



ASH INB-100 Clinical Update

December 12, 2023



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Deep Experience Across Development and Biotechnology



William Ho
Co-Founder,
President and Chief
Executive Officer



**Lawrence
Lamb, PhD**
Co-Founder and Chief
Scientific Officer



**Patrick
McCall, CPA**
Chief Financial
Officer



**Trishna
Goswami, MD**
Chief Medical Officer



**Kate Rochlin,
PhD**
Chief Operating
Officer

IN8bio's team has deep experience in cell therapy & oncology expertise:

- Diverse leadership team brings extensive background in oncology discovery, business insights, franchise creation, product development, regulatory affairs, and commercialization
- Business development and licensing expertise across biopharmaceutical and biotechnology companies. Founding of a private healthcare investment fund and management of public investments and cross-over portfolio at leading healthcare venture capital firm, New Leaf Venture Partners
- Specialization in transplantation immunology and recognized innovation in the field of $\gamma\delta$ T cells
- Leadership of Curadigm's spin-out from Nanobiotix and platform collaborations and partnerships
- Proven and measurable successes in bringing high profile candidates to market including Stemline, Immunomedics and Gilead Sciences



Guest Speakers



Michael Bishop, MD, University of Chicago

- Michael R. Bishop, MD, specializes in the diagnosis and treatment of lymphomas. In particular, he cares for patients with hematologic malignancies that have not responded to first-line treatments. An expert in hematopoietic stem cell transplantation (bone marrow transplantation) and cellular therapy, Dr. Bishop and his team are working to address the unique social, economic, physiological and biological issues that patients face while undergoing this treatment. Dr. Bishop's research focuses on the prevention and treatment of relapse after stem cell transplantation. Relapse is the primary cause of treatment failure and death after stem cell transplantation. He has served as the primary investigator on studies designed to prevent and treat disease recurrence after transplantation. Specifically, he works on ways to enhance immune effects of the transplanted cells against cancer. An active contributor to medical literature, Dr. Bishop has authored more than 150 peer-reviewed articles, in addition to more than 30 book chapters and two books on cancer treatment and research. He also serves on the editorial board of numerous scientific journals, including Biology of Blood and Marrow Transplantation. Since 2001, Dr. Bishop has consistently been named one of the "Best Doctors in America" by Best Doctors, Inc. He previously served as a senior investigator and as the clinical head of stem cell transplantation for the National Cancer Institute at the National Institutes of Health. He is a faculty member and on the planning committee of the ASTCT/EBMT Conference on Relapse After Transplant and Cellular Therapy.



AT THE FOREFRONT
UChicago
Medicine

IN8bio Cell Therapy Thesis

IN8bio's three-pronged approach to targeting cancers:

Durability

Meaningful **duration of response** can be achieved by increasing the **depth of response** through novel **synergistic combinations**.

Tolerability

Utilize **novel cell types** with a natural ability to identify and kill malignant cells while **preserving healthy tissue** to avoid toxicities seen with other cell therapy approaches.

Heterogeneity

Employ an approach that can leverage **endogenous immune mechanisms** to **cover tumor heterogeneity** and drive broader immune activation.

Robust Pipeline with Multiple Near-Term Clinical Readouts

Product Candidate	Approach	Initial Indication	Stage of Development				Next Anticipated Milestone(s)
			Preclinical	Phase 1	Phase 2	Phase 3	
INB-200	DeltEx DRI*	Glioblastoma (GBM)					<ul style="list-style-type: none"> Complete enrollment of Cohort 3 in 2023 Clinical update at SNO 2023 Phase 1 long-term follow-up in 1H24
INB-100	DeltEx Allo	Leukemia					<ul style="list-style-type: none"> Updated results at ASH 2023 Phase 1 long-term follow-up results in 2024 Potentially submit IND for Phase 3; 2:1 RCT Trial in AML & MDS in 2024^
INB-400	DeltEx DRI Auto	GBM (front-line)					<ul style="list-style-type: none"> Initial enrollment in 2H23
	DeltEx DRI Allo	GBM (relapsed and front-line) Ovarian					<ul style="list-style-type: none"> Potentially submit IND for Allo Phase 1b in relapsed GBM in 2024^
INB-300	Non-signaling CAR-T	TBD					<ul style="list-style-type: none"> Updated proof-of-concept data on nsCAR platform targeting AML at medical meeting in 1H24
INB-500	iPSC gamma-delta T cells	TBD					

* DRI = Drug Resistant Immunotherapy, or a chemotherapy resistant cell therapy

^Timing of Next Anticipated Milestones are estimates based on the successful raise of additional capital to fund our programs

The background of the slide features a microscopic image of cells, likely cancer cells, rendered in shades of teal and green. The cells are clustered and have a textured, irregular appearance. The overall aesthetic is clean and scientific.

