Cabaletta Bio®

Corporate Presentation

MARCH 2024

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Words such as, but not limited to, "look forward to," "believe," "expect," "anticipate," "estimate," "intend," "plan," "would," "should" and "could," and similar expressions or words, identify forward-looking statements.

Various risks, uncertainties and assumptions could cause actual results to differ materially from those anticipated or implied in our forward-looking statements. Such risks and uncertainties include, but are not limited to, risks related to the success, cost, and timing of our product candidate development activities and preclinical studies and clinical trials, risks related to our ability to demonstrate sufficient evidence of safety, efficacy and tolerability in our preclinical studies and clinical trials of CABA-201, DSG3-CAART and MuSK-CAART, the risk that the results observed with the similarly-designed construct, including, but not limited to, due to dosing regimen, are not indicative of the results we seek to achieve with CABA-201, our plans to evaluate additional cohorts in the DesCAARTes™ trial, including a cohort implementing a pre-treatment regimen, the risk that signs of biologic activity or persistence may not inform long-term results, the risk that persistence observed with effective CART-19 oncology studies in combination with lymphodepletion is not indicative of, or applicable to, clinical responses in patients with mPV, risks related to clinical trial site activation or enrollment rates that are lower than expected, our ability to protect and maintain our intellectual property position, risks related to our relationships with third parties, uncertainties related to regulatory agencies' evaluation of regulatory filings and other information related to our product candidates, our ability to retain and recognize the intended incentives conferred by any Orphan Drug Designations and Fast Track Designations, risks related to regulatory filings and potential clearance, the risk that any one or more of our product candidates will not be successfully developed and commercialized, the risk that the results of preclinical studies or clinical studies will not be predictive of future results in connection with future studies, and risks related to volatile market and economic conditions and public health crises. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Accordingly, you are cautioned not to place undue reliance on these forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause our actual results to differ materially from those contained in the forward-looking statements, see the section entitled "Risk Factors" in our most recent annual report on Form 10-K, as well as discussions of potential risks, uncertainties, and other important factors in our other and subsequent 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.

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

Cabaletta Bio®

Realizing the vision to transform autoimmune disease treatment

Engineered CABA-201 specifically for use in autoimmune patients

- *Aim to build on academic report which demonstrated favorable safety data & durable, drug free remissions[1]*

Designed novel Phase 1/2 trials to accelerate path to approval

- *no requirement for dose escalation*
- *independent, parallel 6-patient cohorts*
- *broad portfolio of indications*

Initiated dosing in CABA-201 program

Cash runway into 1H26

1H24:
Initial clinical data from each of the first patients in myositis & SLE trials

2H24:
Follow-up & additional data in myositis & SLE

Initial clinical data in SSc & gMG

- **Securing scalable commercial manufacturing**
- **Expanding to multiple additional indications**
- **Innovating to optimize patient & physician experience**

SLE – Systemic lupus erythematosus; SSc – Systemic sclerosis; gMG – Generalized myasthenia gravis

1. Müller, Fabian, et al. "CD19 CAR T-Cell Therapy in Autoimmune Disease—A Case Series with Follow-up." New England Journal of Medicine 390.8 (2024): 687-700. The construct utilized in these studies has a similar design to CABA-201, sharing the 4-1BB costimulatory domain, but is a different construct.

Cabaletta Bio®

Pipeline targeting autoimmune diseases with high unmet need

Innovative and scalable clinical strategy with potential for accelerated development path

Program	Trial	Preclinical	Phase 1/2	Pivotal
CABA-201 FTD *4-1BB CD19-CAR T*	**RESET-Myositis™**	*Dermatomyositis*		
		Anti-synthetase syndrome		
		IMNM		
	RESET-SLE™	*Lupus Nephritis*		
		Non-Renal SLE		
	RESET-SSc™	*Skin + Organ Cohort*	*IND cleared*	
		Skin Cohort		
	RESET-MG™	*AChR-Ab pos. gMG*	*IND cleared*	
		AChR-Ab neg. gMG		
CAART FTD *Chimeric AutoAntibody Receptor T cells*	**DesCAARTes™**	*Mucosal pemphigus vulgaris*[1]		
	MusCAARTes™	*MuSK-Ab positive MG*[1]		

