ACTengine® IMA200 Clinical Trial Series
Phase 1a Data Update

Cedrik Britten, Chief Medical Officer
Harpreet Singh, Chief Executive Officer
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Key Takeaways from ACTengine® Phase 1a Data Update

Clinical Overview

3 Clinical ACTengine® (TCR-T) Programs: IMA201, IMA202, IMA203

14 Patients infused as of data cut-off on Feb 16, 2021*

<1bn T cells infused per patient at dose levels 1 and 2 – presumed to be sub-therapeutic

Key Findings

Transient and manageable treatment-emergent adverse events as expected for cell therapies

Robust T cell engraftment and persistence post infusion and tumor infiltration in all evaluable patients

Tumor shrinkage observed in 8/10 evaluable patients including one unconfirmed partial response (RECIST1.1)

First anti-tumor activity observed consistent with robust biological activity during early phases of dose escalation

* Thereof 10 patients evaluable for biological activity and clinical efficacy analysis at data cut-off

ACTengine® IMA200 Series – Key Features

Differentiated Targets, TCRs and Cellular Manufacturing Designed to Enhance Safety and Activity

	IMA201	IMA202	IMA203
Peptide Target	HLA-A*02-presented peptide derived from		
	MAGEA4/8	**MAGEA1**	**PRAME**
	shown to be naturally and specifically presented on native tumor tissues at differentiated high peptide target density[1]		
	100-1,000 copies/cell	50-900 copies/cell	100-1,000 copies/cell
T cell Receptor (TCR)	High-affinity specific TCRs with high functional avidity[2]		
	Natural TCR ~10 ng/ml	Natural TCR ~15 ng/ml	Pairing-enhanced TCR ~5 ng/ml
T cell Product	Autologous T cells gene-engineered with lentiviral vector expressing TCR and applying proprietary short-term manufacturing process designed to achieve better T cell engraftment and persistence		
	7-10 days	7-10 days	6-7 days

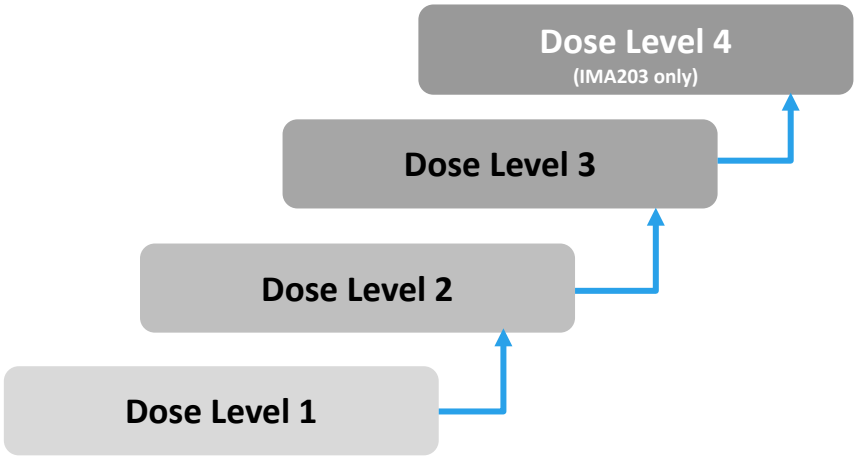
[1] Applying XPRESIDENT® quantitative mass spectrometry engine; target density: peptide copy number per tumor cell, approximate range representing the majority of tumor samples analyzed

[2] Applying XCEPTOR® TCR discovery and engineering platform incl. XPRESIDENT®-guided off-target toxicity and similar peptide screening to minimize off-target reactivity; functional avidity: EC50 half maximal effective concentration

ACTengine® Trial Design and Key Study Objectives

Each IMA200 Series Clinical Trial Includes Dose Escalation and Dose Expansion Cohorts

Phase 1a: Dose Escalation



Phase 1b: Dose Expansion

Additional 10-12 patients at recommended Phase 2 Dose

- IMA201
- IMA202
- IMA203

Trial Design: IMA201 and IMA202: 2+2 Design; IMA203 3+3 Design

	Dose Level 1*	Dose Level 2*	Dose Level 3*	Dose Level 4*
IMA201/202	~50m /m^2	~300m /m^2	~1000m /m^2	NA
IMA203	40-60m /m^2	120-180m /m^2	200-480m /m^2	up to 1200m /m^2

Key Objectives	Dose Level 1 & 2	Dose Level 3 & 4
Primary: Safety	●	●
Secondary: Biological Activity	●	●
Secondary: Clinical Activity		●

* Dose is shown as transduced viable CD8 T cells per m^2 total body surface area; NA: not available

ACTengine® Patient Flow

High Enrollment Efficiency through Combined Screening for Three Targets

Screening & Manufacturing Phase | **Treatment & Observation Phase** | **Long Term Follow-up**

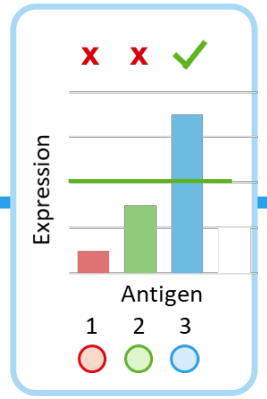
Safety and efficacy monitoring for 12 months