Michael Bishop, MD

UChicago Medicine



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Relapse after Allogeneic Hematopoietic Stem Cell Transplantation

Michael Bishop, MD

INB-100

Haploidentical Stem Cell Transplantation (HSCT)

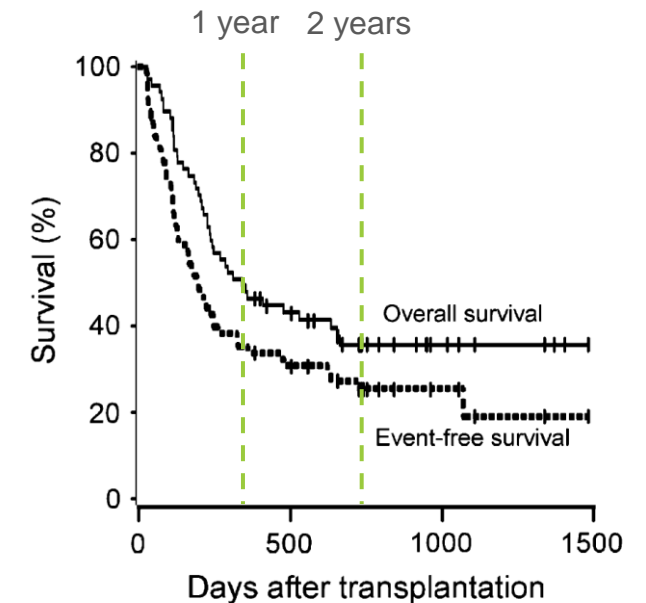
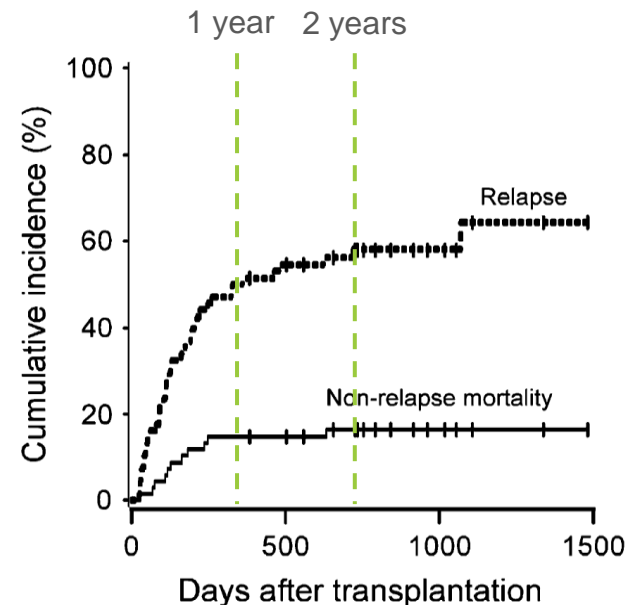
Relapse is the biggest HSCT problem

- Haploidentical transplants have expanded access to stem cell transplantation
- However, relapse remains the biggest risk post-transplant with a ~51% risk of relapse at 1-year
- Gamma- delta ($\gamma\delta$) T cells are an inherent anti-cancer immune cell that may be able to preempt relapse in the post-transplant setting
- $\gamma\delta$ T cells respond to stress ligands expressed on tumor cells to eliminate residual leukemia

HLA-Haploidentical Bone Marrow Transplantation for Hematologic Malignancies Using Nonmyeloablative Conditioning and High-Dose, Posttransplantation Cyclophosphamide

Leo Luznik,^{1*} Paul V. O'Donnell,^{2,3*} Heather J. Symons,¹ Allen R. Chen,¹ M. Susan Leffell,¹ Marianna Zauburak,¹ Ted A. Gooley,^{2,3} Steve Piantadosi,¹ Michele Kaup,¹ Richard F. Ambinder,¹ Carol Ann Huff,¹ William Matsui,¹ Javier Bolaños-Meade,¹ Ivan Borrello,¹ Jonathan D. Powell,¹ Elizabeth Harrington,² Sandy Warnock,² Mary Flowers,^{2,3} Robert A. Brodsky,¹ Brenda M. Sandmaier,^{2,3} Rainer F. Storb,^{2,3} Richard J. Jones,¹ Ephraim J. Fuchs¹

¹ Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, Maryland; ² Fred Hutchinson Cancer Research Center, Seattle, Washington; and ³ University of Washington School of Medicine Seattle, Washington