Rheumatology
Neurology
Dermatology

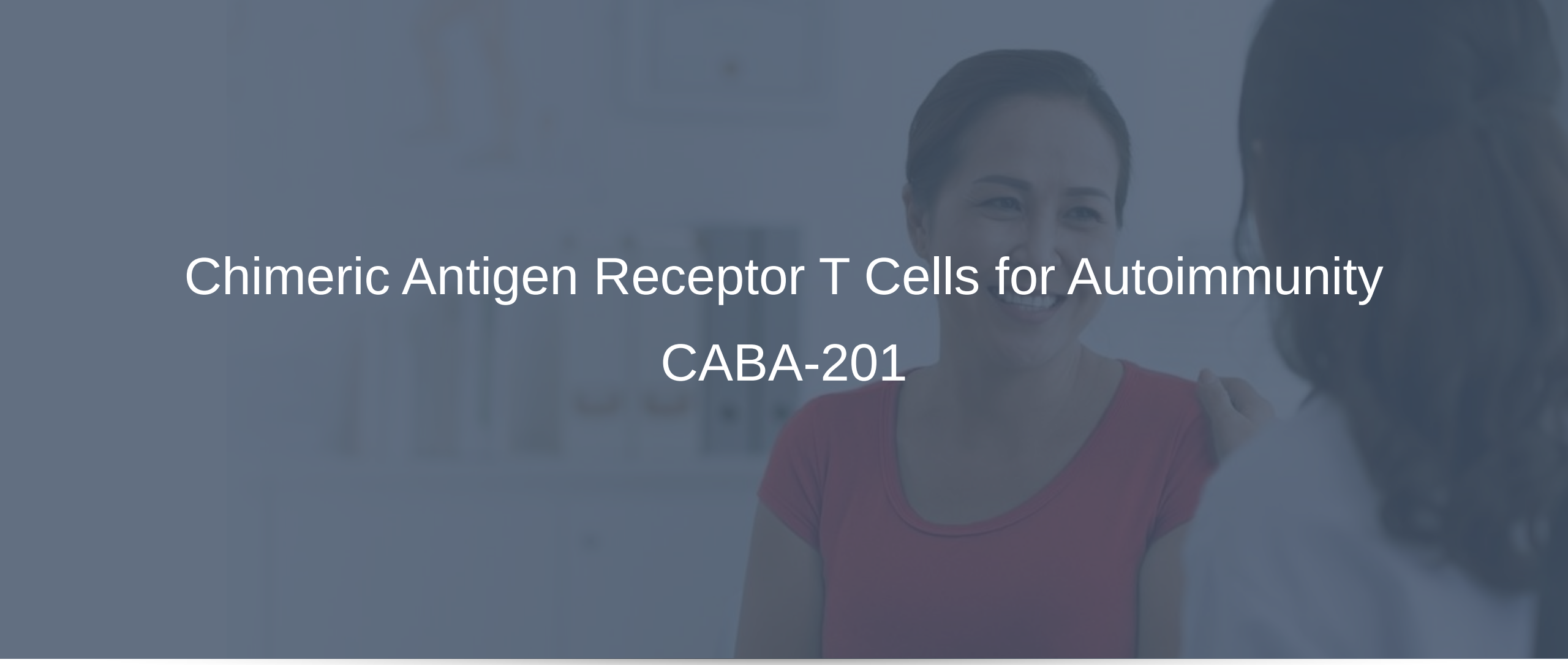
Expanding the potential application of CABA-201 to multiple additional indications in 2024

RESET™ – **RE**storing **SE**lf-**T**olerance; IMNM – Immune-mediated necrotizing myopathy; SLE – Systemic lupus erythematosus; Ab – Antibody; AChR – Acetylcholine receptor; gMG – Generalized myasthenia gravis

1. Currently being evaluated in a Phase 1 trial.

● FDA Fast Track Designation received in dermatomyositis, SLE and lupus nephritis, systemic sclerosis, mucosal pemphigus vulgaris, and MuSK-Ab positive MG.

