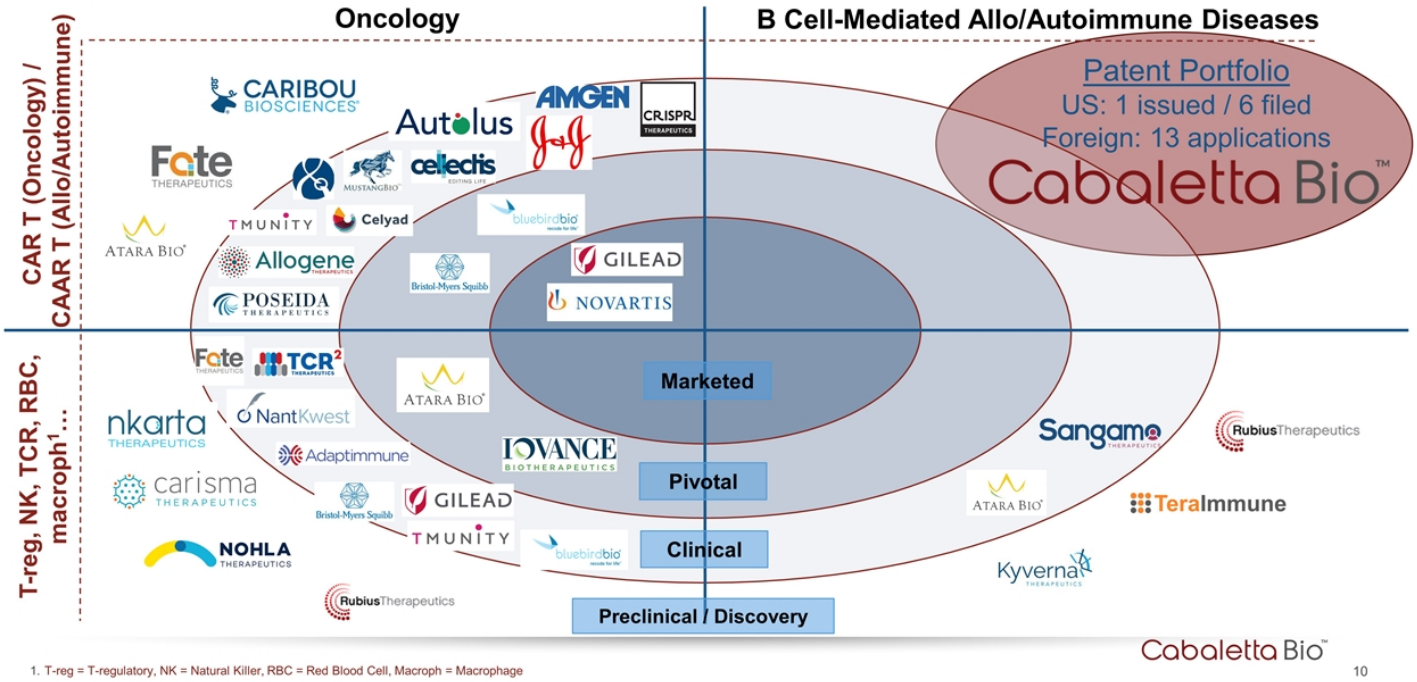
* = non-cell therapy Cabaletta pipeline competitors

= Cabaletta pipeline products

Cabaletta Bio™

Cabaletta product candidates are filling an adjacent white space

CAR T therapy products are approved for B cell cancers



1. T-reg = T-regulatory, NK = Natural Killer, RBC = Red Blood Cell, Macroph = Macrophage

Overview of Intellectual Property Strategy

Distinct from CD19 directed CAR T patents, initial CAAR T patent covers entire human antigen

- Patent rights pursued on a target by target basis
  - Pursuing multiple levels of protection for CAAR constructs
    - protein, nucleic acid, and engineered cells; and their use
  - Expiration Dates: 2035-2039 (without patent term extensions)

- First issued US patent for CAAR therapy in pemphigus
  - Exemplary Composition of Matter Claim
    - "A genetically modified cell comprising a CAAR comprising an extracellular domain **comprising DSG1, DSG3, or a fragment thereof that binds an autoantibody expressed on a B-cell**, a transmembrane domain, and an intracellular signaling domain, wherein the cell expresses the CAAR and binds the autoantibody expressed on the B cell or induces killing of the B cell expressing the autoantibody."

- Patent rights owned by the University of Pennsylvania (Penn) or co-owned by Penn and the Children's Hospital of Philadelphia and exclusively licensed globally to Cabaletta

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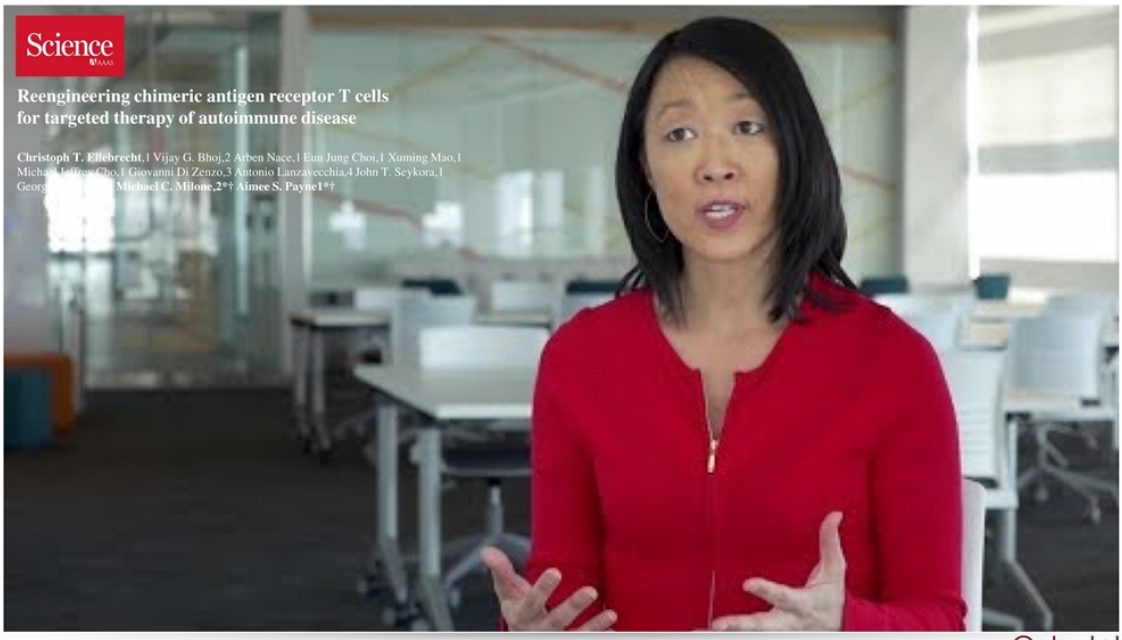
DSG3-CAART for mucosal pemphigus vulgaris patients