An Allogeneic Therapy to Reduce Leukemic Relapse

INB-100: Single-center, dose-escalation trial of DeltEx Allo gamma-delta T cells post-haploidentical HSCT

Treatment Arms

Single, ascending dose levels in a 3+3 design:

1. N = 3 (up to 6) patients, single dose of 1×10^6 cells/kg
2. N = 3 (up to 6) patients, single dose of 3×10^6 cells/kg
3. N = 3 (up to 6) patients, single dose of 1×10^7 cells/kg

 RP2D

Treatment Regimen & Timing

Fludarabine +
cyclophosphamide + TBI =
6 days



Haploidentical
HSCT*



INB-100 infusion within
7 days after
engraftment

*Neutrophil engraftment is ~15-20 days following HSCT

Primary Endpoints

- Safety
- Maximum tolerated dose (MTD) of DeltEx Allo gamma-delta T cell infusion
- Dose limiting toxicity (DLT)

Secondary Endpoints

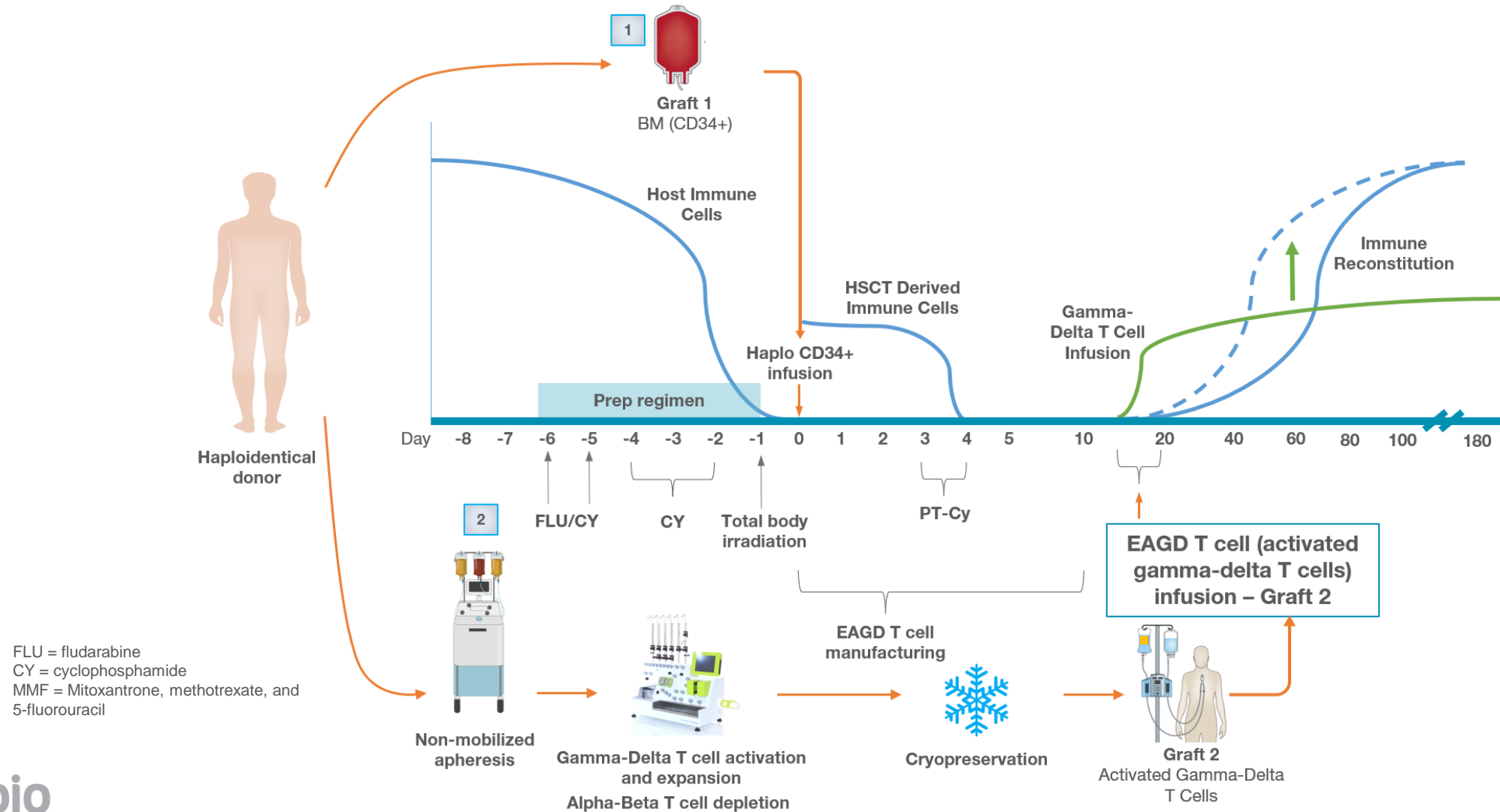
- Rate of acute and chronic graft versus host disease (aGVHD), relapse, and overall survival