HLA-A*02 Testing
Blood sample;
Central lab

Leuka-pheresis

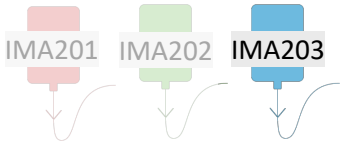
Infusion of ACTengine® T cell Product

IL-2
1m IU twice daily
for 14 days



Target Profiling
Fresh Tumor Biopsy;
IMADetect®

ACTengine® Manufacturing
by Immatics



Lymphodepletion
40 mg/m² Fludarabine and
500 mg/m² Cyclophosphamide
for 4 days*

* Dose modifications of lymphodepletion regimen for certain risk groups (e.g. patients with HCC & patients with reduced renal-clearance)

Patient Characteristics

Heavily Pre-treated Patients Suffering from Diverse Solid Cancers Enrolled in ACTengine® Trials

Patient Distribution (N=16)	Number
Patients lymphodepleted	16
Thereof patients infused[1]	14
Patients in Safety Population[2]	16
Patients in Efficacy Population[3]	**10**
Patients with serial biopsies	6
Patients in IMA201 study	1
Patients in IMA202 study	7
Patients in IMA203 study	8

Characteristics in Efficacy Pop. (N=10)	Median (range)
Age [years]	61 (33 - 68)
Number of prior lines of systemic therapies	5 (2 - 7)
Years from diagnosis[4]	4 (1 - 12)
Total transduced T cells[5] [x10^9]	0.11 (0.08 – 0.65)

- At data cut-off, 10 patients across multiple tumor indications (including NSCLC, head & neck cancer, melanoma, synovial sarcoma and others) received ACTengine® T cell products and had at least one tumor response assessment
- All patients infused were heavily pre-treated, failed all previous therapies and entered the study with recurrent and/or refractory solid tumors

Data cut-off – February 16, 2021

[1] Infusion of one patient pending; [2] Patients that started lymphodepletion; [3] Patients with at least one tumor response assessment post baseline; [4] Until start of lymphodepletion; [5] viable CD8 T cells

Safety Profile

Treatment-emergent Adverse Events Are Manageable, Transient and Expected for Cell Therapies

Adverse Events:

- Most frequent adverse events were transient cytopenias associated with lymphodepletion
- Transient CRS[3] (Grade 1-2) in 13/14 infused patients.
- Transient Grade 1 or 2 ICANS in 3/14 infused patients, resolved within 48h in all cases

Dose-limiting toxicities:

- IMA201 and IMA202: No DLT[5] observed
- IMA203: One transient, Grade 3 atrial fibrillation with onset on day 5 post infusion that resolved within 48h after onset. DLT triggered expansion of dose level 2 from three to six patients

TEAEs by maximum severity (N=16)

	All Grades		≥ Grade 3	
Adverse event	**No.**	**%**	**No.**	**%**
Patients with any adverse event	**16**	**100.0**	**16**	**100.0**
Lymphopenia	16	100.0	16	100.0
Leukopenia	16	100.0	16	100.0
Neutropenia	16	100.0	15	93.8
Anaemia	16	100.0	10	62.5
Thrombocytopenia	15	93.8	6	37.5
Nausea	11	68.8	0	0
Pyrexia	8	50.0	0	0
Vomiting	6	37.5	1	6.3
Fatigue	5	31.3	1	6.3
Hypoxia	5	31.3	1	6.3
Hyponatraemia	5	31.3	0	0
Dyspnoea[1]	3	18.8	1	6.3
Atrial fibrillation	2	12.5	1	6.3
Hypertension	2	12.5	1	6.3
Muscular weakness	2	12.5	1	6.3
Pleural effusion	2	12.5	1	6.3
Tumor pain	2	12.5	1	6.3
Blood alkaline phosphatase increased	1	6.3	1	6.3
Candida infection	1	6.3	1	6.3
Corona virus infection	1	6.3	1	6.3
Febrile neutropenia	1	6.3	1	6.3
Infection	1	6.3	1	6.3
Pneumonia[1]	1	6.3	1	6.3
Sepsis[2]	1	6.3	1	6.3
Adverse Events of Special Interest				
Cytokine release syndrome[3]	13	81.3	0	0
ICANS[4]	3	18.8	0	0

All treatment-emergent adverse events (TEAEs) with grade 1-2 occurring in at least 5 patients (incidence ≥31.3%) and additionally all events with grade 3-5 regardless of relatedness to study treatment are presented. Data source: clinical and safety database; hematological adverse events were derived from lab values. Grades were determined according to National Cancer Institute Common Terminology Criteria of Adverse Events, version 5.0. Grades for CRS and ICANS were determined according to CARTOX criteria (Neelapu et al, 2018). Patients are counted only once per adverse event and severity classification.