Pemphigus Vulgaris CAAR T Preclinical Development (video)

Ellebrecht…Milone, Payne, *Science* 2016



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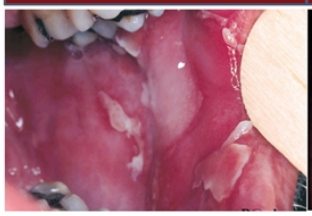
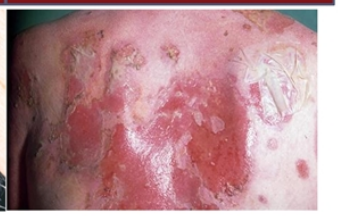
Pemphigus Vulgaris

Epidemiology, clinical signs and treatment

Mucosal PV: 25% of U.S. pemphigus vulgaris	Mucocutaneous PV: 75% of U.S. pemphigus vulgaris
	
http://www.danderm-pdv.is.kkh.dk/atlas/3-157.html	http://www.dermis.net/bilder/CD008/550px/img0042.jpg

Associated Antibody	Anti-DSG3	Anti-DSG3 + Anti-DSG1
Clinical Signs	Painful blisters of the orifices (mouth, nose, larynx, esophagus, eyes, genitalia, rectum)	Blisters on orifices and skin
Disease Incidence (US / EU)	350 / 600	1,050 / 1,800
Disease Prevalence (US / EU)	4,250 / 6,250	12,750 / 18,750

Current Treatment

- **Broad immunosuppression** with steroids, methotrexate, mycophenolate and/or azathioprine is **modestly effective and/or poorly tolerated.** Similar challenges with intravenous immunoglobulin (IVIG)
- B cell depletion with **rituximab**[1,2,3] offers **transient remission** (clinical & serologic) with **up to 90% of responders relapsing** without chronic therapy
- Chronic B cell depletion with rituximab: **5.4% annual risk of severe infection** and up to **1.9% lifetime risk of fatal infection**

Patients and physicians want safer and more effective treatment options

Image credit: D@nderm

1. 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.
2. Kushner, Carolyn J., et al. "Factors Associated With Complete Remission After Rituximab Therapy for Pemphigus." JAMA dermatology (2019).
3. Jancin, Bruce. "Rituximab bests mycophenolate in pemphigus vulgaris," Dermatology News, Nov 2019, Vol. 50:11, p. 2.; Press Release, Roche, 14 Oct 2019.

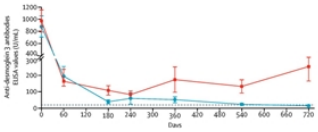
PV is an optimal lead indication for CAAR T therapy

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

1

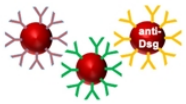
Serum anti-DSG3 **antibodies are 98 - 100% sensitive *and* specific**

2



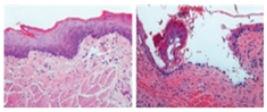
Depletion of B cells by rituximab[2] or antibody by plasmapheresis **transiently improves clinical disease**

3



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

4

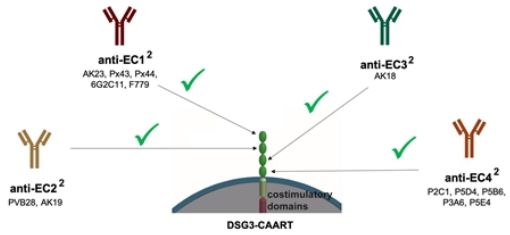


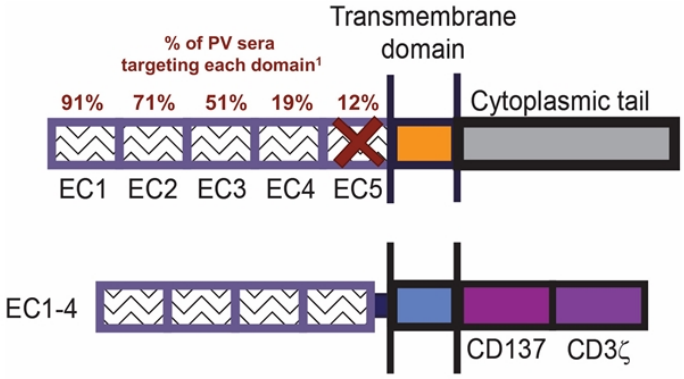
The DSG3 CAAR has **published animal model** proof-of-concept validation

1. Spindler, Volker, et al. "Mechanisms causing loss of keratinocyte cohesion in pemphigus." Journal of Investigative Dermatology 138.1 (2018): 32-37.
2. 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.

DSG3-CAART encompasses all known pathogenic epitopes

DSG3 EC1-4 CAAR is designed to target all known pathogenic B cells in mPV





EC5 directed antibodies are not known to be pathogenic

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.

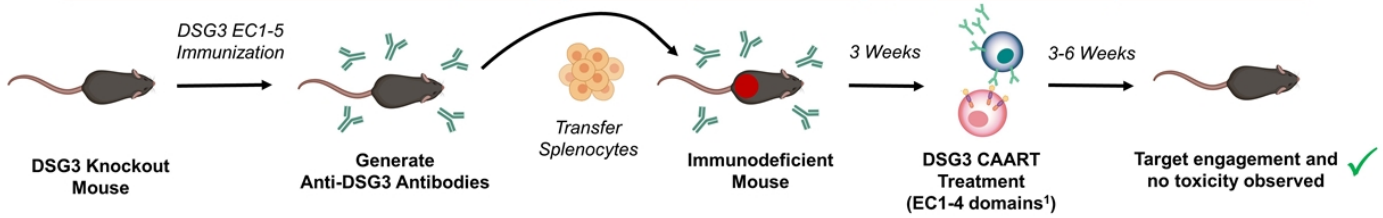
DSG3-CAART preclinical program summary of results