Site

THE UNIVERSITY OF KANSAS
CANCER CENTER

Potential to Provide Protection During a Vulnerable Period

Expanded + activated gamma-delta T cells (EAGD) to prevent leukemic relapse



Key Eligibility Criteria

- Adult patients with a haploidentical donor identified
- KPS \geq 70
- Acute myeloid leukemia (AML) in morphologic complete remission (mCR) with intermediate/high-risk features or relapsed disease
- Chronic myelogenous leukemia (CML) in any chronic phase
- Myelodysplastic syndromes (MDS) with intermediate/high risk features
- Acute lymphocytic leukemia (ALL) in mCR with high-risk features or relapsed disease

Patient Demographics and Summary

Patient	Dose Level	Age / Sex	Prior Therapies	Disease	Acute / Chronic GvHD	mCR Duration (mos)
002	1	63 / female	Idasanutlin + 7+3	High-risk AML trisomy 8+ and del7	Acute G2 skin GvHD Chronic limited mild skin GvHD	42.7+
003	1	44 / female	7+3	High-risk AML trisomy 8+ and del7	Acute G2 GI, Acute G2 rash GvHD	40.3+
006	1	66 / male	7+3 IDAC	Relapsed AML	Acute G2 rash GvHD Chronic extensive GvHD	28.6+
007	1	71 / male	Ven/Aza+Pembrolizumab	AML	Acute G2 rash GvHD Chronic limited mod GvHD	14.3+
009	2	68 / male	R-CHOP Blinatumomab Inotuzumab Flu/Mel/TBI Vincristine/steroids Flu/cy/brentuximab CAR-T with Tecartus	Relapsed Ph- ALL; p53 mutated by FISH and NGS	Acute G2c rash GvHD	12.2+
010	2	63 / female	7 cycles Venetoclax/Aza	AML	Acute G2b rash - GvHD	12.0+
011	2	68 / male	Hydrea/Peg-IFN	ET with MDS/MPN overlap	Acute G1 rash - <u>not</u> GvHD Acute G1 diarrhea - <u>not</u> GvHD	9.0+
012	2	69 / male	2 cycles Venetoclax/Aza	AML		5.6+
013	2	71 / female	1 cycle Ven/aza/gliteritinib 2 cycles Venetoclax/Aza	AML, FLT3	Acute G1 diarrhea - <u>not</u> GvHD	5.3+
014	2	71 / male	Venetoclax/Dacogen	AML	Acute G1 diarrhea - <u>not</u> GvHD Acute G1 rash - <u>not</u> GvHD	4.9+

14 enrolled, n=10 dosed and evaluable for safety

- 1 patient expired prior to dosing
- 1 patient received an out of specification product at 6 x 10⁵ EAGD/kg
- 1 manufacturing failure
- 1 screen failure