Cabaletta Bio®



Chimeric Antigen Receptor T Cells for Autoimmunity

CABA-201

Cabaletta Bio®

Academic data: Immune system reset in autoimmune patients

Promising clinical responses in 15 patients across several autoimmune diseases with 4-1BB CD19-CAR T[1,2]

100%

Objective clinical response rate in SLE, myositis, SSc

T cell expansion & B cell depletion within 1st month enabled robust clinical improvement by 3 months

<7%

Rate of CRS more severe than fever (1/15)

11/15 patients reported by Erlangen group with CRS, 10/11 with fever*

Single grade 1 ICANS event reported (transient dizziness)

**One grade 2 CRS (increased oxygen requirement in patient with pre-existing lung disease[3])*

2+

Years of SLE durable drug-free remission

Up to 29 months of follow-up with no relapses in any of the 15 patients reported by Erlangen group, off immunosuppressive agents

3-7

Months to naïve B cell repopulation

In patients with ≥5 months of follow-up, complete B cell elimination followed by return of healthy naïve B cells within median of ~3 months

CRS – Cytokine release syndrome; ICANS – Immune effector cell-associated neurotoxicity syndrome

1. Müller, Fabian, et al. "CD19 CAR T-Cell Therapy in Autoimmune Disease—A Case Series with Follow-up." New England Journal of Medicine 390.8 (2024): 687-700.
2. The construct utilized in these studies has a similar design to CABA-201, sharing the 4-1BB costimulatory domain, but is a different construct.
3. Taubmann J, et al. Efficacy and Safety of CAR-T-Cell Treatment in Refractory Antisynthetase Syndrome – Data of the First Three Patients [ACR abstract; Nov 14, 2023].

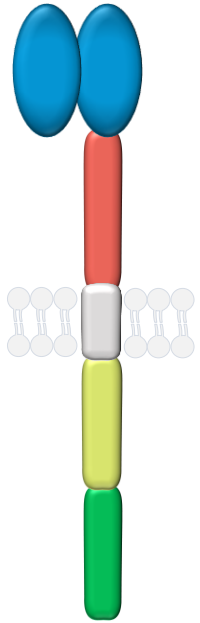
CABA-201: CD19-CAR T specifically designed for autoimmunity

Cabaletta's CD19 binder with similar *in vitro* & *in vivo* activity to FMC63[1,2] (binder used in academic report[3])

Fully human anti-CD19 binder
Similar binding affinity & biologic activity to FMC63, with binding to the same epitope[1,2]

4-1BB costimulatory domain
Same co-stim. domain as used in academic studies

CD3-Zeta signaling domain



CABA-201[5]

Clinical data reported by IASO using licensed CD19 binder in oncology[4]

- **Fully human binder**
  Evaluated as dual-CAR combined with CD22 binder with standard Flu/Cy preconditioning
- **Data reported in ~20 patients to date**
  B cell leukemia and lymphoma in IIT in China
- **Safety data supports autoimmune development**

IIT – Investigator-initiated trial; Flu/Cy – Fludarabine/Cyclophosphamide

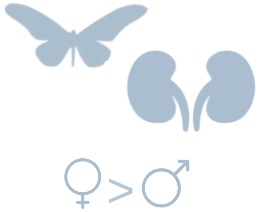
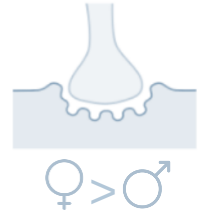
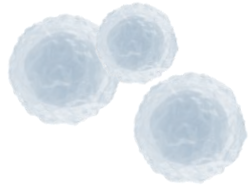
1. Peng, Binghao J, et al. "Preclinical specificity and activity of CABA-201, a fully human 4-1BB containing CD19 CAR T therapy for treatment-resistant autoimmune disease." Poster presented at: American Society Gene and Cell Therapy 26th Annual Meeting; 2023 May 19; Los Angeles, CA.
2. Dai, Zhenyu, et al. "Development and functional characterization of novel fully human anti-CD19 chimeric antigen receptors for T-cell therapy." Journal of Cellular Physiology 236.8 (2021): 5832-5847.
3. Müller, Fabian, et al. "CD19 CAR T-Cell Therapy in Autoimmune Disease—A Case Series with Follow-up." New England Journal of Medicine 390.8 (2024): 687-700.
4. Evaluated as part of CT120, a dual-CD19xCD22 CAR T product candidate under development by Nanjing IASO Biotherapeutics, Co., Ltd. (IASO Bio).
5. Transmembrane domain in CABA-201 is CD8α vs. TNFRSF19 (Troy) utilized in the academic construct. The two transmembrane domains have not been shown to have a significant difference in function or IFN-γ production in preclinical studies. The CD8α transmembrane domain is employed in tisagenlecleucel.