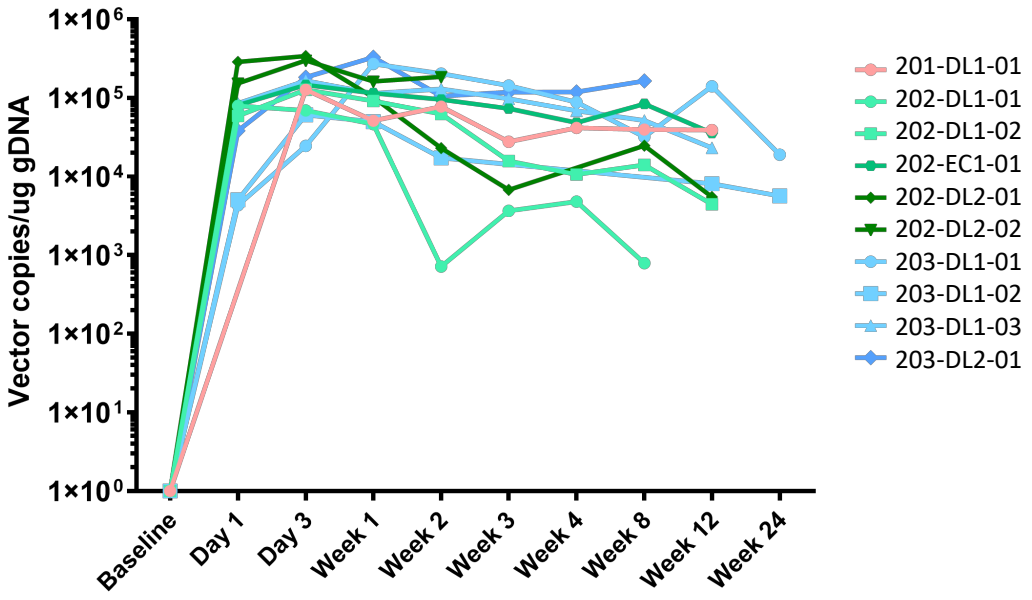
Data cut-off – February 16, 2021

[1] Patient died from tumor progression and pneumonia 69 days after IMA202 T cell infusion (determined not related to any study medication), [2] Patient died from sepsis of unknown origin and did not receive IMA203 T cells, [3] CRS: Cytokine release syndrome, [4]ICANS: Immune effector cell associated neurotoxicity syndrome, [5]DLT: Dose limiting toxicities

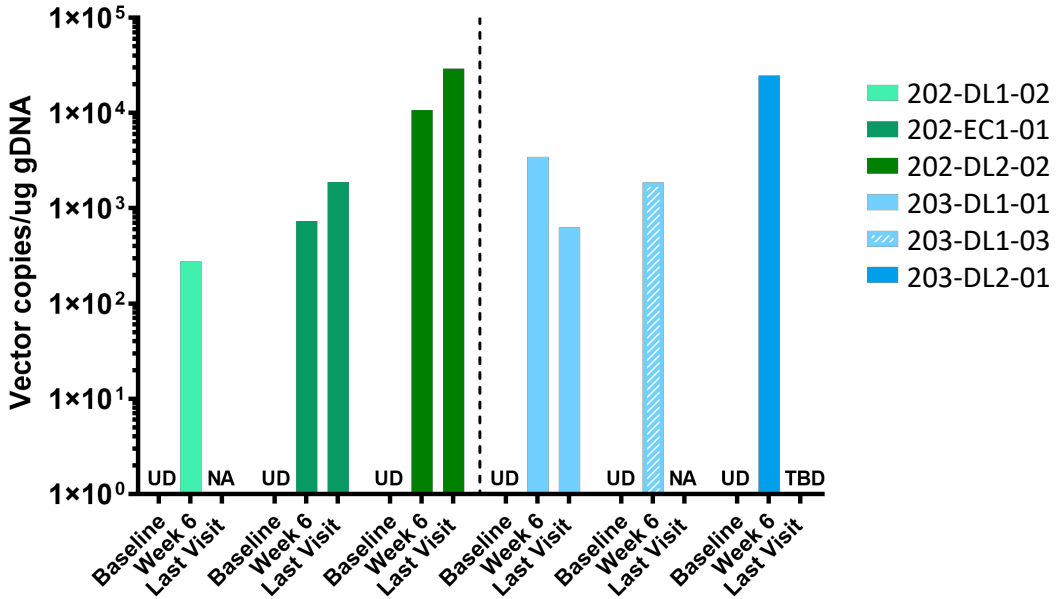
Biological Activity

T cells Robustly Engraft, Persist and Infiltrate into Tumor after Infusion of Low Doses of ACTengine®

Engraftment & T cell Persistence in the Blood



Detection of T cells in the Tumor



- Robust T cell engraftment and persistence post infusion until the end of the observation period as assessed by qPCR*
- Engineered T cells are detectable in serial tumor biopsies post T cell infusion in all evaluable patients by qPCR

Data cut-off – February 16, 2021

* Up to 9 months (data not shown), UD: Undetected, NA: Not available, DL: Dose level, EC1: Enrichment cohort with intermediate dose level between DL1 and DL2 , TBD: To be determined

Clinical Activity – Best Overall Response (BOR) Assessment

Disease Control in 9 out of 10 Patients at Dose Level 1 and 2 (below 1 Billion Transduced CD8 T cells)