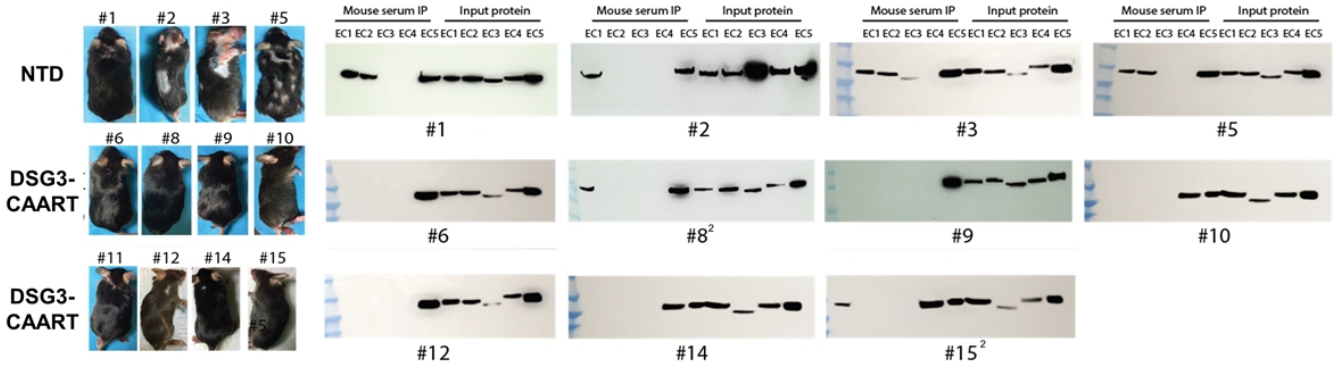
No evidence of toxicity at clinically relevant doses with selective and specific target engagement

	Indicator	Final Preclinical Results
Tolerability	*In vitro* off-target toxicity	**No specific cytotoxicity observed** • at clinically relevant cell numbers toward a panel of primary human & FcγR-expressing cells **No confirmed interactions with** human membrane proteins
Tolerability	*In vivo* off-target toxicity	**No detected off-target effects** at clinically relevant doses
Target Engagement	Anti-DSG3 autoantibody titer	Dose-dependent elimination of anti-DSG3 B cells and anti-DSG3 antibody reduction (**serologic 'remission'**)
Target Engagement	CAAR T cell engraftment	Dose-dependent increase in CAAR-positive cells observed via flow cytometry
Target Engagement	Tissue blistering	**No** blistering of oral mucosa (**histologic 'remission'**)
Target Engagement	Anti-DSG3 hybridoma outgrowth	**Significantly delayed growth or reduction of anti-DSG3 hybridomas, even in the presence of soluble anti-DSG antibodies**

Active immune model: target engagement despite soluble antibody

DSG3-CAART demonstrates target engagement in presence of high polyclonal antibody titer





1. The DSG3 protein is made of up of 5 extracellular (EC) domains, EC1-5. Antibodies against EC1-4 can be pathogenic, but antibodies against EC5 are not. Therefore, antibodies against EC5 are not targeted by the CAAR by design.
2. In this model, the human DSG3-CAART product is rapidly rejected. In these two animals, an incomplete response against EC1 was observed, which correlated with loss of persistence.

DesCAARTes phase 1 clinical trial (IND reviewed and accepted within 30 days)

Open-label study of DSG3-CAART in mucosal-dominant PV patients (mPV)

Open-label study to determine the maximum tolerated dose & fractionation of DSG3-CAART in 30 (up to 48) r/r mPV patients

Major Inclusion Criteria

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

Major Exclusion Criteria

- Rituximab in last 6 months
- Prednisone > 0.25mg/kg/day
- Other autoimmune disorder requiring immunosuppressive therapies
- Recent investigational treatment
- ALC < 1,000 at screening

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

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

Go: Identification of a dosing regimen with evidence of target engagement and an acceptable safety profile

1. FDA has requested, and the Company has agreed, that we will share data from cohort A to inform a discussion on the optimal design of cohort C. According to FDA guidance, the submission of cohort A data is not gating to planned enrollment in cohort B.

Clinical trial assessments and timeframes

Safety assessed acutely and at 3 months, with ability to measure CAART engagement by 6 months

Up to Week -18: *Screening*	***Week -6 to -1:*** *Apheresis and manufacturing*	***Day -7 to -3:*** *Pre-infusion visit*	*CAART infusion*	***8 Days:*** *Acute safety*	***3 Months:*** *Primary safety endpoint*	***6 Months:*** *Evidence of target engagement*	***3 years:*** *Efficacy*	***15 yrs:*** *Long-term follow-up*

Key Risks	Context and Mitigating Strategies	Options to Consider
CRS / Neurotoxicity	• CAAR T cells are designed to kill only 0.01-1% of total B cells • No lymphodepletion, low initial dose, dose fractionation	• Manage with standard protocols
Soluble antibody	• Toxicity mitigated with conservative dose escalation with fractionation	• Pretreatment with plasmapheresis or IVIG
Insufficient efficacy / CAAR T engraftment	• Wide cell dose range planned across cohorts A1 through A4	• Consider increased dose and/or preconditioning / lymphodepletion
Disease flare with medication taper or skin toxicity from cross-reactivity	• Absence of skin toxicity and/or disease flare in preclinical studies	• Topical steroids, oral steroids, or plasmapheresis.
New autoimmune disorder or worsening	• Exclude patients with active autoimmune disorders requiring immunosuppressants	• Manage with autoimmune therapies as needed

Declining trend in DSG3 antibody titers[1]

Assuming selective B cell ablation in 2-4 weeks, serum IgG (half-life ~3 wks) should fall within 6 months

Key Potential Efficacy Measures

- DSG3 antibody titer (ELISA)[1]
- Disease activity (clinical)
- Use of steroid / immunosuppressive tx

1. Spindler, Volker, et al. "Mechanisms causing loss of keratinocyte cohesion in pemphigus." Journal of Investigative Dermatology 138.1 (2018): 32-37.