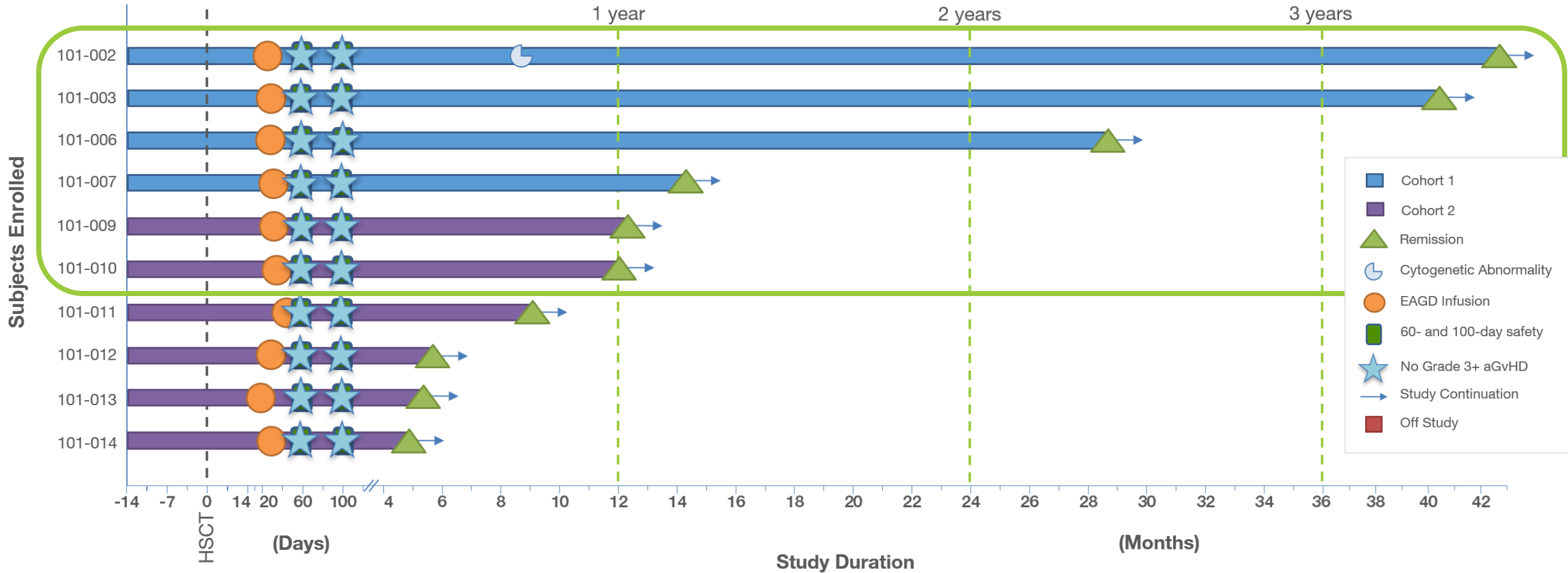
Treatment Emergent AE's in $\geq 20\%$ of Patients (n=10)

Adverse Events	Total (%)	Grade 1/2	Grade 3	Grade 4
Platelet count decreased	100	36.3	45.5	18.2
WBC decreased	90.9	45.4	27.3	18.2
Anemia	90.9	36.4	54.5	
ANC decreased	90.9	36.3	18.2	36.4
ALC decreased	54.5		36.4	18.2
Hypomagnesemia	54.5	54.5		
Creatinine increased	54.5	54.5		
Rash maculopapular	54.5	54.5		
Vomiting	36.4	36.4		
Hypokalemia	36.4	36.4		
Hyponatremia	36.4	36.4		
Dyspnea	27.3	27.3		
Peripheral edema	27.3	27.3		
Hypertension	27.3	27.3		
Pollakiuria	27.3	27.3		
Diarrhea	18.2	18.2		
Decreased appetite	18.2		18.2	

- No DLT's to date
- 2 patients with CMV reactivation
- Treatment-related SAE's:
 - G2 Rash maculopapular (18.2%)
 - G3 Nausea (aGvHD 2B GI)
 - G3 Anemia
- Other non-treatment related SAE's include:
 - G3 Acute Kidney Injury
 - G3 CMV reactivation
 - G3 Fall
 - G3 Decreased appetite
- No treatment-related deaths
- No SUSAR's or unexpected safety events
- No change in AE profile from DL1 to DL2