REstoring **SE**lf-**T**olerance (**RESET™**) Phase 1/2 trials advancing

SLE & myositis trials currently enrolling, with a broadening portfolio to realize the potential of CABA-201

Phase 1/2 Trials — **Preclinical**

Rheum
Neuro
Undiscl.

Myositis	SLE	SSc	gMG	2024
				
Typical onset middle age Only FDA-approved therapy is IVIg in DM High mortality due to lung & cardiac involvement	Affects young women & people of color ~40% with lupus nephritis, which carries ~25% risk of death or ESRD within 10y	Middle age onset common Progressive skin & organ fibrosis with lung, cardiac, renal damage Average survival of 12y	Bimodal age of onset Profound weakness that can be disabling Risk for myasthenic crises, with respiratory failure	Autoimmune diseases in which B cells play a key role
U.S. Prevalence				
~66k	**~160-320k**	**~88k**	**~55k**	**Over 1 million**

Current therapies offer modest efficacy & often result in chronic and broad immunosuppression

SLE – Systemic lupus erythematosus; DM – Dermatomyositis; SSc – Systemic sclerosis; gMG – Generalized myasthenia gravis; ESRD – End-stage renal disease

Clinical strategy to reduce risk, maximize reach & accelerate timelines

Broad investigation of CABA-201 in well-defined patient populations with the same dose & similar design

RESET-Myositis™

- ASyS Cohort — CABA-201 — Single infusion[1]
- DM Cohort — CABA-201 — Single infusion[1]
- IMNM Cohort — CABA-201 — Single infusion[1]

RESET-SLE™

- Lupus Nephritis Cohort — CABA-201 — Single infusion[1]
- Non-renal SLE Cohort — CABA-201 — Single infusion[1]

RESET-SSc™

- Skin + Organ Involvement Cohort — CABA-201 — Single infusion[1]
- Severe Skin Involvement Cohort — CABA-201 — Single infusion[1]

RESET-MG™

- AChR+ gMG Cohort — CABA-201 — Single infusion[1]
- AChR- gMG Cohort — CABA-201 — Single infusion[1]

CD19-CAR T clinical data reported in academic literature[2]

No CD19-CAR T clinical data

Each cohort to include 6 patients treated with an identical dose – without dose escalation requirement – and designed to inform discussions with FDA on registrational path for each indication

SLE – Systemic lupus erythematosus; SSc – Systemic sclerosis; gMG – Generalized myasthenia gravis; ASyS – Anti-synthetase syndrome; DM – Dermatomyositis; IMNM – Immune-mediated necrotizing myopathy

1. Subjects will be treated with a standard preconditioning regimen consisting of fludarabine and cyclophosphamide prior to a single dose CABA-201, followed by short inpatient stay.
2. The data reported in the academic literature does not employ CABA-201.

RESET-Myositis™: Phase 1/2 study design for CABA-201

Patient dosing commenced; enrolling patients with active myositis with DM, ASyS or IMNM subtypes

Screening

Key inclusion criteria

- Adults 18-65y
- Clinical IIM diagnosis
- Subtype based on serology
- Disease activity despite standard of care
- Recommended vaccines

Key exclusion criteria

- Cancer associated myositis
- Significant lung or cardiac impairment
- Treatment with anti-B cell agent within prior ~6 months
- Treatment with biologic agent within prior ~3 months

Phase 1/2 Study Design

Open-label trial with parallel 6-subject cohorts

CABA-201

DM — *Single dose of 1x10^6 cells/kg*[1]