Clinical trial communication plan

By dosing cohort except for serious adverse events that materially change timelines or protocol

- Enrollment
  - Patients dosed over 1-3 weeks for initial cohorts, then followed for at least 2-4 weeks before next patient
  - Timelines may be delayed due to non-material changes or challenges, including among others:
    - identifying appropriate patients for 1st trial of cell therapy in autoimmune disease
    - mitigating risks observed in earlier patients
    - manufacturing prioritization or outcomes

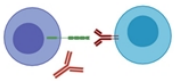
- Safety updates by dosing cohort – limited top-line updates
  - Acute – within 8 days of infusion
  - Primary endpoint safety measures – 3 months

- Target engagement updates by dosing cohort – possible but not expected in lowest dose
  - DSG3 antibody is **necessary and sufficient** to cause mPV (per consensus document[1])
    - DSG3 antibody half-life ~3 weeks
      - Potential evidence of reduction of DSG3 antibody levels within six months
    - Clinical responses including mucosal lesion response and absence of recurrence may take longer

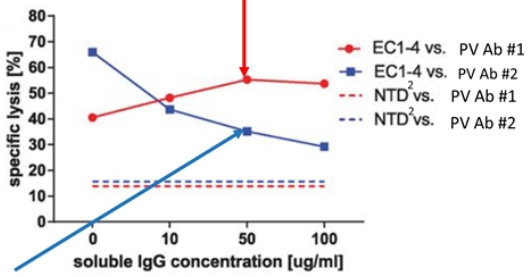
1. Spindler V, Eming R, Schmidt E, et al. Mechanisms Causing Loss of Keratinocyte Cohesion in Pemphigus. J Invest Dermatol 2018;138:32-7.

Soluble antibodies may alter the dynamics of DSG3-CAART proliferation

They can partially activate or inhibit DSG3 CAAR T cells[1]

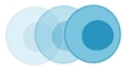


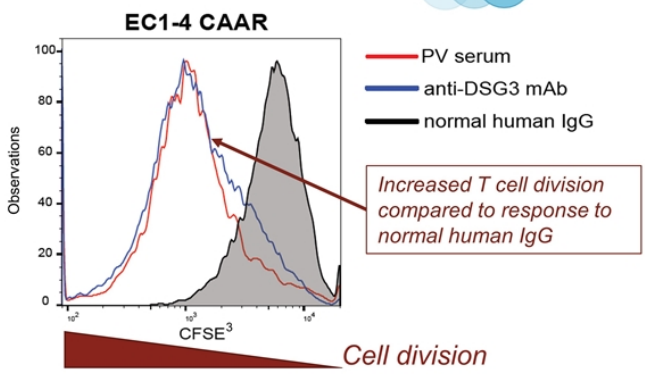
Increased target engagement



Decreased target engagement

Inhibitory antibodies reduce but do not fully prevent DSG3-CAART target engagement





Antibody induces T cell proliferation

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. Non-transduced T cell.
3. CFSE (carboxyfluorescein diacetate succinimidyl ester) is a dye used in flow cytometric monitoring that reduces in intensity as it is distributed in actively dividing cells. Non-dividing cells will retain more CFSE dye.

Preconditioning regimens in CAAR T cell therapy may not be required

Past successes in HIV and multiple myeloma without preconditioning plus differences in patient populations are relevant[1,2]

- Preconditioning may not be necessary to drive responses in the non-leukemia / lymphoma setting
  - not standard in this patient population and carries safety implications
- Potential activating effect of soluble antibody on engraftment and function is a key consideration
- Multiple infusions, higher dose, and cytokine support may offer safer approach for autoimmune patients
- Recent data in patients with multiple myeloma showed non-significant differences in objective response rate and rate of cytokine release syndrome in patients receiving CART-BCMA with and without lymphodepletion[1]

Lymphodepletion Mechanism	Oncology	Autoimmunity
Reduction of T cell growth cytokine sinks[3]	+	+
Depletion of suppressor cells[4]	+	-

\+ *Lymphodepletion mechanism likely to apply*

— *Lymphodepletion mechanism unlikely to apply*

The DesCAARTes trial will begin without a preconditioning regimen, but with a data-driven approach to potential incorporation as warranted

1. Cohen, Adam D., et al. "B cell maturation antigen–specific CAR T cells are clinically active in multiple myeloma." *The Journal of clinical investigation* 129.6 (2019).
2. Scholler, John, et al. "Decade-long safety and function of retroviral-modified chimeric antigen receptor T cells." *Science translational medicine* 4.132 (2012): 132ra53-132ra53.
3. Gattinoni et al. "Removal of homeostatic cytokine sinks by lymphodepletion enhances the efficacy of adoptively transferred tumor-specific CD8+ T cells." *The Journal of Experimental Medicine* 202(7):907-912
4. Wang, Shu and Plautz "Host lymphodepletion augments T cell adoptive immunotherapy through enhanced intratumoral proliferation of effector cells: *Cancer Research* 65(20): 9547-54.

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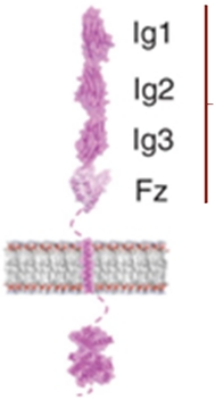
MuSK-CAART for myasthenia gravis patients

MuSK MG is a highly feasible and valuable CAAR target

All known extracellular domains can be included in the CAAR design

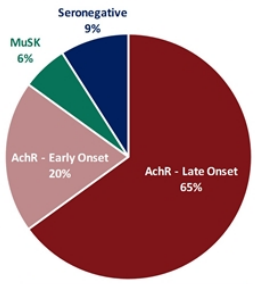
- Clinically high unmet need with limited treatment options
- Like pemphigus, autoantibody titers drop after rituximab[1,2], indicating the clinical potential of B cell depletion strategies in MuSK MG