100% Patients Remain in mCR with Six \geq 12 Months

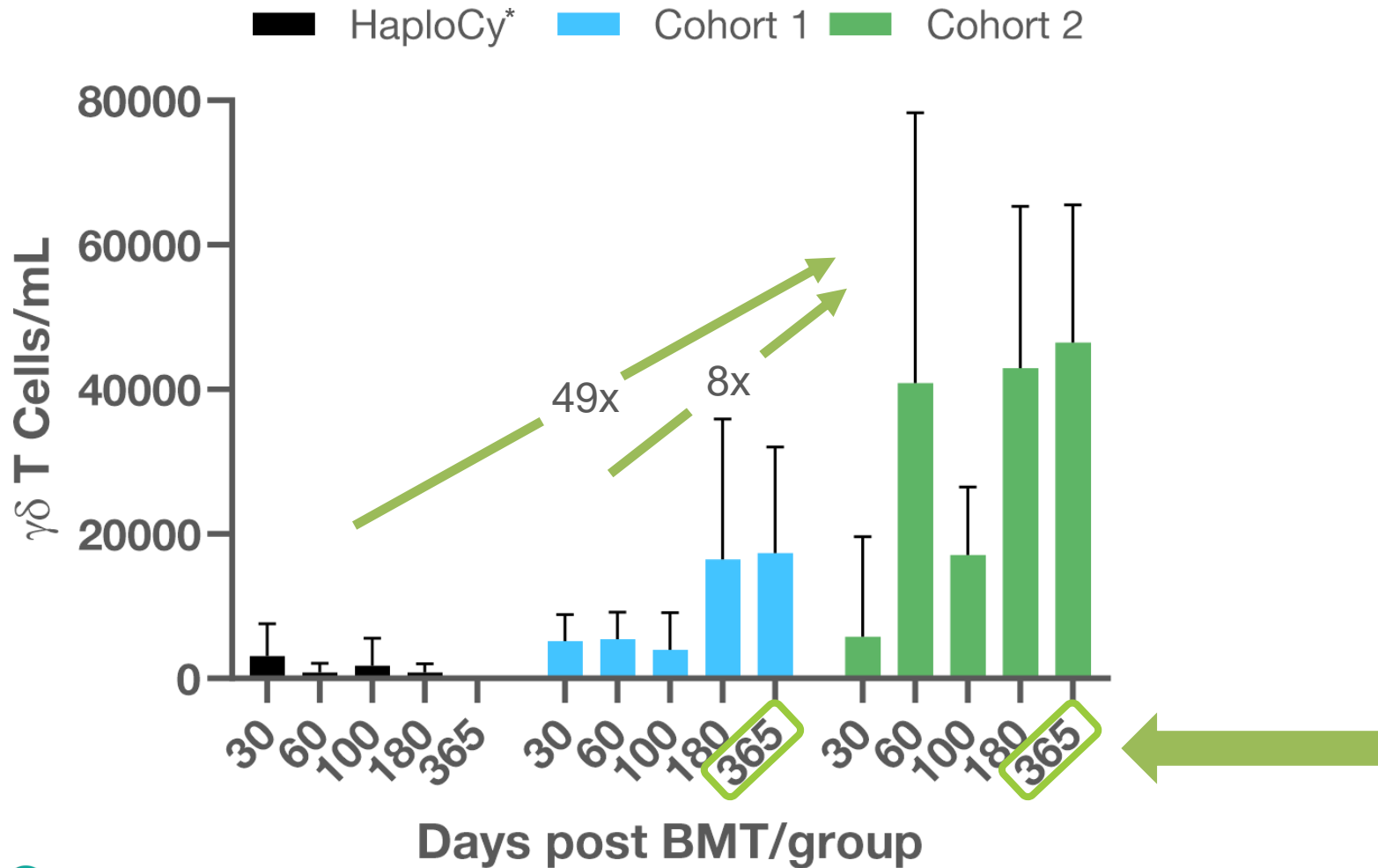
Three patients with high-risk disease remain relapse free for >28 months



Note: As of November 3, 2023; Early trial results are not indicative of future results, including the outcome of this trial.