CABA-201

ASyS — *Single dose of 1x10^6 cells/kg*[1]

CABA-201

IMNM — *Single dose of 1x10^6 cells/kg*[1]

Equivalent to dose of 4-1BB CD19-CAR T used in academic report along with standard preconditioning[1,2]

Study Objectives

Primary objective

Safety & tolerability within 28 days of infusion

Categories of key secondary objectives

- **Myositis clinical activity – Total Improvement Score**
- **Functional & radiographic evidence of disease**
- **Myositis serology**
- **Pharmacokinetics / pharmacodynamics**

IIM – Idiopathic inflammatory myopathy; DM – Dermatomyositis; ASyS – Anti-synthetase syndrome; IMNM – Immune-mediated necrotizing myopathy

1. Subjects will be treated with a standard preconditioning regimen consisting of fludarabine and cyclophosphamide prior to a single dose CABA-201, followed by short inpatient stay.
2. Müller, Fabian, et al. "CD19 CAR T-Cell Therapy in Autoimmune Disease—A Case Series with Follow-up." New England Journal of Medicine 390.8 (2024): 687-700.

RESET-SLE™: Phase 1/2 study design for CABA-201

Currently enrolling patients with active SLE with or without renal involvement

Screening

Key inclusion criteria

Adults 18-65y

Clinical SLE diagnosis

Confirmatory serology

Disease activity despite standard of care

Recommended vaccines

Key exclusion criteria

Treatment with anti-B cell agent within prior ~6 months

Treatment with biologic agent within prior ~3 months

Phase 1/2 Study Design

Open-label trial with parallel 6-subject cohorts

SLE with lupus nephritis — **CABA-201** — *Single dose of 1x10⁶ cells/kg*[1]

SLE without renal disease — **CABA-201** — *Single dose of 1x10⁶ cells/kg*[1]

Equivalent to dose of 4-1BB CD19-CAR T used in academic report along with standard preconditioning[1,2]

Study Objectives

Primary objective

Safety & tolerability within 28 days of infusion

Categories of key secondary objectives

- **SLE clinical activity**
- **SLE serology**
- **Pharmacokinetics / pharmacodynamics**

Similarly designed Phase 1/2 trials – RESET-SSc™ & RESET-MG™ – advancing in SSc & gMG

SLE – Systemic lupus erythematosus; SSc – Systemic sclerosis; gMG – Generalized myasthenia gravis

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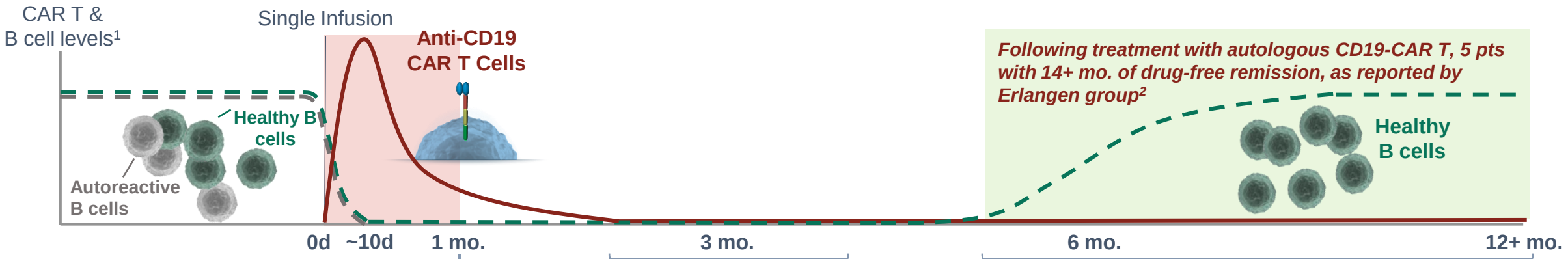
2. Müller, Fabian, et al. "CD19 CAR T-Cell Therapy in Autoimmune Disease—A Case Series with Follow-up." New England Journal of Medicine 390.8 (2024): 687-700.

