



Cabaletta Bio[®]

CABA-201 Initial Clinical Data from the RESET-Myositis[™] & RESET-SLE[™] Phase 1/2 Trials

JUNE 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 CD19-CAR T 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.

Today's Agenda

AGENDA TOPIC	SPEAKER
CABA-201 Overview	Steven Nichtberger, MD <i>Chief Executive Officer</i>
Current & Investigational Treatments for Patients with Autoimmune Disease	Iain McInnes, MD, FRCP, PhD, FRSE, FMedSci <i>Vice Principal and Head of the College of Medical, Veterinary and Life Sciences, Muirhead Chair of Medicine and Versus Arthritis Professor of Rheumatology at the University of Glasgow</i>
Initial CABA-201 Data in Myositis & Lupus	David Chang, MD, MPH, FACR <i>Chief Medical Officer</i>
Conclusions	Steven Nichtberger, MD <i>Chief Executive Officer</i>
Q&A	

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

Designed to replicate and expand on the academic clinical data that generated interest in the field

CABA-201 designed to optimize the potential safety and efficacy of CD19-CAR T for patients with autoimmune disease

Fully human anti-CD19 binder

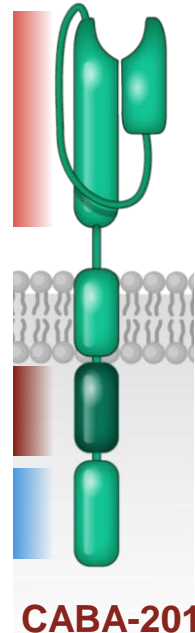
Similar binding affinity and biologic activity to FMC63, with binding to the same epitopes^{1,2}

Safety data in ~20 oncology patients evaluated and reported by IASO as part of a dual-CAR³

4-1BB costimulatory domain

Same domain as used in academic studies

CD3-zeta signaling domain



Key Questions for RESET™ Phase 1/2 Studies

Safety of CABA-201

CABA-201 AE profile
CRS, ICANS, SAEs

Dose selection 1×10^6 cells/kg

PK – CAR T persistence
PD – B cell depletion
Autoantibody reduction
Clinical outcomes

PK, pharmacokinetics; PD, pharmacodynamics; SAEs: serious adverse events

1. Peng, BinghaoJ, et al. Presented at: American Society Gene and Cell Therapy 26th Annual Meeting; 2023 May 19; Los Angeles, CA.

2. Dai, Zhenyu, et al. Journal of Cellular Physiology. 2021;236(8): 5832-5847.

3. Evaluated as part of CT120, a dual-CD19xCD22 CAR T product candidate under development by Nanjing IASO Biotherapeutics, Co., Ltd. (IASO Bio).

CABA-201 pipeline targeting a broad range of autoimmune diseases

Innovative and scalable clinical strategy with potential for accelerated development path

Program	Trial	Preclinical	Phase 1/2	Pivotal
CABA-201 4-1BB CD19-CAR T	RESET-Myositis™	<i>Dermatomyositis</i>		
		<i>Anti-synthetase syndrome</i>		
		<i>IMNM</i>		
		<i>Juvenile Myositis</i>		
	RESET-SLE™	<i>Lupus Nephritis</i>		
		<i>Non-Renal SLE</i>		
	RESET-SSc™	<i>Skin + Organ Cohort</i>		
		<i>Skin Cohort</i>		
	RESET-MG™	<i>AChR-Ab pos. gMG</i>		
		<i>AChR-Ab neg. gMG</i>		
	RESET-PV™ Sub-study¹	<i>Mucocutaneous & mucosal pemphigus vulgaris</i>		

- Rheumatology
- Neurology
- Dermatology
- Contains cohort(s) without preconditioning
- Pediatric Indication

Clinical & translational data² support the selected single dose of CABA-201 at 1 x 10⁶ cells/kg

RESET™ – REstoring SElf-Tolerance; IMNM – Immune-mediated necrotizing myopathy; SLE – Systemic lupus erythematosus; Ab – Antibody; AChR – Acetylcholine receptor; gMG – Generalized myasthenia gravis, PV – Pemphigus vulgaris

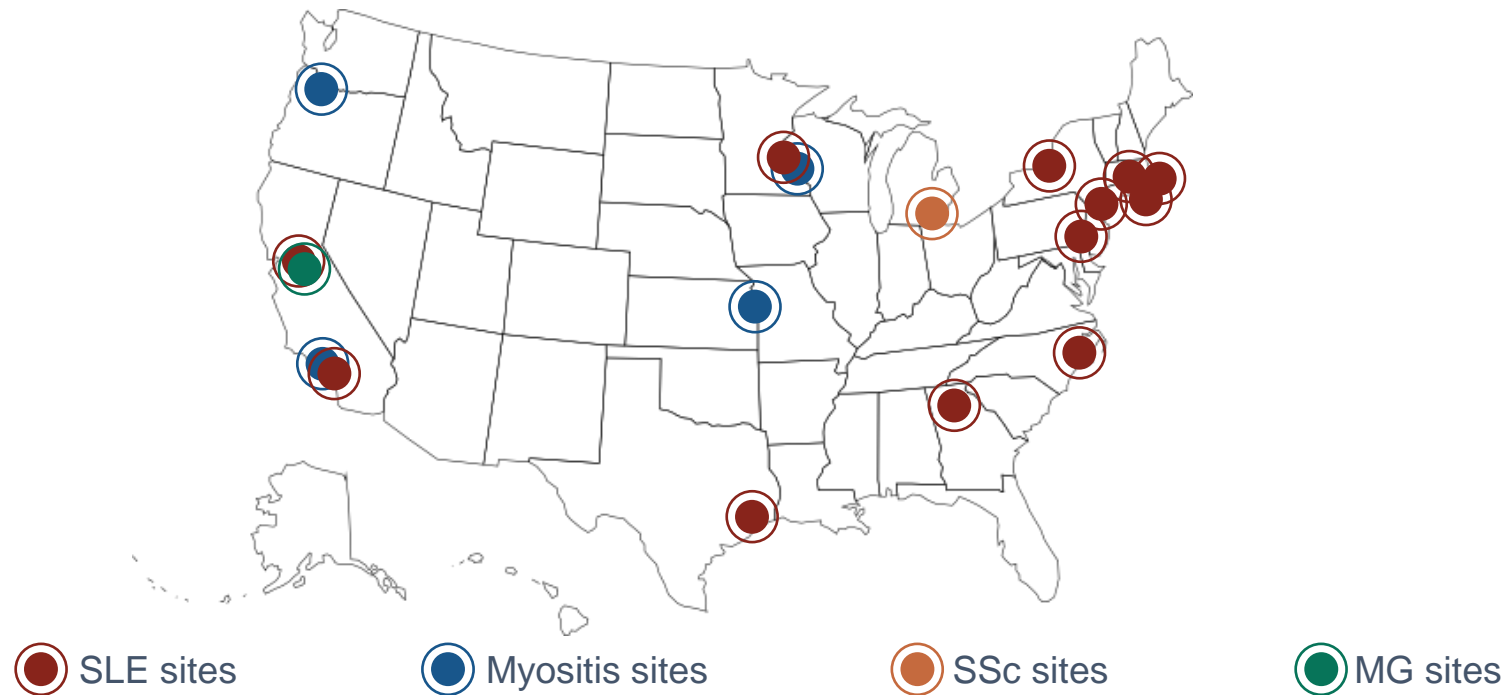
● FDA Fast Track Designation received in dermatomyositis, SLE and lupus nephritis, systemic sclerosis, mucosal pemphigus vulgaris, and MuSK-Ab positive MG.