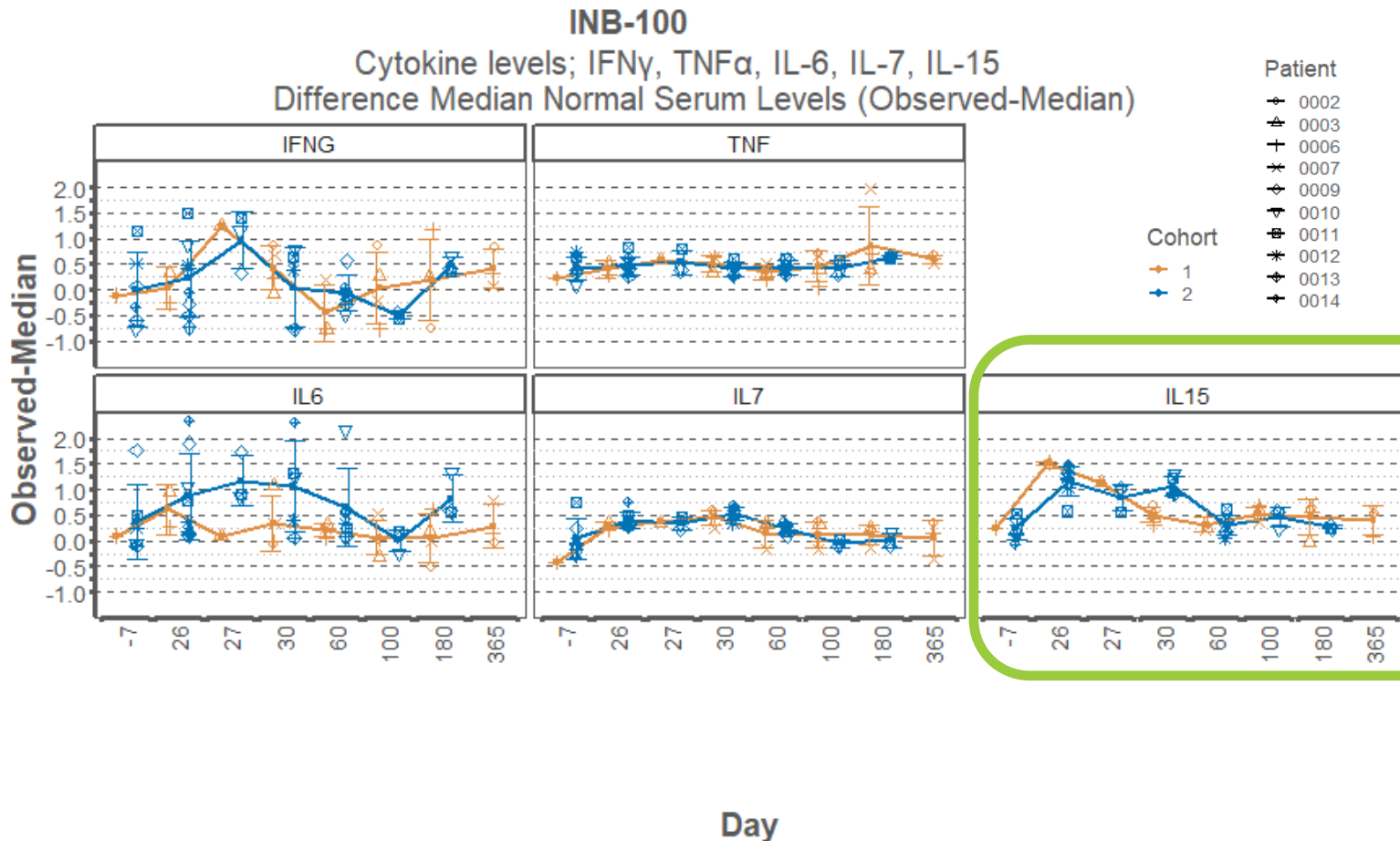
One –Year In Vivo Persistence and Expansion of $\gamma\delta$ T Cells

Haplo-Cy vs INB-100



- Comparison of $\gamma\delta$ T cell count recovery between patients who received haploidentical BMT + post-BMT Cy without $\gamma\delta$ T cell infusion and INB-100 patients from Cohort 1 and Cohort 2
- Cohort 2 patients receive 3x the $\gamma\delta$ T cell dose as Cohort 1
- Dose dependent increase of circulating $\gamma\delta$ T cells at Days +60, +100, +180 and +365 for INB-100 treated patients
- At 1 year Cohort 2 $\gamma\delta$ T cells are 2.7x greater than Cohort 1