Evaluation metrics to assess outcomes of CAR T in autoimmunity

For CABA-201, translational effects in 1st month may inform clinical outcomes at 3 months



Metrics of evaluation	Within 1 month	~3 months	5-12+ months
Translational measures	❑ CAR T expansion: Magnitude & timing ❑ B cell depletion: Timing & depth	❑ Autoantibody changes ❑ Vaccine titer changes ❑ Inflammatory marker changes	❑ Time to B cell repopulation ❑ Autoantibody changes ❑ Vaccine titer changes
Clinical data	❑ Rate of CRS more severe than fever ❑ Rate & grade of ICANS ❑ Rate & severity of infection	❑ Early efficacy signals ❑ Rate & severity of infection	❑ Durability of clinical activity ❑ Rate & severity of infection
Patient experience	❑ Hospitalization requirements ❑ Preconditioning & infusion regimen	❑ Concomitant medications, if any	❑ Concomitant medications, if any

SLE – Systemic lupus erythematosus; SSc – Systemic sclerosis; gMG – Generalized myasthenia gravis

1. Illustrative graphic, adapted from Taubmann, J., et al. "OP0141 Long Term Safety and Efficacy Of CAR-T Cell Treatment in Refractory SLE-Data from the First Seven Patients." (2023): 93-94.
2. Müller, Fabian, et al. "CD19 CAR T-Cell Therapy in Autoimmune Disease—A Case Series with Follow-up." New England Journal of Medicine 390.8 (2024): 687-700.

Manufacturing strategy

Staged approach allows for efficient allocation of capital while leveraging experienced partners

Early Phase:
Penn, CDMOs & CABA Process

Ongoing

- **Penn has reliably provided timely product for years**
- **Commercial CDMO partnerships have expanded our vector and cell product supply**
  - **Oxford: Lentiviral supply partner**
  - **WuXi: Additional cell processing supply partner**

Late Phase & Commercial:
Scale-Up & Commercialization

Data-gated, staged investment

- **Evaluating potential paths to commercial-ready manufacturing:**
  - **Expansion of CDMO relationships**
  - **Cabaletta-operated facility**
  - **Strategic partnership(s)**
- **Continuous focus on innovations to address scale**

Preparations ongoing to implement commercial-ready process in advance of pivotal studies

Securing & expanding our leadership in autoimmune cell therapy

Rapidly advancing to address patient need

Advancing the RESET™ clinical trials with the goal of delivering on our commitment to patients

Myositis

Systemic lupus erythematosus

Systemic sclerosis

Generalized myasthenia gravis

- Minimizing the requirement for inpatient stay
- Optimizing the preconditioning regimen
- Reducing the burden of apheresis
- Innovating to address scale in autoimmune disease

Broadening potential to serve patients

Biologic opportunity for potential cure or paradigm-shifting treatment may be possible in dozens of autoimmune diseases

Rheumatology	• Rheumatoid arthritis • ANCA-associated vasculitis • Sjogren's syndrome
Neurology	• Multiple sclerosis • Neuromyelitis optica • CIDP
Nephrology	• Membranous nephropathy • Goodpasture's syndrome
Dermatology	• Pemphigus vulgaris • Pemphigus foliaceus • Epidermolysis bullosa acquisita • Bullous pemphigoid
Hematology	• Immune thrombocytopenic purpura • Thrombotic thrombocytopenic purpura • Antiphospholipid syndrome • Autoimmune hemolytic anemia
Endocrinology	• Type 1 diabetes • Graves' disease • Hashimoto's disease

Corporate Summary

Cabaletta Bio®

Cabaletta Bio leadership

Track record of operational success evaluating novel cell therapy candidates in autoimmunity

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tengion
Penn

Samik Basu, M.D.
Chief Scientific Officer

Adaptimmune
MERCK

Gwendolyn Binder, Ph.D.
President, Science & Technology

Adaptimmune
Penn

David J. Chang, M.D., M.P.H., FACR
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AstraZeneca
gsk
Penn

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Goldman Sachs
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Spark
SANDOZ A Novartis Division

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Adaptimmune
Pfizer

Anup Marda
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accentureconsulting

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FORTUNE BEST SMALL WORKPLACES 2023
FORTUNE BEST WORKPLACES IN BIOPHARMA 2023

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