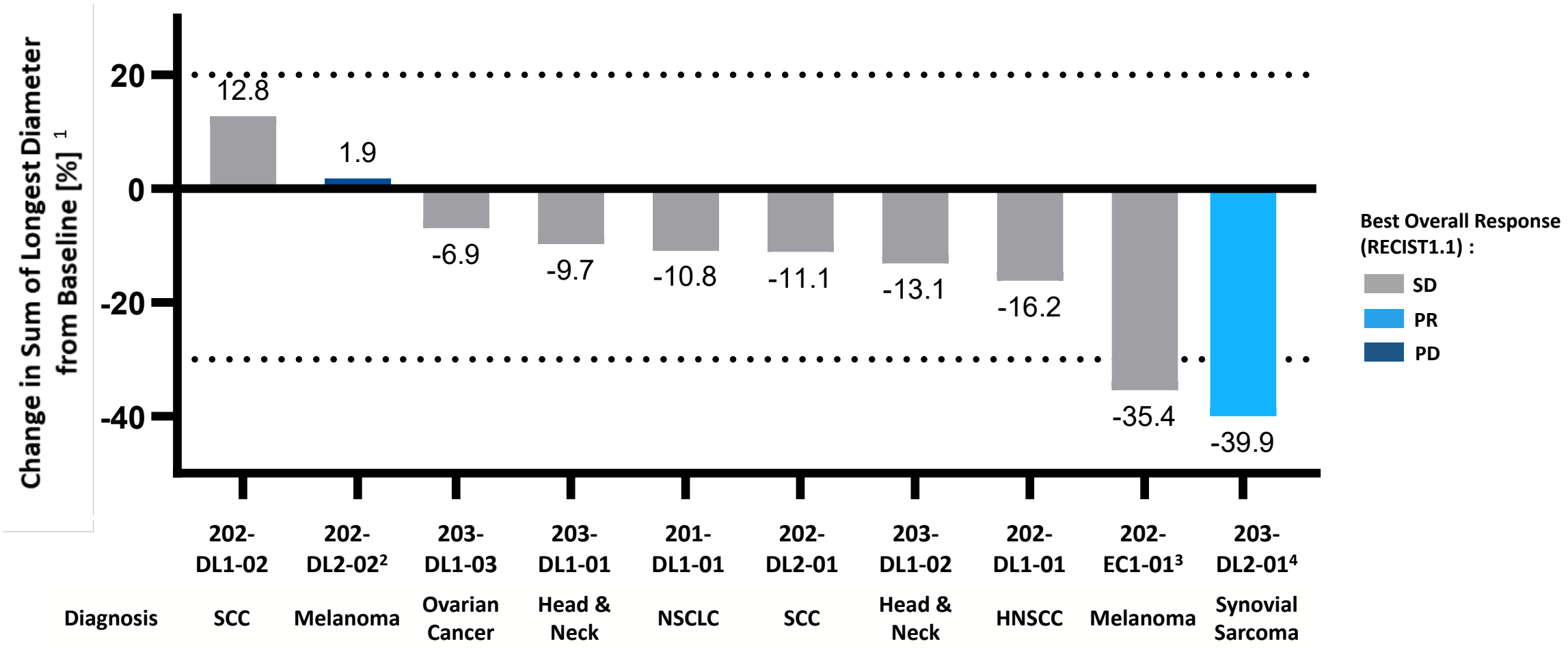
	IMA201	IMA202					IMA203			
Patient	201-DL1-01	202-DL1-01	202-DL1-02	202-EC1-01	202-DL2-01	202-DL2-02	203-DL1-01	203-DL1-02	203-DL1-03	203-DL2-01
Dose level	DL1	DL1	DL1	EC1	DL2	DL2	DL1	DL1	DL1	DL2
Total transduced cells[1]	$0.11x10^9$	$0.11x10^9$	$0.09x10^9$	$0.19x10^9$	$0.51x10^9$	$0.65x10^9$	$0.12x10^9$	$0.11x10^9$	$0.08x10^9$	$0.35x10^9$
Age (gender)	60 (M)	33 (M)	63 (F)	64 (F)	68 (F)	49 (M)	40 (F)	63 (M)	61 (F)	57 (M)
Diagnosis	NSCLC	HNSCC	Squamous Cell Cancer	Melanoma	Squamous Cell Cancer	Melanoma	Head and Neck Cancer		Ovarian Cancer	Synovial Sarcoma
Prior lines of systemic therapy	4	5	6	4	3	7	6	4	7	2
Prior lines of ICI[2] treatment	1	3	1	2	1	3	2	-	1	-
Disease status at infusion	Patients with recurrent and/or refractory solid tumors									
Best response RECIST1.1	SD	SD	SD	SD	SD	PD	SD	SD	SD	PR[3]

Data cut-off – February 16, 2021

[1] Total infused dose of transduced viable CD8 T cells; [2] Immune checkpoint inhibitor; [3] Unconfirmed as of data cut-off; DL: Dose level, EC1: Enrichment cohort with intermediate dose level between DL1 and DL2 , SD: stable disease, PD, progressive disease, PR: partial response

Clinical Activity – Change of Sum of Diameters in Target Lesions

Tumor Shrinkage Observed in 8 of 10 Patients at Low Dose Levels



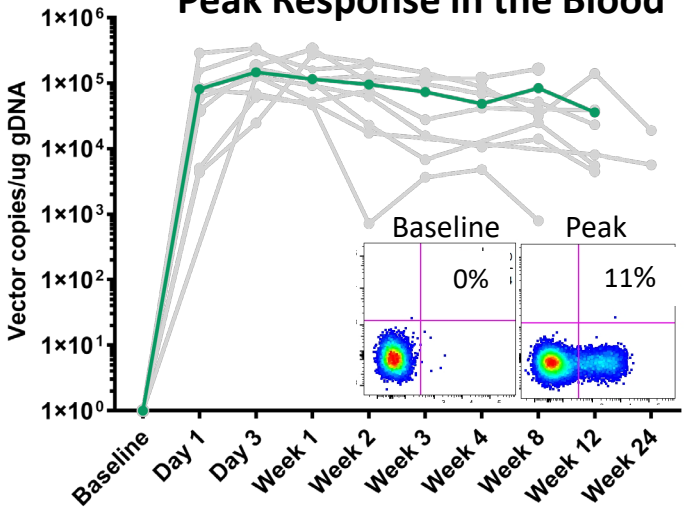
Data cut-off – February 16, 2021

[1] Shortest diameter for nodal lesions; [2] Stable target lesions with parallel growth of a CNS non-target lesion;
[3] RECIST1.1 response at timepoint of maximum in change of target lesions (week 12): PD due to growth of non-target lesion; [4] PR unconfirmed as of data cut-off