1. Sub-study incorporated into DesCAARTes™ study.

2. Data cut-off as of 28 May 2024.

Sites actively recruiting patients in the RESET™ clinical program¹

Acceleration in enrollment anticipated in 2H24 with initial CABA-201 data & engaged clinical investigators



- 5 patients enrolled across RESET-SLE™ & RESET-Myositis™, with 3 patients enrolled over the last 2 months
- 18 actively recruiting clinical sites in the U.S. across the RESET™ studies
- RESET-SSc™ and RESET-MG™ trials now open for enrollment



Current & Investigational Treatments for Patients with Autoimmune Diseases

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Current therapies for autoimmunity do not achieve drug-free remission

Broad immunosuppression and chronic administration often required to achieve partial, transient responses

High Unmet Clinical Need in SLE & Myositis

Myositis



- High mortality due to lung & cardiac involvement¹
- Only FDA & EMA-approved therapy is IVIg in DM²
- Many patients remain refractory to standard of care therapies – particularly high unmet need in IMNM¹

- Potential for life-threatening complications
- ~40% of patients with SLE develop LN^{3,4}
 - ~25% risk of death or ESRD within 10y
- Incomplete responses despite chronic therapy

Lupus



Current Therapies in Autoimmunity

- Broad immunosuppression
- Modest & inconsistent clinical responses
- Chronic therapy requirements

There is a need for durable, effective and safe therapies that reestablish immune tolerance to eliminate the need for long-term therapy^{5,6}

(Hematopoietic stem cell transplant has been shown to be curative in systemic sclerosis but has increased mortality in the first year⁶)

1. Khoo T, et al. *Nat Rev Rheumatol*. 2023;19(11):695-712.
2. Octapharma. Accessed June 10, 2024.
3. Hoover PJ, Costenbader KH. *Kidney Int*. 2016;90(3):487-92.

4. Hahn BH, et al. *Arthritis Care Res (Hoboken)*. 2012; 64(6): 797–808.
5. Rosenblum MD, et al. *Sci Transl Med*. 2012;4(125):125sr1.
6. Swart J, et al. *Nat Rev Rheumatol*. 2017;13:244-256.

Potential for treatment paradigm to evolve in autoimmunity

CAR T therapy has the potential to provide drug-free, durable & reliable responses

What are the clinical outcomes with autologous 4-1BB CD19-CAR T cell therapy?

Promising clinical responses reported in 15 patients with an academic 4-1BB CD19-CAR T¹⁻³

100%

Clinical responses in SLE, myositis, SSc off immunosuppressive therapies

<7%

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

Within 7 months

Repopulation of naïve B cells post-infusion

2+ years

SLE drug-free remission with single infusion of CD19-CAR T³

How is CAR T cell therapy designed to reset the immune system?

A ‘living drug’ potentially enabling complete B cell depletion in the blood, tissues, lymph nodes & secondary lymphoid organs

While autologous CD19-CAR T has potential to deliver drug-free, durable & reliable responses, multiple other therapeutic modalities may find a role within the future treatment paradigm

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. It has been publicly reported that one idiopathic inflammatory myopathy subject in this academic study had a reoccurrence of disease following ~18 months of clinical remission.

A photograph of a female doctor with dark hair in a teal scrub top, smiling and using a stethoscope to examine an elderly female patient with short grey hair. The patient is wearing a white hospital gown. The image is overlaid with a semi-transparent dark blue filter.

Initial CABA-201 Data in Myositis & Lupus

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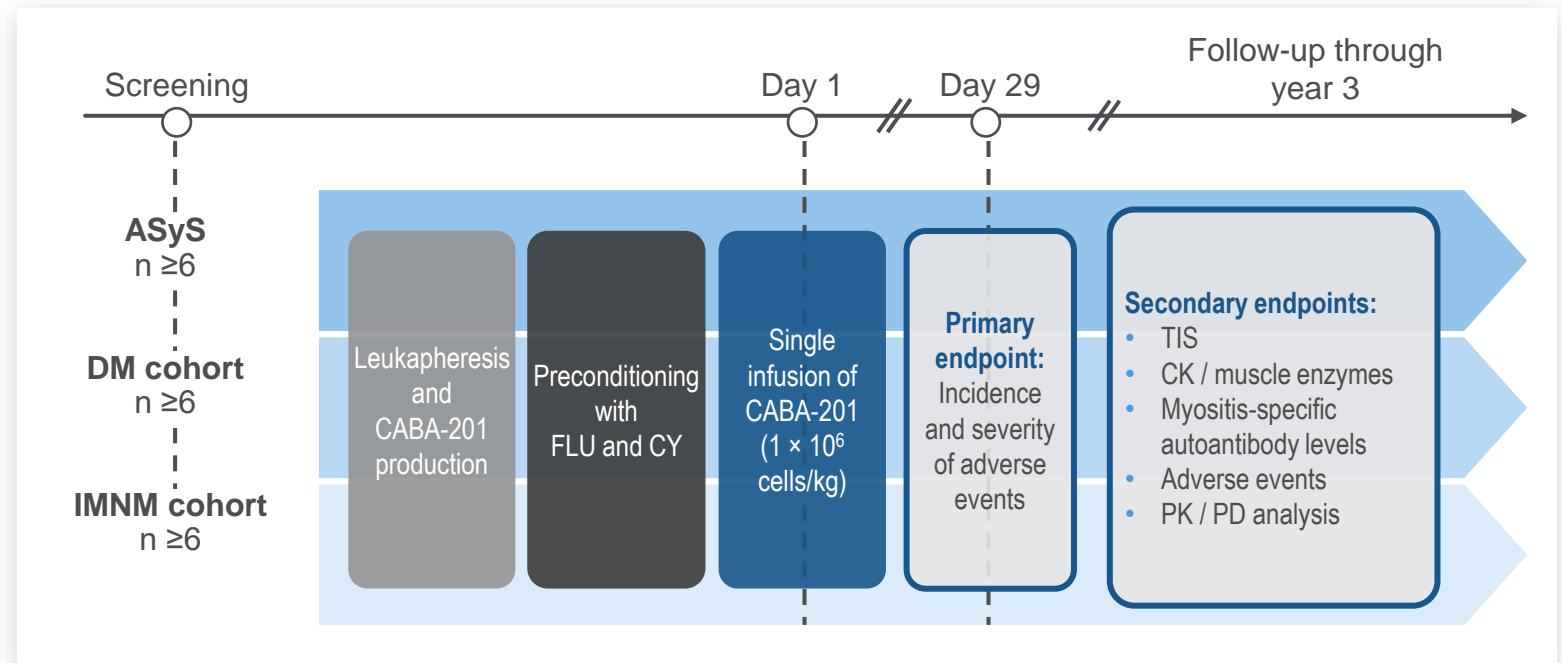
Phase 1/2 Myositis Study for CABA-201

Key inclusion criteria

- Age ≥ 18 and ≤ 75 with a definite or probable clinical diagnosis of IIM (2017 EULAR/ACR classification criteria)
- Diagnosis of antisynthetase syndrome (ASyS), dermatomyositis (DM), or immune-mediated necrotizing myopathy (IMNM) based on presence of serum myositis-specific antibodies
- Evidence of active disease despite prior or current treatment with standard of care

Key exclusion criteria

- Cancer-associated myositis
- Significant lung or cardiac impairment
- B cell-depleting agent within prior ~6 months
- Previous CAR T cell therapy and/or HSCT



Juvenile idiopathic inflammatory myopathy (JIIM, juvenile myositis) cohort recently incorporated into trial