MuSK has similar modular structure and size as Dsg3

Seronegative MG
Low affinity AChR, LRP4

MuSK MG
Early onset
7:1 female to male ratio
Typically more severe



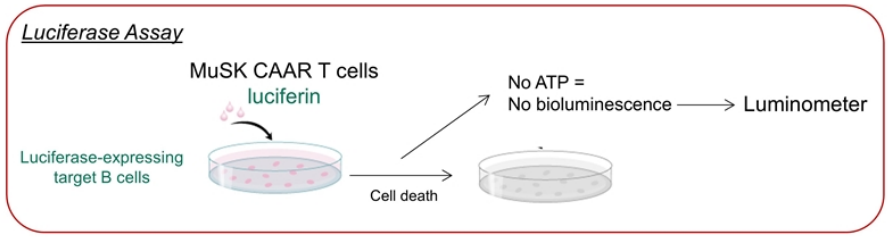
AChR MG Early Onset
Age <50 ; F>M

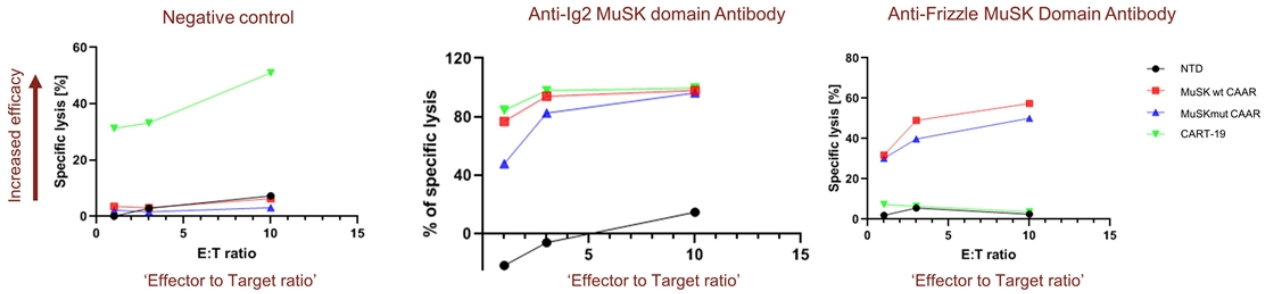
AChR MG Late Onset
Age >50 ; M>F

Prevalence: ~65,000 patients in the US

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.

MuSK CAAR T cells specifically kill anti-MuSK target cells *in vitro*





1. Sangwook Oh. "Antigen-specific B cell depletion for myasthenia gravis with chimeric autoantibody receptor (CAAR) T cells." American Neurology Associated Annual Conference. November 2019. Poster Presentation.

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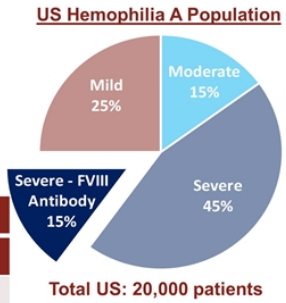
FVIII-CAART for Hemophilia A inhibitor patients

Hemophilia A and neutralizing alloantibodies

B cell-mediated inhibition of Factor VIII reduces efficacy of replacement therapy

- FVIII neutralizing alloantibodies can block protein or gene replacement therapy
  - Increased incidence in severe disease where native FVIII is not present
- Inhibitors persist in 70% of patients despite tolerance induction therapy[3]

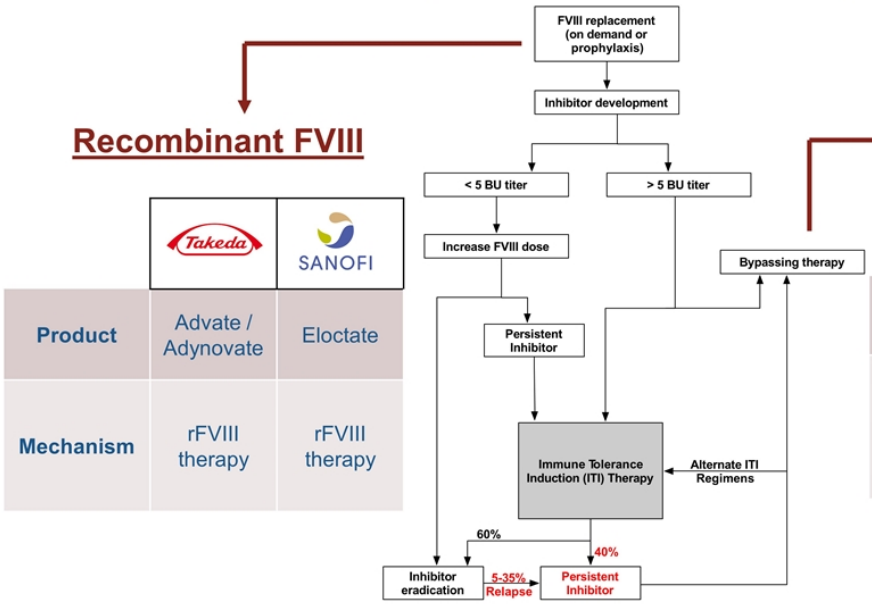


	Hemophilia A Population (US only)		
	Mild	Moderate	Severe
FVIII levels	5-40%	1-5%	<1%
% of cases	25%[1]	15%[1]	60% (~12,000 patients)[1,2]
Consequence	Bleeding after trauma or surgery	Hemarthrosis, synovitis muscle contracture cerebral stroke, death	Debilitating hemarthrosis muscle necrosis strokes, death
Risk of FVIII neutralizing alloantibodies	Minimal	Moderate (~10%)[3]	High (~25%)[3] ~3,000 US patients

1. https://www.hemophilia.org/Bleeding-Disorders/Types-of-Bleeding-Disorders/Hemophilia-A.
2. Peyvandi, Flora, et al. "A randomized trial of factor VIII and neutralizing antibodies in hemophilia A." New England Journal of Medicine 374.21 (2016): 2054-2064.
3. Arruda, Valder R., and Ben J. Samelson-Jones. "Gene therapy for immune tolerance induction in hemophilia with inhibitors." Journal of Thrombosis and Haemostasis 14.6 (2016): 1121-1134.

Current management of FVIII neutralizing alloantibodies

3-fold increased risk of hemophilia related death; overall 40% higher mortality



Recombinant FVIII

	Takeda	SANOFI
Product	Advate / Adynovate	Eloctate
Mechanism	rFVIII therapy	rFVIII therapy