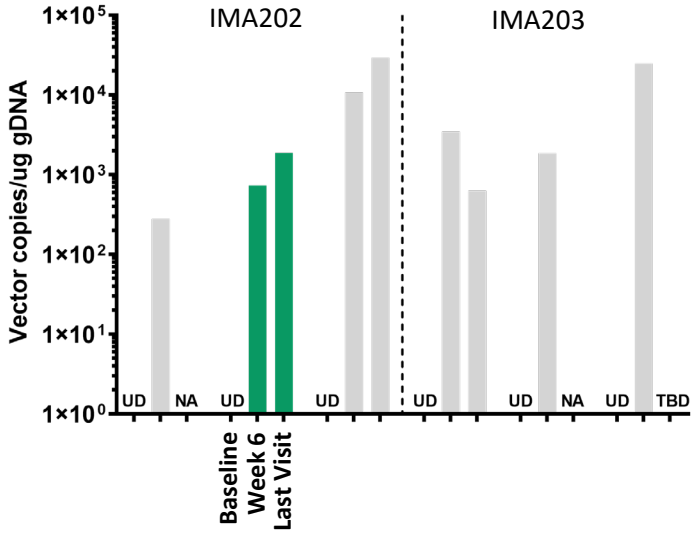
Case Study – Melanoma Patient 202-EC1-01

Tumor Shrinkage Associated with T cell Persistence in Blood and Tumor Infiltration

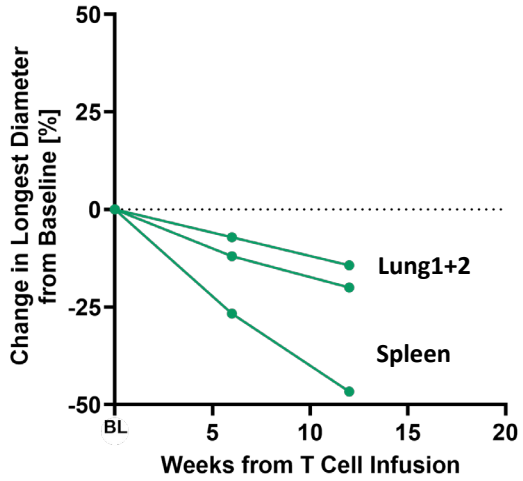
T cell Persistence & Peak Response in the Blood[1]

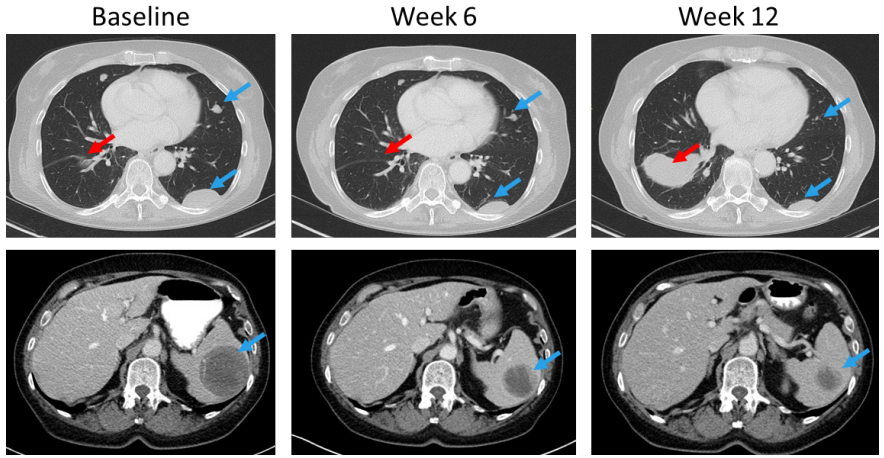


T cell Detection in the Tumor



Change in Target Lesions





- 64-year-old female; Stage 4 melanoma
- Infused at progressive disease after failing 4 prior systemic lines of treatment including immune checkpoint inhibitors
- Patient received total dose of 189m transduced CD8 IMA202 T cells following lymphodepletion

- **T cells persisted until end of observation and were detected in the tumor**
- **20% and 35% decrease in target lesions (RECIST1.1) at week 6 and 12, respectively**
- **Best Response: SD (week 6), Patient off-study (week 12) due to growth of an existing non-target lung lesion**