Phase 1/2 Lupus Study for CABA-201

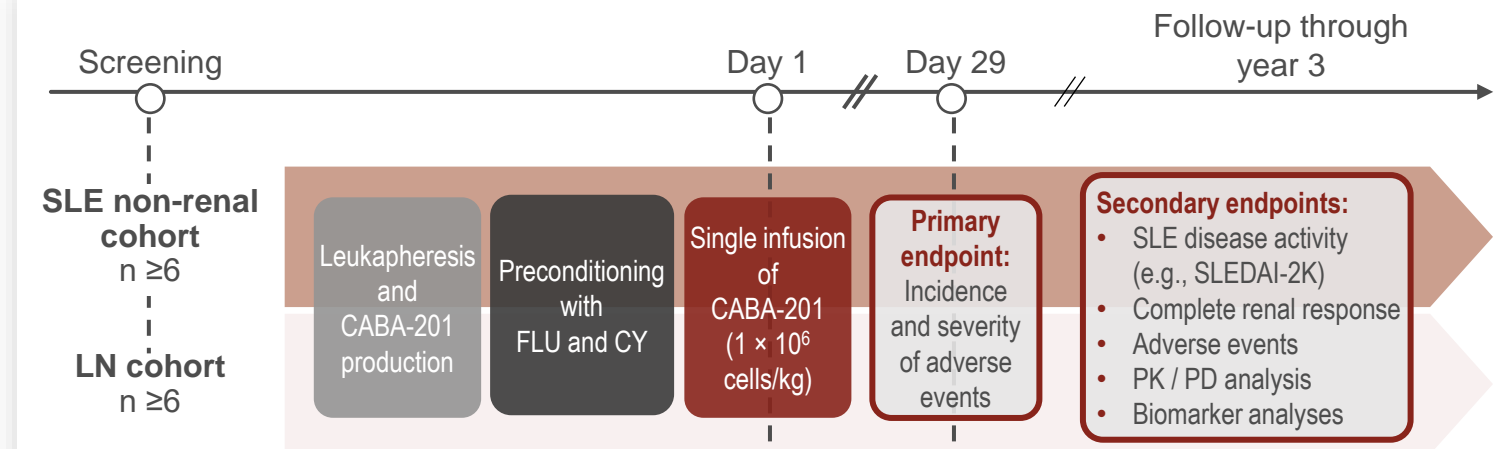


Key inclusion criteria

- Age ≥ 18 to ≤ 65 with an SLE diagnosis (2019 EULAR/ACR classification criteria)
- ANA+ or anti-dsDNA+ at screening
- For SLE (non-renal) cohort: active, moderate to severe SLE, SLEDAI 2K ≥ 8 despite standard therapy
- For Lupus Nephritis cohort: active, biopsy-proven LN class III or IV, \pm class V

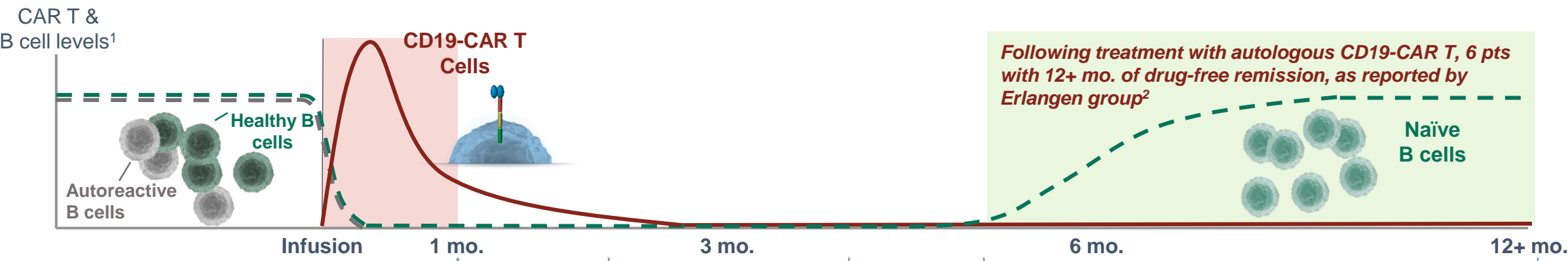
Key exclusion criteria

- B cell-depleting agent within prior ~ 6 months
- Previous CAR T cell therapy and/or HSCT
- Presence of kidney disease other than LN



Metrics to assess outcomes of B cell depletion in autoimmunity

Translational & clinical parameters inform framework to evaluate advanced modalities in autoimmunity



Metrics of evaluation	Within 1 month	~3 months	Up to 12+ months
Translational measures	<div><input checked="" type="checkbox"/> B cell depletion: Timing & depth</div> <div><input checked="" type="checkbox"/> CAR T expansion: Magnitude & timing</div>	<div><input checked="" type="checkbox"/> Autoantibody changes</div> <div><input checked="" type="checkbox"/> Vaccine titer changes</div> <div><input checked="" type="checkbox"/> Inflammatory marker changes</div>	<div><input checked="" type="checkbox"/> Time to B cell repopulation</div> <div><input checked="" type="checkbox"/> B cell phenotype³</div> <div><input type="checkbox"/> Autoantibody changes</div>
Clinical data	<div><input checked="" type="checkbox"/> Rate of CRS more severe than fever</div> <div><input checked="" type="checkbox"/> Rate & grade of ICANS</div> <div><input checked="" type="checkbox"/> Rate & severity of infection</div>	<div><input checked="" type="checkbox"/> Early efficacy signals</div> <div><input checked="" type="checkbox"/> Rate & severity of infection</div>	<div><input type="checkbox"/> Durability of clinical activity</div> <div><input type="checkbox"/> Rate & severity of infection</div>
Patient experience	<div><input checked="" type="checkbox"/> Hospitalization requirements</div> <div><input checked="" type="checkbox"/> Apheresis & preconditioning</div> <div><input checked="" type="checkbox"/> Single vs. multiple infusions</div>	<div><input checked="" type="checkbox"/> Chronic maintenance therapy / concomitant medications, if any</div>	<div><input type="checkbox"/> Chronic maintenance / concomitant medications, if any</div>

✓ Indicates data being presented for either or both of the first two patients in the RESET clinical program.

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.

3. Flow phenotyping data; confirmatory analyses ongoing.

Baseline characteristics of first two patients in RESET™ trials

Both patients with refractory disease, including to B cell-targeting antibodies & other agents

	RESET-Myositis Patient #1	RESET-SLE Patient #1
Age (years), sex	33, male	26, male
Cohort	IMNM	Non-renal SLE
Disease duration	~2 years	~6 years
Prior disease-specific therapy	IVIg, rituximab, MTX, glucocorticoids	Cyclophosphamide, voclosporin, belimumab, tacrolimus
Disease-specific therapy at screening	MTX, glucocorticoids	MMF, hydroxychloroquine, glucocorticoids
Autoantibodies	SRP, Ro-52	ANA, dsDNA
Disease activity ¹	MMT-8: 130, CK: 617	SLEDAI-2K: 26
Disease manifestations ^{1,2}	Muscle weakness, dysphagia	Vasculitis, arthritis, alopecia, hematuria, proteinuria (isolated class V LN), low complement

Expanding CD19-CAR T experience in IMNM & SLE

dsDNA, double-stranded DNA; IMNM, immune-mediated necrotizing myopathy; MMF, mycophenolate mofetil; MMT-8, manual muscle testing of 8 muscles; MTX, methotrexate; Ro-52, ribonucleoprotein 52; SRP, signal recognition particle.

1. Baseline=pre-preconditioning visit.

2. Disease manifestations were assessed according to Myositis Disease Activity Assessment Tool (MDAAT) and SLEDAI-2K for myositis and SLE, respectively.