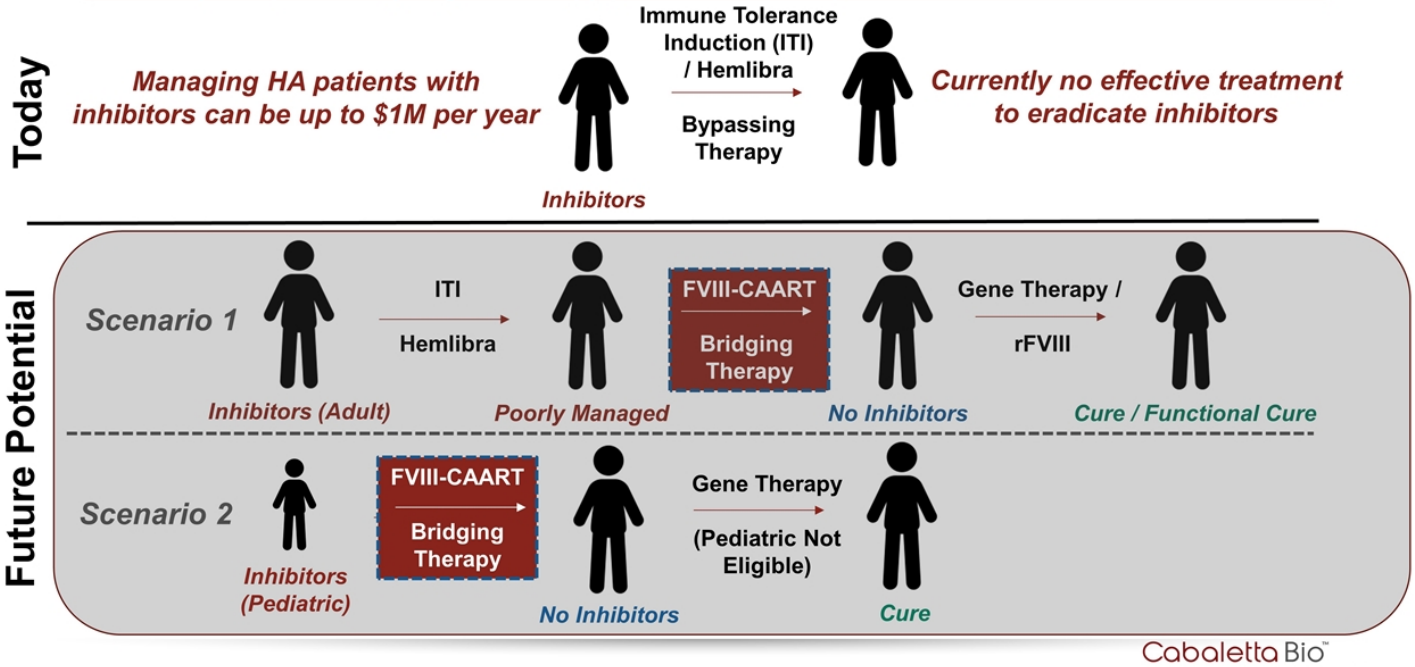
Bypassing Therapy

	Roche	Takeda	novo nordisk
Product	Hemlibra	FEIBA	NovoSeven
Mechanism	Bispecific antibody binding FIX / FX	Bypass inhibitor	Bypass inhibitor

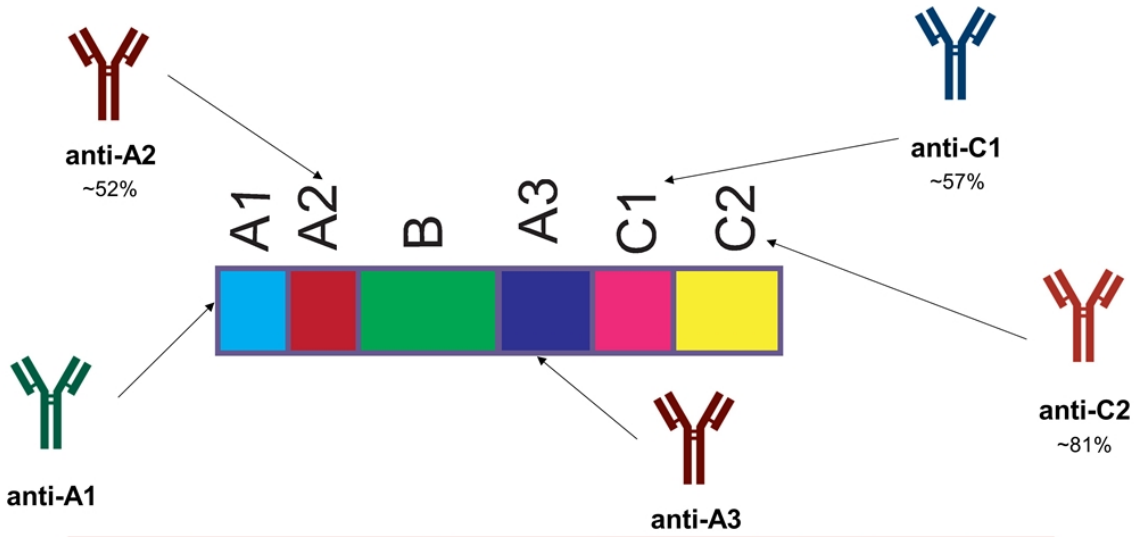
1. Kempton, Christine L., and Gilbert C. White. "How we treat a hemophilia A patient with a factor VIII inhibitor." Blood 113.1 (2009): 11-17.
2. Wermke, Martin, et al. "Successful eradication of acquired factor-VIII-inhibitor using single low-dose rituximab." Haematologica 95.3 (2010): 521.

FVIII-CAART value proposition is unique

Potentially complementary to gene therapy products in development



FVIII-CAART for hemophilia A patients with inhibitors



Epitopes on several domains of FVIII may bind pathogenic alloantibodies (inhibitors) in patients with Hemophilia A

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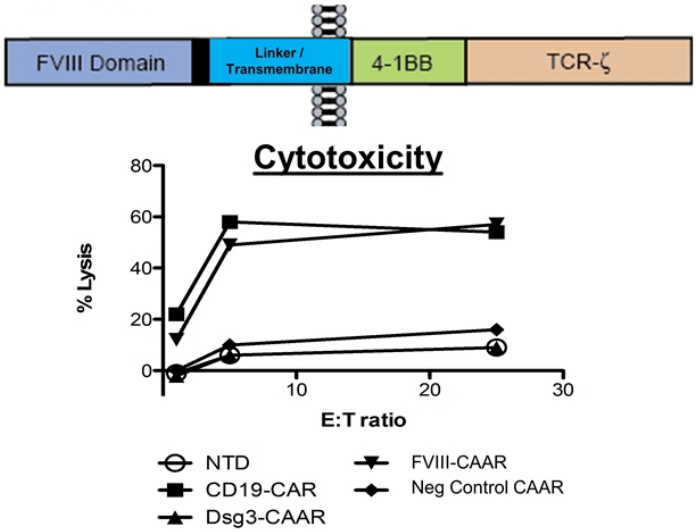
Kahle, Joerg, et al. "Frequency and epitope specificity of anti–factor VIII C1 domain antibodies in acquired and congenital hemophilia A." *Blood* 130.6 (2017): 808-816.