Data cut-off – February 16, 2021

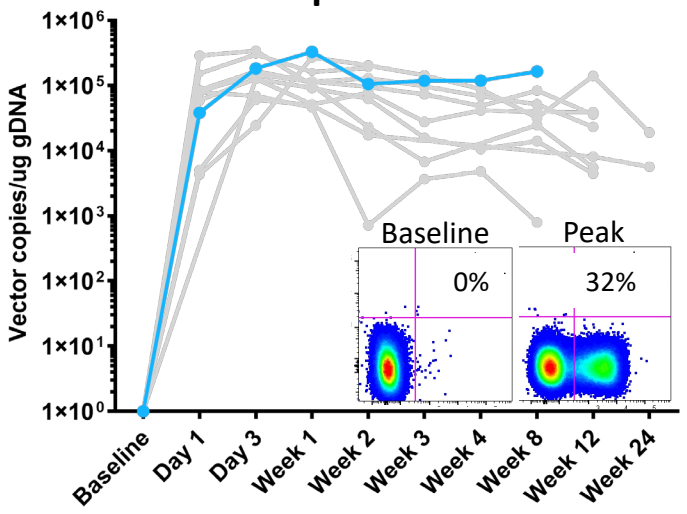
UD: undetected, NA: not available, TBD: to be determined, [1] T cell levels prior to and at peak post infusion as assessed by flow cytometry, T cell persistence as assessed by qPCR

Scans by courtesy of Dr. Wermke

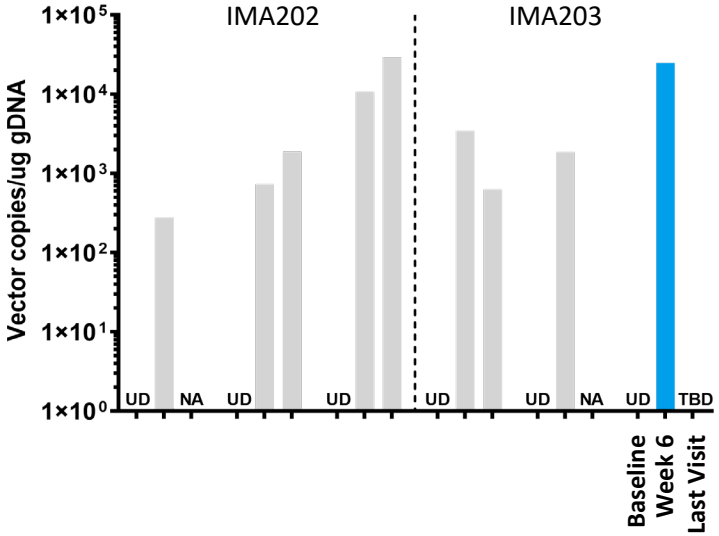
Case Study – Synovial Sarcoma Patient 203-DL2-01

RECIST Response in Patient with High Tumor Burden Observed at Dose Level 2

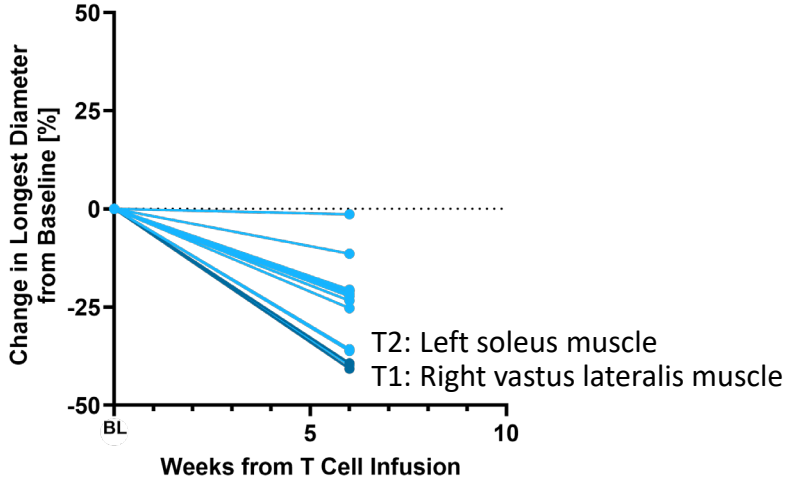
T cell Persistence & Peak Response in the Blood[1]



T cell Detection in the Tumor



Size Changes across 14 Lesions

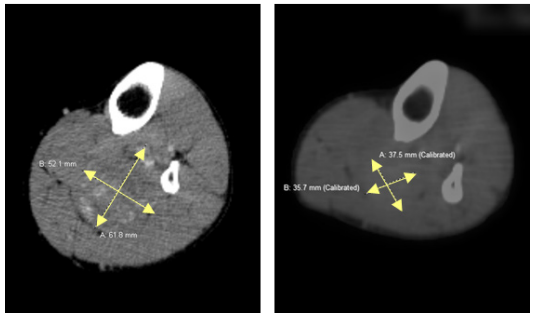


- 57-year-old male; Stage 4 synovial sarcoma
- Infused at refractory disease after failing previous lines of therapy
- Patient received total dose of 350m transduced CD8 IMA203 T cells (DL2) following lymphodepletion

- **T cells persisted at high levels until end of observation and were detected in the tumor**
- **All 14 lesions (22-62 mm longest diameter) decreased at week 6 with 40% decrease in target lesions (RECIST1.1)**
- **Best Response: PR (unconfirmed, week 6)**

Target Lesion T2: Left soleus muscle

Baseline | Week 6



Data cut-off – February 16, 2021

UD: undetected, NA: not available, TBD: to be determined, [1] T cell levels prior to and at peak post infusion as assessed by flow cytometry, T cell persistence as assessed by qPCR

Scans by courtesy of Dr. Araujo

Summary and Future Directions

Key Findings

Transient and manageable treatment-emergent adverse events as expected for cell therapies

Robust T cell engraftment and persistence post infusion and tumor infiltration in all evaluable patients