CABA-201 was well-tolerated in initial patients

No CRS, ICANS or infections of any grade reported through follow-up period¹

	RESET-Myositis Patient #1	RESET-SLE Patient #1
Dose of CABA-201	83 million (1 x 10 ⁶ /kg) CAR ⁺ cells	63 million (1 x 10 ⁶ /kg) CAR ⁺ cells
Duration of inpatient monitoring²	4 days	4 days
Adverse events⁴	CRS	None
	ICANS	None
	Infections	None
	Hypogammaglobulinemia	None
	Serious adverse events	None
Concomitant disease-specific therapy	Discontinued MTX prior to infusion; Prednisone discontinued day 3 post-infusion	Discontinued MMF and HCQ prior to infusion; Ongoing taper from prednisone 10mg daily by 8 weeks ³
Duration of follow-up¹	84 days	28 days

Vaccination titers preserved post-infusion, with no reported infections in the duration of follow-up period¹

Both patients discharged after 4 days of monitoring post-infusion & neither received tocilizumab

1. Data cut-off as of 28 May 2024.

2. Protocol requires a minimum of 4-day hospitalization for monitoring.

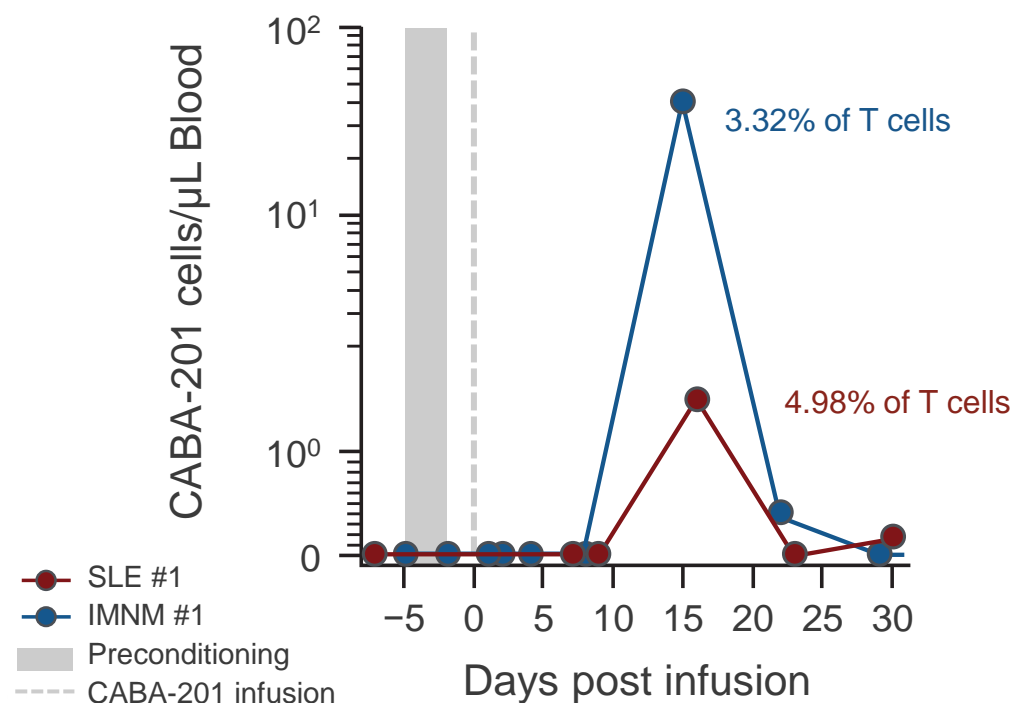
3. PI-directed taper from 10mg daily prednisone.

4. Grade 4 leukopenia, neutropenia and lymphopenia reported for SLE Patient #1, the Grade 4 cytopenias resolved and were attributed to the preconditioning regimen (fludarabine and cyclophosphamide).

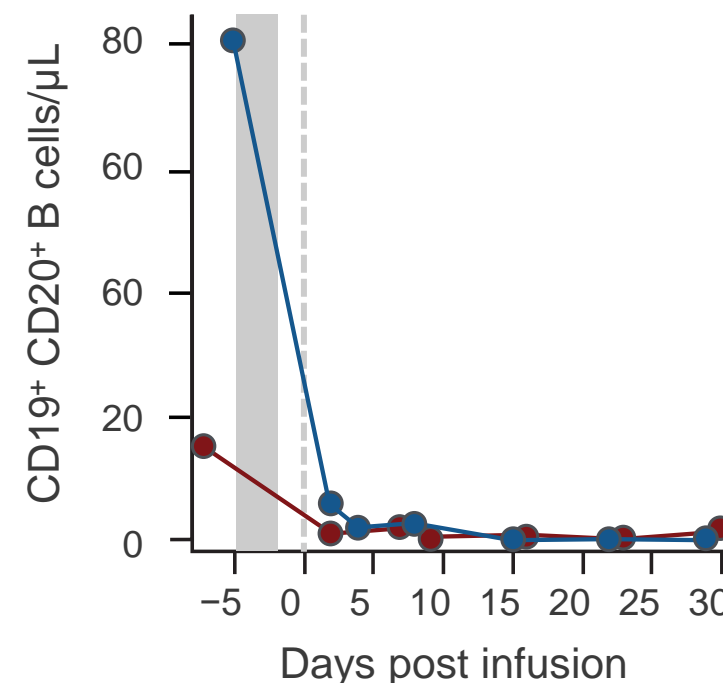
CABA-201 demonstrated expansion & targeted B cell depletion

CABA-201 exhibited anticipated profile of expansion and contraction¹

Expansion of CAR T cells to anticipated range suggests target engagement



Complete B cell depletion achieved by day 15 on flow cytometry



Peripheral peak CAR T expansion occurred at approximately 2 weeks & rapid contraction suggests systemic B cell aplasia was achieved

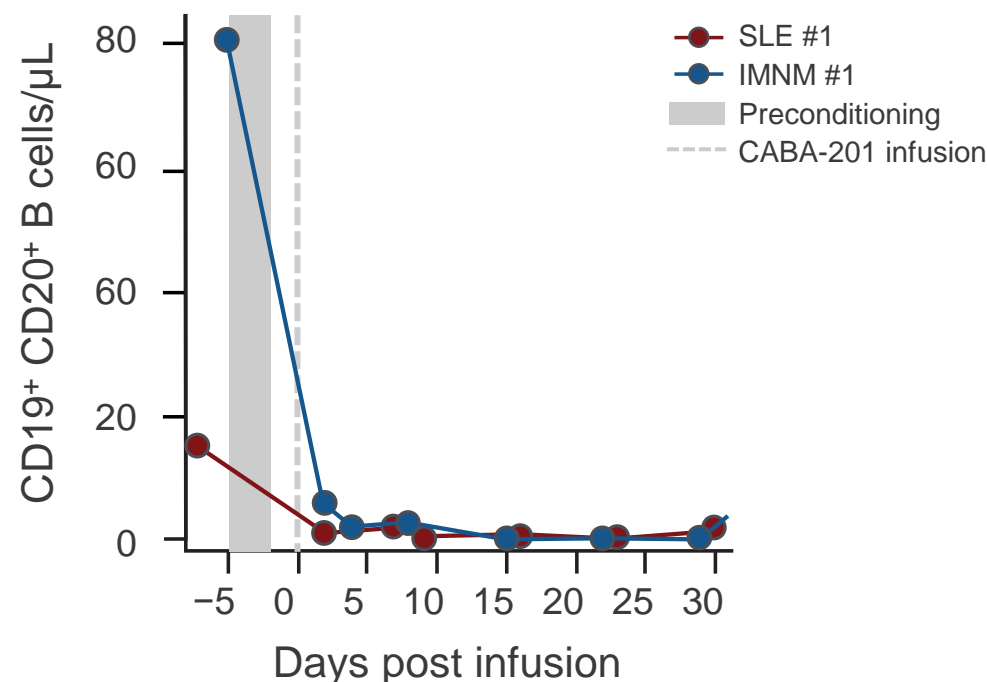
1. Response appears to be consistent with published data of cryopreserved CAR T products as well as the expansion profile of BCMA-CAR T products in patients with multiple myeloma, in which the number of target cells is more similar to autoimmune disease than to B cell leukemias and lymphomas.²⁻⁶
 2. Shah BD, et al. *Lancet*. 2021;398(10299):491-502.
 3. Awasthi R, et al. *Blood Adv*. 2020;4(3):560-572.