FVIII-CAART *in vitro* proof of concept data

Selective and specific target engagement



Cabaletta is developing optimized constructs designed to maximize the number of pathogenic domains and patients covered by the potential product candidate

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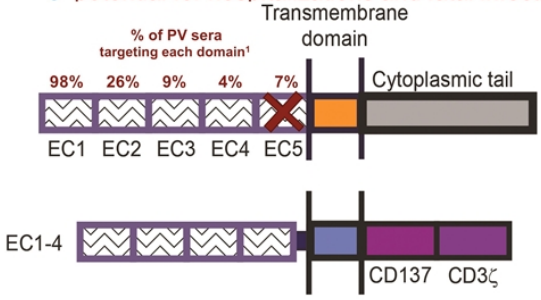
DSG3/1-CAART for mucocutaneous PV patients

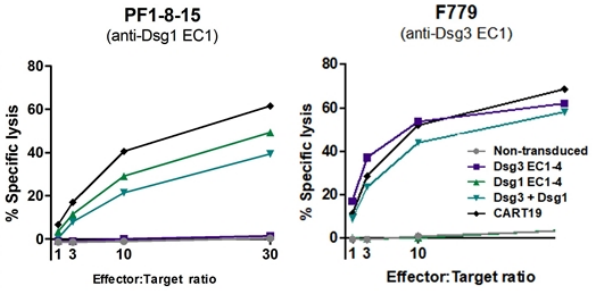
DSG3/1-CAART for mucocutaneous PV (mcPV)

Designed to cover all known pathogenic epitopes

- 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



- DSG1-CAART demonstrated specific cytotoxicity *in vitro to anti-DSG1 B cells*
  - DSG1-CAART + DSG3-CAART together demonstrated cytotoxicity toward both anti-DSG3 and anti-DSG1 B cells

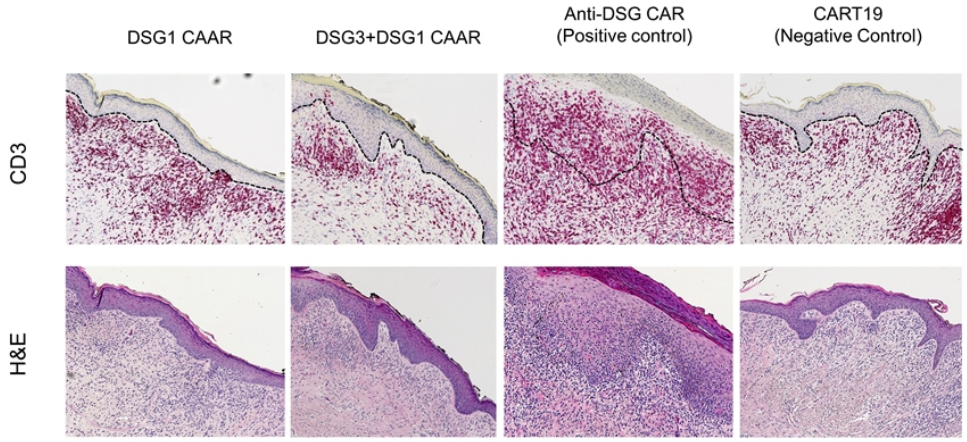


DSG1 EC1- 4 CAAR showed robust & specific *in vitro* cytotoxicity towards all known pathogenic epitopes

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.

No detected *in vivo* skin toxicity induced by DSG3/1-CAART

DSG1 CAAR T cells and DSG1 + DSG3 CAAR T



Designing optimal construct with both antigens in a single CAAR

1. Lee, Jinmin, et al., "Preclinical development of desmoglein chimeric autoantibody receptor (CAAR) T cells for pemphigus therapy", Poster presented at: *International Investigative Dermatology 2018*, Orlando, FL.

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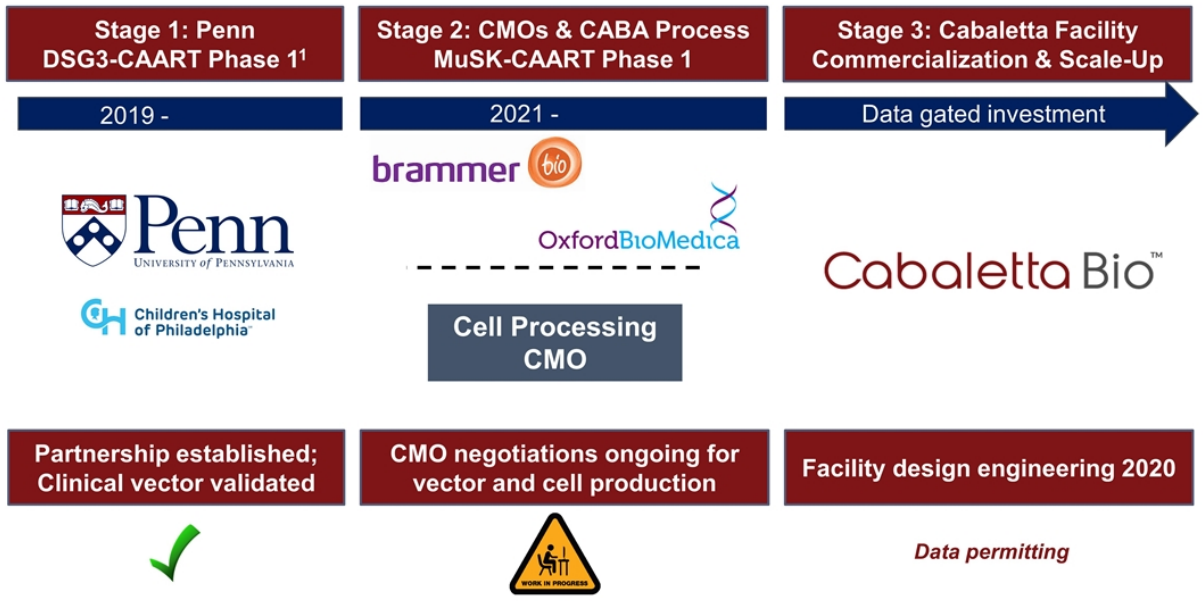
Manufacturing

Manufacturing strategy: three stages

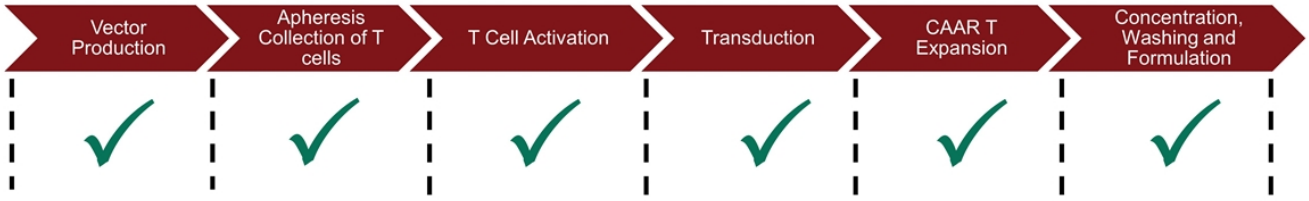
Risk mitigating, capital efficient, milestone gated progression proceeding as planned



1. Penn-sponsored CD19 CAR IND CMC data has been cross-referenced in DSG3-CAART IND to provide additional data reflecting alignment.