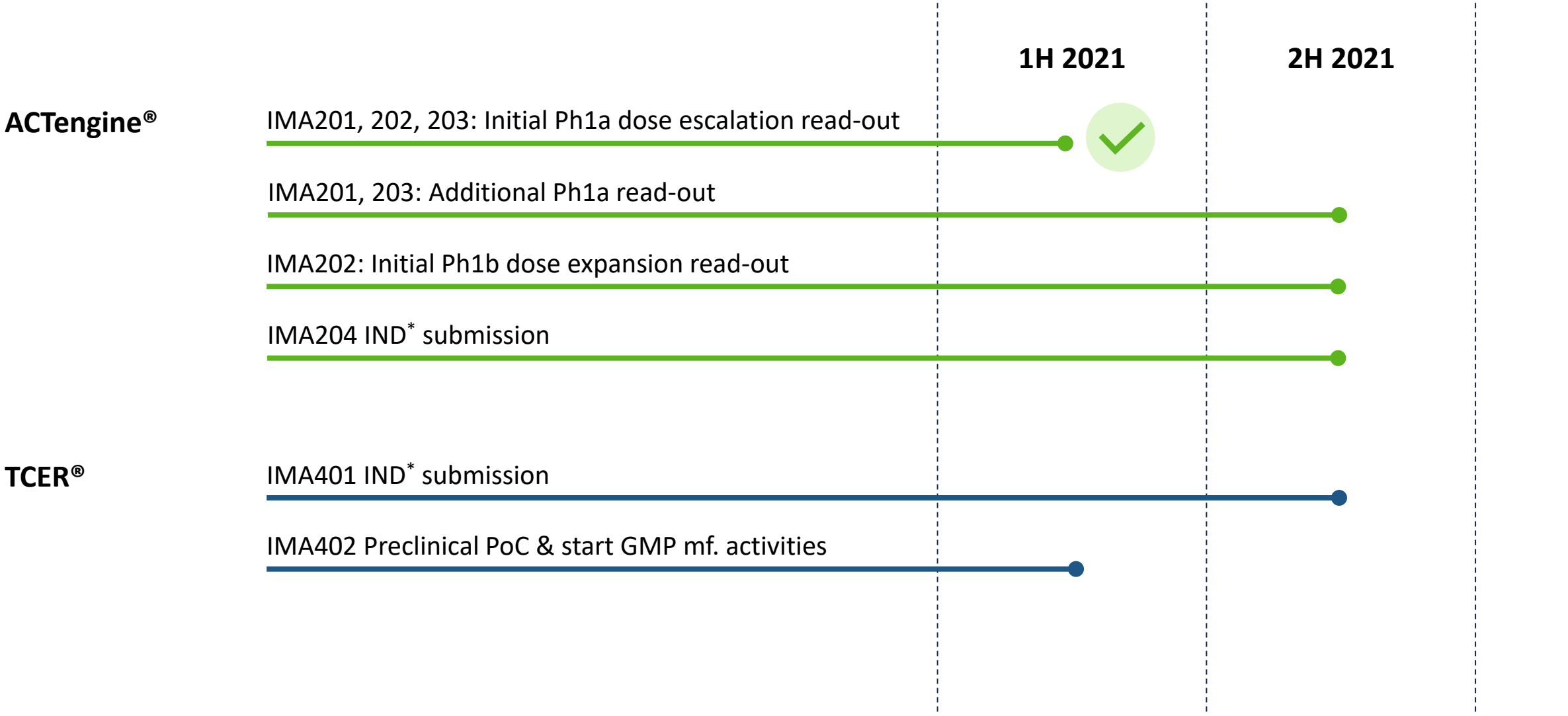
Tumor shrinkage observed in 8/10 evaluable patients including one unconfirmed partial response (RECIST1.1)

Next Steps

- Complete Dose Escalation for IMA201, IMA202, IMA203 clinical trials
- Initiate Dose Expansion and treat patients at target dose
- Update on patients treated at target dose expected for 2H2021

First anti-tumor activity observed consistent with robust biological activity during early phases of dose escalation