4. Munshi NC, et al. *N Engl J Med*. 2021;384(8):705-716.
 5. Cohen AD, et al. *Blood Cancer J*. 2022;12(2):32.
 6. Müller F, et al. *N Engl J Med*. 2024;390(8):687-700.

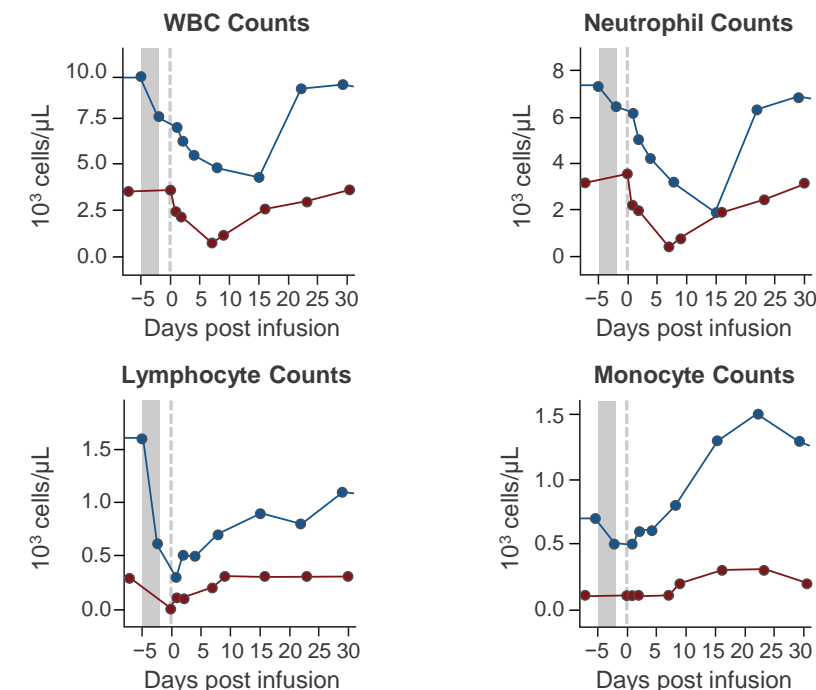
Systemic B cell depletion with CABA-201

Complete B cell depletion achieved by day 15 on flow cytometry & maintained in context of WBC recovery

CD19⁺ CD20⁺ B cell count



Leukocyte counts



B cell depletion was achieved & maintained in follow up or until naïve B cell recovery; early, transient leukopenia observed in both patients, as expected with preconditioning¹

WBC, white blood cell.

1. Nadir of lymphocyte count following fludarabine and cyclophosphamide administration estimated based on respective product labels.^{2,3}

2. Fludarabine phosphate injection. Prescribing information. 2010. https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/022137s003lbl.pdf.

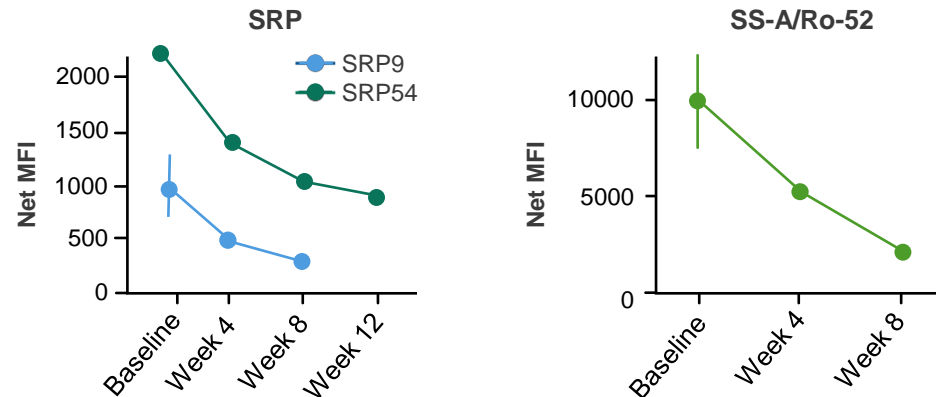
3. Cyclophosphamide. Prescribing information. 2013. https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/012141s090,012142s112lbl.pdf.

CK reduction & clinical improvement observed in SRP IMNM

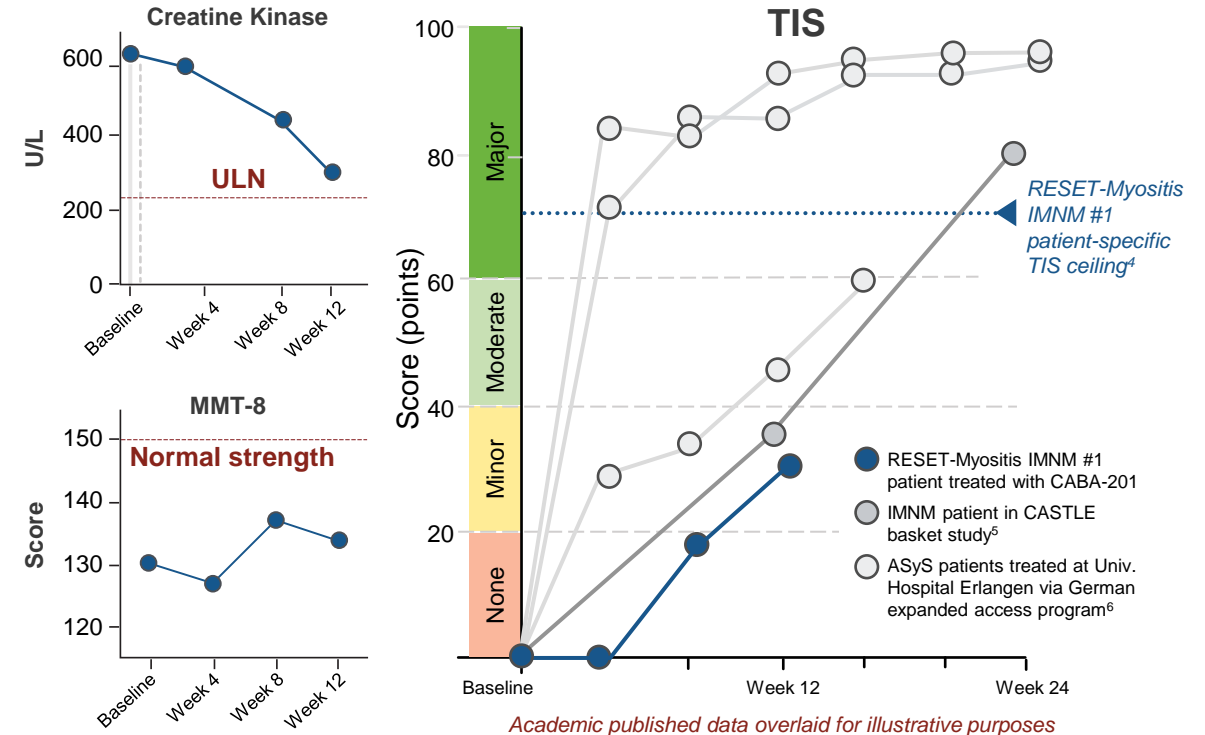
Antibody reduction & clinical improvement in disease activity as anticipated with follow-up of 12 weeks¹

- Discontinued all disease-specific therapies
- Disease markers continuing to trend positively
- Patient reported symptoms as much improved

Quantitative translational assay shows ongoing reduction in SRP & Ro-52 antibodies^{2,3}



Disease activity & improvement measures



12-week TIS consistent with IMNM case report⁵

1. Data cut-off as of May 28, 2024.

2. Luminex assay developed and performed by Cabaletta Labs.

3. Qualitative commercial assay (Myositis Antigen Panel, performed at National Jewish Health Advanced Diagnostic Laboratories) suggests SRP54 antibody remains strongly positive at Week 12; Ro-52 normalizes by week 8.