CAR T vs CAAR T manufacturing process[1]

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

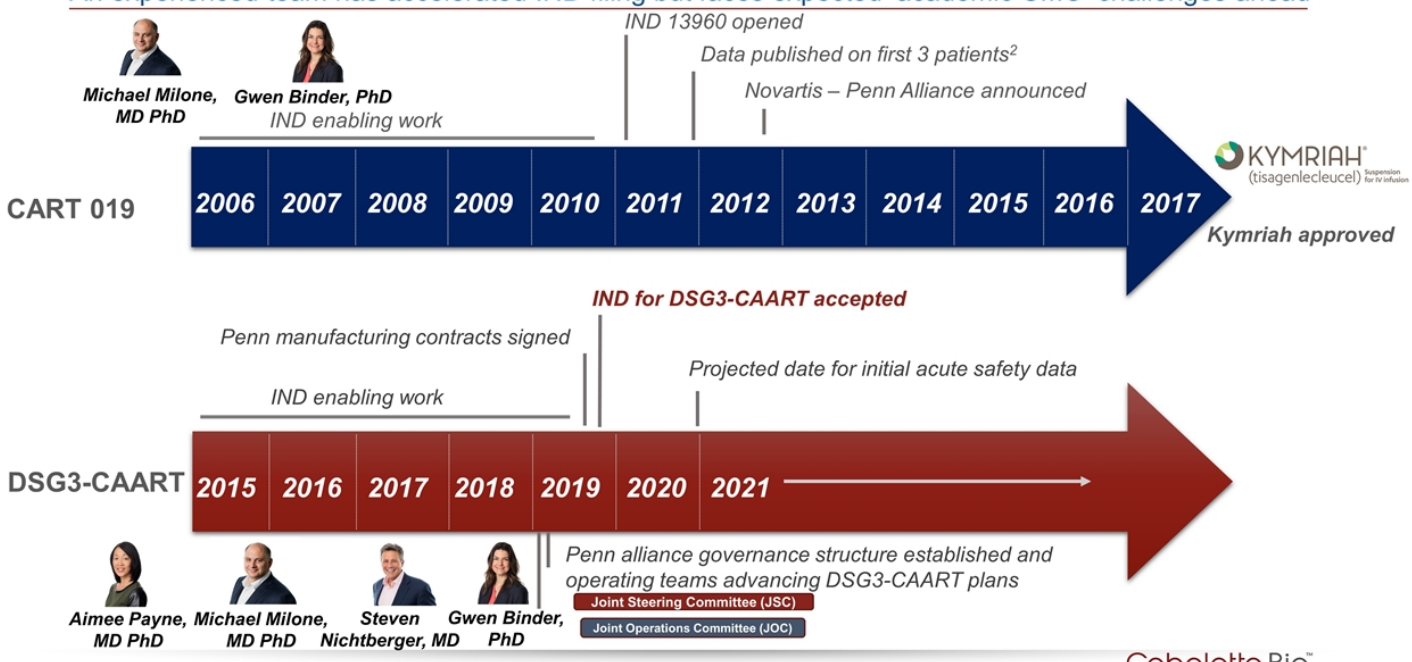


- Conserving the clinically validated CD19 CAR cell manufacturing process minimizes confounding risks
  - Supported Kymriah BLA approval; sufficient for commercial use
  - Penn process, not Novartis process; avoids Kymriah release challenges[2]
- Cross referenced the Penn IND to minimize operational risk
  - DSG3-CAART IND accepted within routine 30 day window following submission using Penn standard operating procedures
  - Clinical scale engineering runs have delivered successful DSG3-CAART product
  - Development work has demonstrated efficient manufacture of T cells from PV patients[3]
- Capacity of up to 3 runs a month has been contractually secured with Penn
- DSG3 vector supply secured for next 2-3 years

1. Penn-sponsored CD19 CAR IND CMC data has been cross-referenced in DSG3-CAART IND to provide additional data reflecting alignment.
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.

The Penn-Cabaletta[1] Alliance

An experienced team has accelerated IND filing but faces expected 'academic CMO' challenges ahead



1. In addition to the cofounders, Steven Nichtberger, MD is a professor at Penn, and Gwendolyn Binder PhD is a former employee at Penn.
2. Porter, David L., et al. "Chimeric antigen receptor–modified T cells in chronic lymphoid leukemia." New England Journal of Medicine 365.8 (2011): 725-733.

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Financial Update

Key financial highlights and funding history

Financial Highlights		
	9 months ended 09/30/2019	**Proforma 09/30/2019**
Cash and Cash Equivalents	$71.0mn	$142.1mn[1]
Operating Expenses	$12.8mn	$12.8mn
Cash Runway	-	At least through 1Q 2022

Funding History			
Round	**Date**	**Amount ($mn)**	**New Investors**
Convertible Notes	May 2018	$12.5	Adage Capital Management, L.P. · Baker Brothers Advisors LLC · Penn
Series A	October 2018	$25.3	5AM Ventures
Series B	January 2019	$50.0	Cormorant Asset Management · Deerfield Capital Management LLC · Redmile Group · Boxer Capital
IPO	October 2019	$80.0[2]	All prior financial investors plus new investors

1. Includes $71mn in net proceeds from IPO.
2. Includes partial exercise of the option to purchase additional shares in November 2019.

Recent and anticipated catalysts

- 2019
  - ✓ Recruited uniquely qualified leadership team with longstanding connections
  - ✓ Established broad alliance with Penn to accelerate DSG3-CAART clinical development
  - ✓ Secured first issued US product patent and expanded portfolio
  - ✓ Expanded Penn license to include filed patents for one additional target
  - ✓ Manufactured and qualified vector for clinical trial, completed manufacturing engineering runs
  - ✓ IND accepted for DSG3-CAART, IRB process being initiated
  - ✓ *In vitro* MuSK-CAART data presented at scientific meeting

- 2020
  - DesCAARTes clinical trial
    - Initiate trial and generate acute tolerability (8 day) data from initial patient cohort
  - MuSK-CAART
    - Present *in vivo* target engagement data and initiate IND-enabling studies
  - Initiate validation of manufacturing with CMO for clinical program
    - Incorporate advanced technologies as warranted

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Selective B cell ablation for autoimmune disease

February 2020