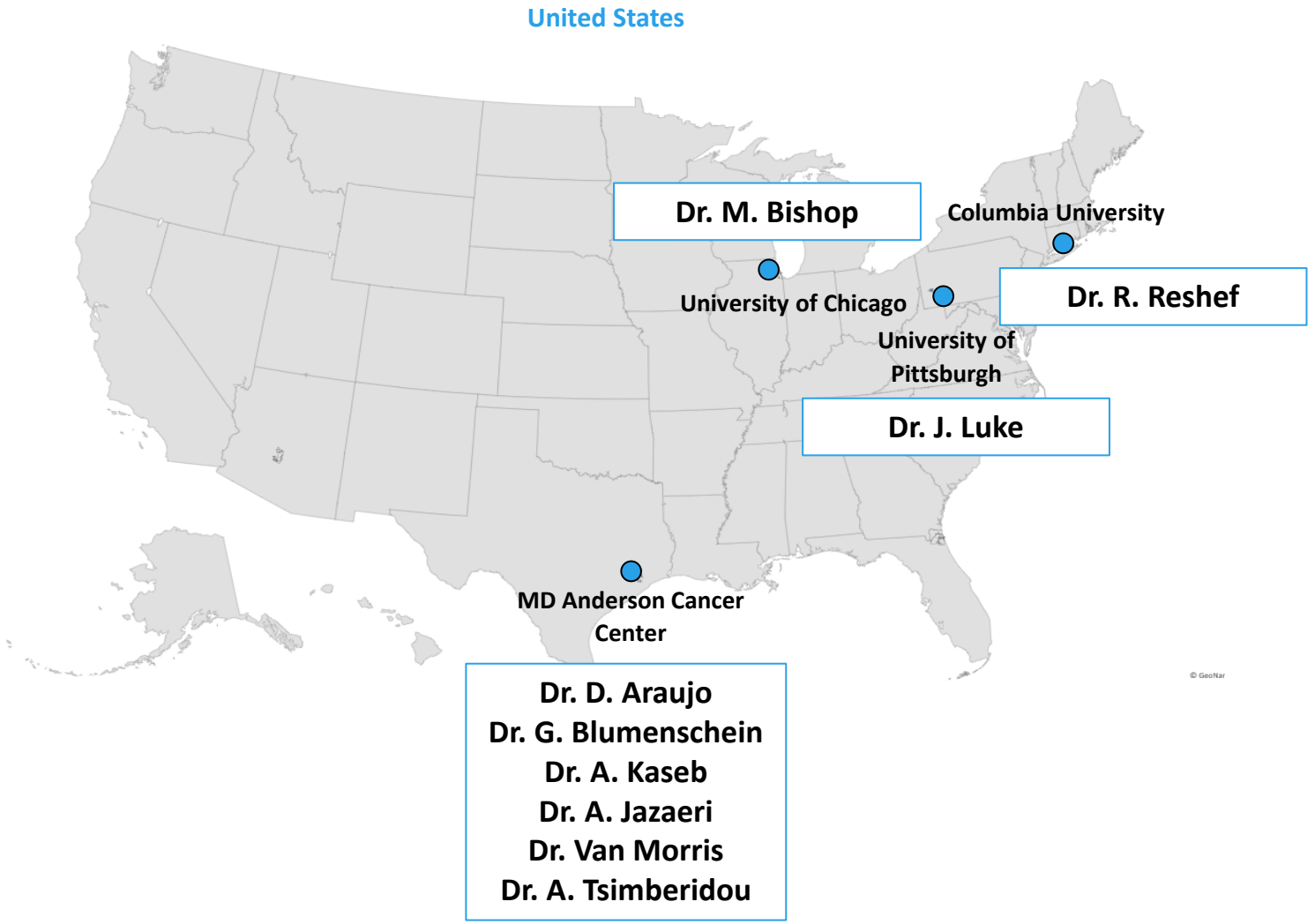
Upcoming R&D Milestones in 2021

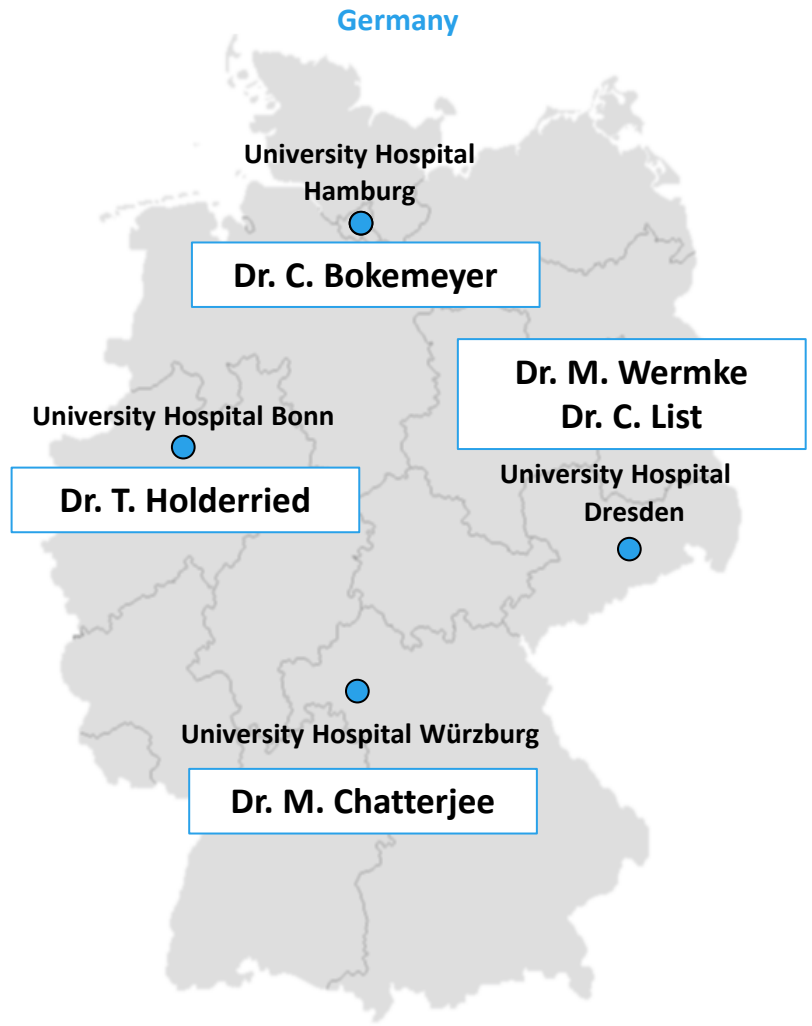


* IND: May be investigational drug application with FDA or analogous clinical trial application (CTA) to a European regulatory agency

Special Thanks to Our Patients, Their Families

… and Our Investigators at the Clinical Sites





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