4. Based on patient's moderate level of muscle disease at baseline, mild-moderate disability and limited extramuscular manifestations, the maximum achievable score is 70 points on the 100-point TIS scale.

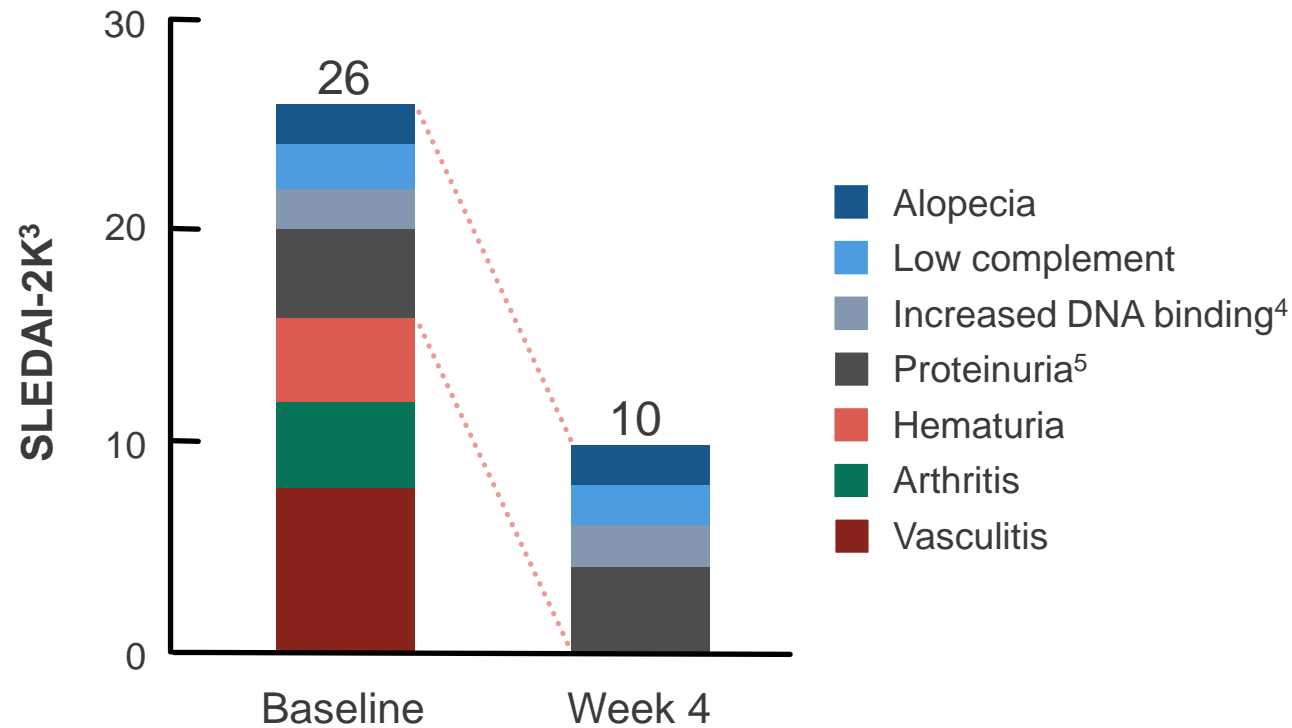
5. Patient treated in third-party CASTLE Phase I/II basket study, TIS data at Week 12 and 24 provided via personal communication with and as presented by Dr. Georg Schett at the EULAR 2024 symposium.

6. Müller F, et al. *N Engl J Med.* 2024;390(8):687-700.

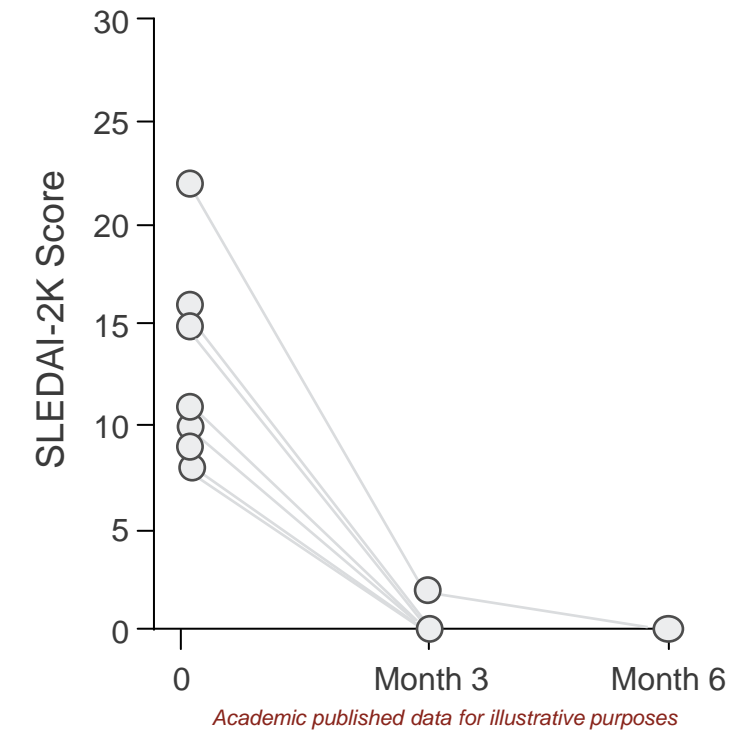
Early efficacy signals in first patient in non-renal SLE cohort¹

Trend toward improvement in disease manifestations with follow up of 4 weeks²

SLE patient #1



Academic SLE data⁶



Vasculitis, arthritis and hematuria resolved within 4 weeks despite discontinuation of all therapies at infusion other than ongoing taper from prednisone 10mg per day

1. Patient in non-renal SLE cohort due to isolated Class V LN.

2. Data cut-off as of 28 May 2024.

3. Baseline and Day 29 SLEDAI-2K score are reflective of disease activity at study visit day.

4. Anti-dsDNA antibody titer decreased from 1:40 to 1:10 from Baseline to Week 4.

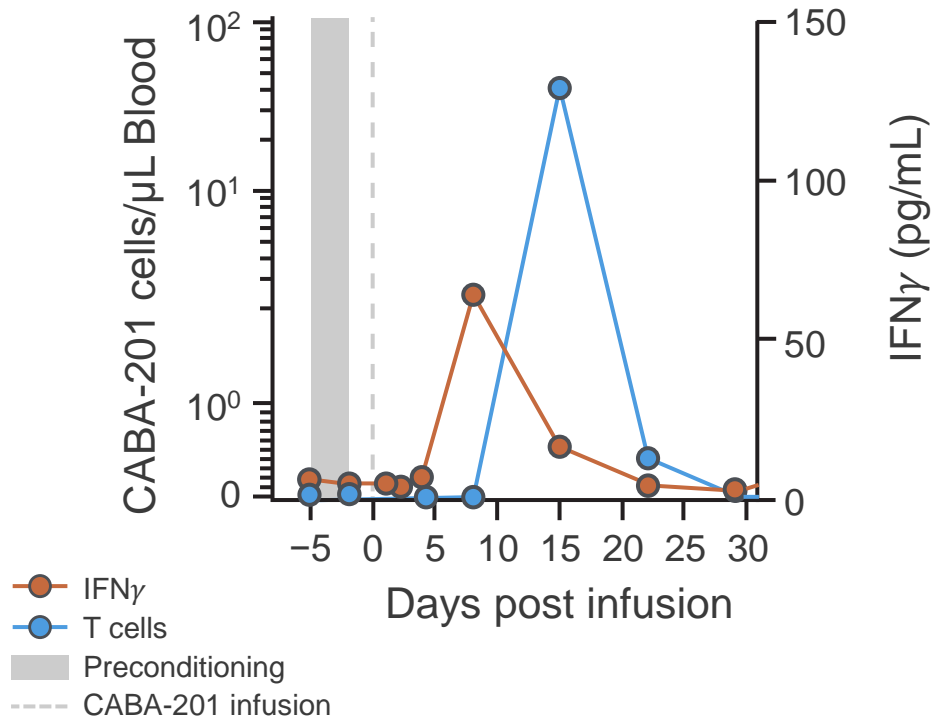
5. Urine Protein Creatinine Ratio decreased from 1.08 to 0.80 from Baseline to Week 4.