Immune Recovery: Serum Cytokine Profile



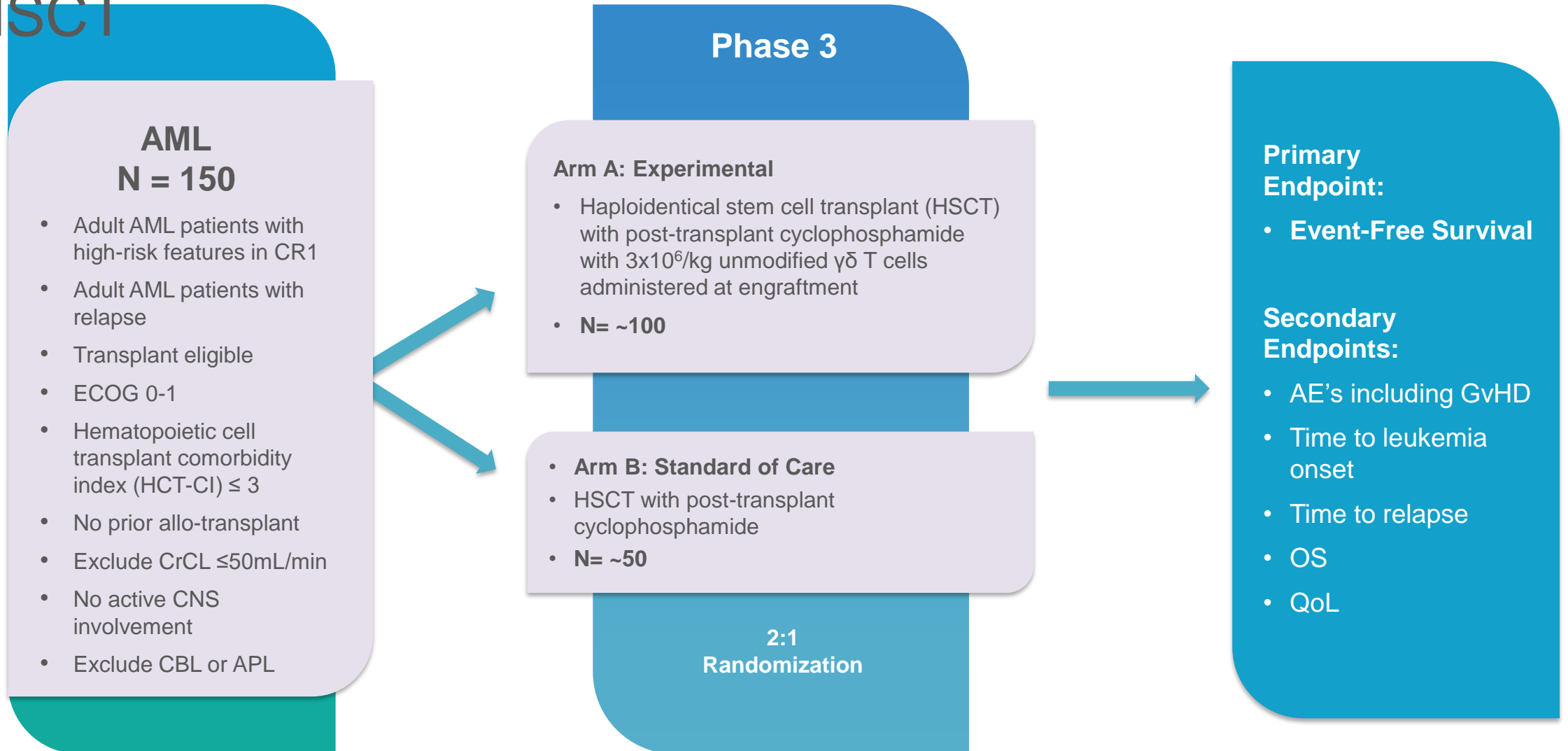
- IL-6 concentration is higher in the second cohort but insufficient to initiate clinical manifestations of CRS. This is also evidenced by decreases of inflammatory cytokines TNF- α , IFN- γ , and IL-7 following transplant and infusion. These data are consistent with a favorable clinical safety profile

Initial higher concentrations of serum IL-15 are favorable for homeostatic reconstitution, expansion, and durability of the infused $\gamma\delta$ T cell population consistent with the observed intermediate and longer-term impact on cytokine levels

Conclusions & Next Steps

- Expected **~51% relapse rate at 1-year** post-transplant with haploidentical transplant alone
 - Median follow-up of **12.1 months**
 - Two patients with high-risk cytogenetic AML remaining in mCR for 3+ years and another patient with relapsed AML for 2+ years
- **100%** of patients achieved and remain in **CR**
 - **70%** of patients with **CR ≥ 6 months** with **60%** of patients remaining in **CR ≥12 months**
- Safety profile remains manageable and consistent across dose cohorts with primarily grade 2 acute GvHD with no cytokine release syndrome (CRS), neurotoxicity (ICANS) or ≥ grade 3 acute GvHD reported
- This is the first trial to demonstrate **in vivo expansion and persistence of $\gamma\delta$ T cells for up to 1-year post-HSCT** suggesting continued $\gamma\delta$ T cell surveillance against leukemic relapse
- Given favorable risk-benefit ratio and prolonged event-free survival (EFS), a Phase 1b expansion trial of 10 patients at DL2 is underway to further validate this signal

Phase 2/3 $\gamma\delta$ T Cell Maintenance in AML Patients with HSCT



Q&A

The Unmet Need in Oncology Trials is Significant

“When I was first diagnosed with AML, we (my wife and I) were updating the will and planning for the worst. Dr. McGuirk and his team discussed the gamma-delta clinical trial and asked if I wanted to participate. I was hoping for a cure, but I figured if I were not to make it, others might learn something from my participation in the trial. We were resigned for the worst but Dr. McGuirk and this trial gave us hope. Today we are living a pretty normal life with people in our community, the church and family. They prayed for us and for a successful treatment. Right now I am feeling good and we are so thankful.” – INB-100 patient

IN8bio Harnessing the Power of $\gamma\delta$ T Cells



- Utilizing innovative approaches to efficiently advance our programs
- Demonstrating the ability to execute and to build our business methodically and intentionally
- Pursuing rigorous science to achieve better patient outcomes
- Completed enrollment in INB-100 Phase 1 trial
- Initiating enrollment in INB-400 Phase 2 trial
- Near-term value creating milestones with presentations and clinical data updates at SITC, SNO and ASH in 4Q 2023 and multiple key data readouts expected in 2024



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