6. SLE patients treated at Univ. Hospital Erlangen via German expanded access program; Müller F, et al. *N Engl J Med.* 2024;390(8):687-700.

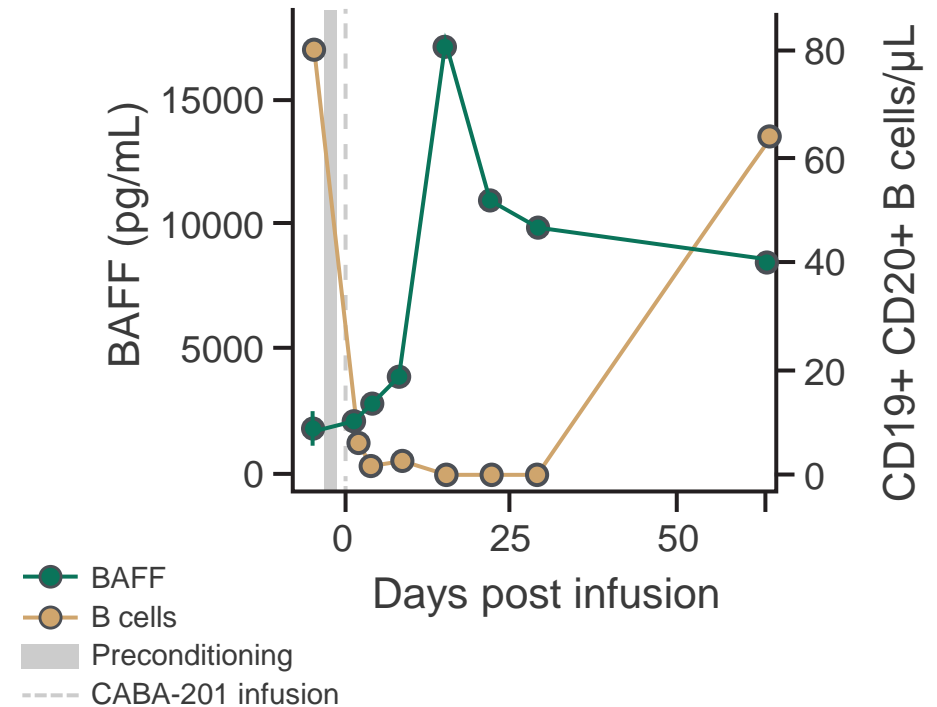
B cell repopulation occurred at 2 months in first IMNM patient

IMNM patient data provides insights supporting tissue-level effects of CAR T

IFN γ peak prior to peripheral CABA-201 peak suggests tissue-resident B cell cytotoxicity



Systemic B cell depletion triggers BAFF to encourage bone marrow B cell repopulation



B cell repopulation with naïve B cells

Initial patient phenotyping data consistent with potential immune system reset; confirmatory analyses ongoing

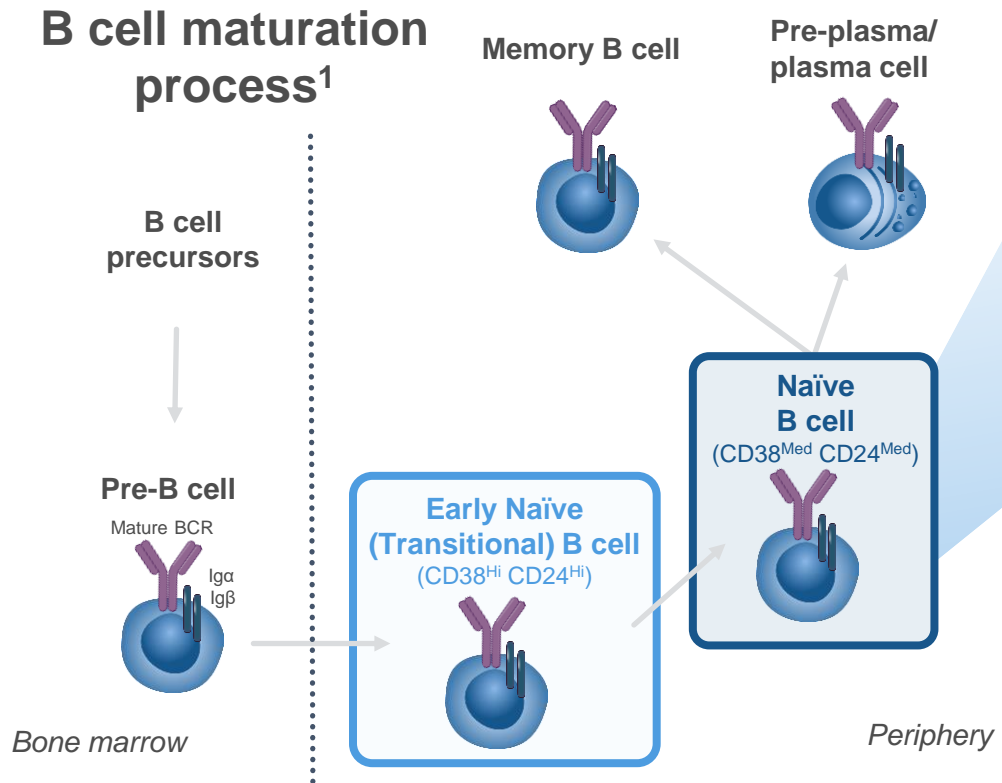
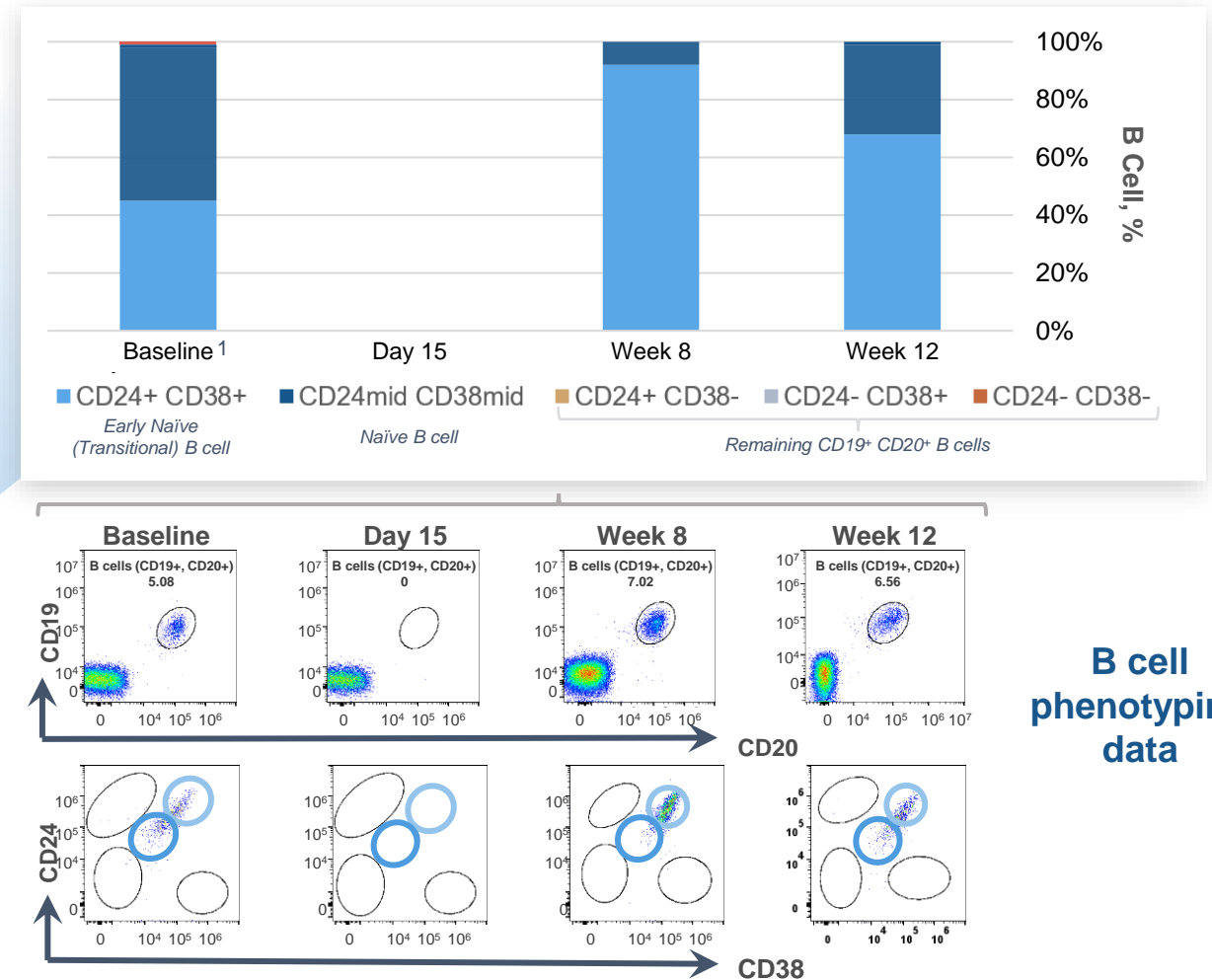


Image adapted from Cambier JC, et al. 2007.²



BCR, B cell receptor; Note: Flow plot gating reflects CD19+ CD20+ live lymphocytes.

1. Patient received multiple courses of rituximab, with most recent dose approximately 9 months prior to CABA-201 infusion.

2. Cambier JC, et al. *Nat Rev Immunol.* 2007;7(8):633-643.



Conclusions

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Key takeaways from initial CABA-201 data in first two patients¹

CABA-201: Engineered specifically for autoimmune patients at the selected dose based on a construct design and function that is similar to the academic CD19-CAR T construct²

Safety of CABA-201

- In the first 2 patients (IMNM & SLE), CABA-201 was well-tolerated
 - No CRS, ICANS or infections reported through follow-up period

Dose selection *1 x 10⁶ cells/kg*

- Clinical & translational data support the selected dose of CABA-201
 - PK: IFN γ peak prior to peak of CABA-201 suggests tissue-level B cell cytotoxicity
 - PD: Systemic B cell depletion followed by repopulation with naïve B cells
 - Autoantibody levels: Decline generally consistent with Univ. Hospital Erlangen data²
 - Clinical & translational data: Improvement consistent with reported CD19-CAR T data^{2,3}

18 clinical sites now enrolling patients in the CABA-201 RESET™ program across four trials – myositis, SLE/LN, systemic sclerosis and myasthenia gravis⁴

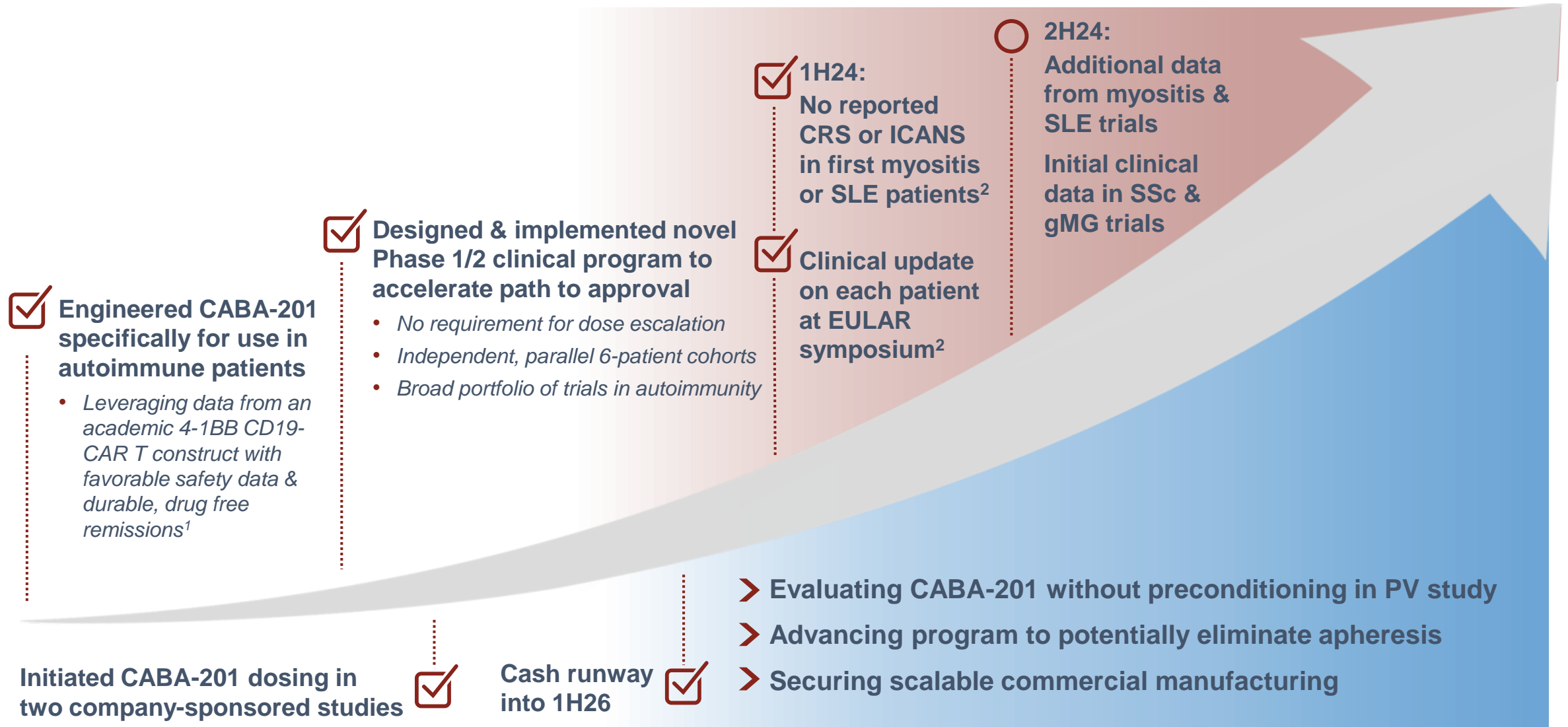
1. Data cut-off as of 28 May 2024.

2. Müller F, et al. N Engl J Med. 2024;390(8):687-700.

3. Third-party CASTLE Phase I/II basket study.

4. As of June 12, 2024.

Realizing the vision to transform autoimmune disease treatment



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

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.

2. Data cut-off as of 28 May 2024.



Q&A

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