



# Transforming the Field of Hematopoietic Stem Cell Therapies

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### Jasper is developing multiple therapies to transform the field of stem and cellular medicine

### JSP191: First in class, targeted anti-CD117 antibody starting pivotal study in AML/ MDS

- **AML/MDS:** Global pivotal study target initiation by Q1 2023 based on recent clinical data and FDA feedback in older AML/MDS patients ineligible for full myeloablative conditioning
- SCID: Potential near-term BLA and PRV opportunity in SCID patients based on clinical data with JSP191 as single-agent, safe conditioning in re-transplant patients
- LR-MDS Therapeutic: Pilot study launching 2H 2022 in lower-risk MDS as a disease-modifying therapeutic to directly deplete diseased stem cells allowing for recovery of blood / immune production by healthy stem cells
- **Other:** Additional ongoing and potential studies for indications in gene therapy, sickle cell disease, mast cell diseases, leukemias and other rare disorders of blood and immune systems



### Jasper mRNA cell programming: Improving the efficacy and safety of cellular therapies

- Gene therapies: Jasper mRNAs designed to improve gene therapy engraftment leading to faster and higher levels of target protein
- Allogeneic grafts: Jasper mRNAs designed to eliminate need for toxic conditioning and reduce risk of GvHD to improve the therapeutic utility of donor grafts (matched, haplo or cord)
- Other: Potential uses in T- and NK cell therapies for homing and immune evasion





# Jasper's expanding pipeline

Indication	R&D Partner	Research	Preclinical	Clinical	Anticipated Milestones
JSP191					
Jasper Sponsored Studies					
MDS/AML					<ul> <li>Clinical data presented at TCT 2022</li> <li>Pivotal trial target initiation by Q1 2023</li> </ul>
SCID					<ul> <li>Targeting FDA registrational feedback 2H 2022</li> </ul>
Lower Risk MDS (primary treatment)	THERAPEOTICS INC.				<ul> <li>2H 2022 clinical study initiation</li> </ul>
Partner Sponsored Studies					
Fanconi Anemia	Stanford University				<ul> <li>First patient dosed Q2 2022, enrollment ongoing</li> </ul>
Sickle Cell & Beta Thalassemia	NIH National Heart, Lung, and Blood Institute				<ul> <li>2022 patient enrollment ongoing</li> </ul>
Chronic Granulomatous Disease	NIH National Institute of Allergy and Infectious Diseases				<ul> <li>2022 patient enrollment</li> </ul>
GATA2 MDS	NIH NATIONAL CANCER INSTITUTE				<ul> <li>2022 patient enrollment</li> </ul>
Gene Therapy – Gaucher Type 1	AVROBIO				2H 2022 first patient enrollment
Gene Therapy – X-SCID	BIO GRAPHITE BIO		•		2H 2022 first collaboration data
Jasper mRNA Stem Cell Graft Platform					
Thalassemias, Sickle Cell Disease	.lasper		·		<ul> <li>2022 in vivo proof of concept</li> </ul>
Autoimmune Diseases	THERAPEUTICS INC.				2023 first IND filing



# JSP191 is designed to specifically block Stem Cell Factor receptor signaling while minimizing effects on mast, germ or Cajal (GI) cells



Inhibition of Stem Cell Survival Signal leads to stem cell depletion in bone marrow JSP191 designed to directly block Stem Cell Factor (SCF) from binding to the CD117 (Stem Cell Factor) Receptor with high affinity and avidity

- · Aglycoslyated IgG1 antibody that inhibits SCF receptor binding site
- Kd < 5pM affinity to human c-Kit Fc dimer with IC50 ~ 70pM
- No Fc mediated ADCC or complement mediated cytotoxicity to reduce risk of adverse effects on germ, mast and Cajal (GI) cells that also express CD117
- GMP production at commercial scale, validation ongoing

# JSP191 preclinical and clinical results show significant potential to improve the efficacy of stem cell transplant and expand to direct therapeutic treatment

- SCID: JSP191 single agent for successful transplant in high risk patients who have previously failed transplant
- AML / MDS: JSP191 in combination with standard of care low dose radiation + fludarabine to improve efficacy for older patients not eligible for full myeloablative conditioning
- Multiple additional JSP191 clinical transplant studies ongoing in various populations with different combinations
- Study of JSP191 as a disease modifying therapeutic in LR-MDS starting in 2022



SCF: Stem Cell Factor

Xue X, et al *Blood. 2010; 116(24):5419-5422.* Bankova AK, Pang WW, Velasco BJ, Long-Boyle JR, Shizuru JA. *Blood Adv.* 2021;5(19):3900-3912.

JSP191 directly blocks key hematopoietic stem cell survival signal leading to depletion of healthy and diseased cells

#### JSP191 depletion of healthy stem cells in non-human primates<sup>1</sup>

#### JSP191 depletion of MDS stem cells in xenograft mouse<sup>2</sup>









# SCID

# Study NCT02963064: JSP191 single agent conditioning for ultra orphan SCID patients who have failed prior curative transplant

JSP191 in SCID granted rare pediatric disease designation and may be eligible for Priority Review Voucher

# SCID patients Re-transplant Newly diagnosed (infants)

#### **Study Endpoints**

- Safety
- Donor stem cell engraftment
- Production of naïve CD4+ T cells
- Clinical benefit (Use of IVIG, infection, vaccine response)

- > SCID is a lethal genetic immune disorder that can be cured with a hematopoietic cell transplant
- > Due to the toxicity of current conditioning agents, patients who fail transplant are not eligible for a repeat procedure
- > Patients who fail transplant have poor clinical status and must rely on lifelong immune therapy
- > 15 re-transplant patients dosed and 3 newly diagnosed

asper

# SCID: Durable clinical benefit in JSP191 conditioned patients with no conditioningrelated toxicity

T-B-NK+ SCID Re-Transplant Subjects

JSP191 dose	Genotype	Follow-up	Outcomes		
0.1 mg/kg	Artemis Artemis	Wk 208 Wk 208	<ul> <li>Off IVIG, Ab response to vaccination</li> <li>IVIG reduced, Chronic norovirus enteritis resolved, Chronic URI resolved</li> </ul>	Key clinical measures	
0.3 mg/kg	PRKDC RAG1 RAG1	Wk 156 Wk 156 Wk 104	<ul> <li>Continues on IVIG, Chronic URI resolved</li> <li>Off IVIG, Ab response to vaccination</li> <li>Continues on IVIG, Improvement in chronic URI</li> </ul>	<ol> <li>Clinical parameters of infection</li> <li>Dependence on exogenous immunoglobulin</li> <li>Response to vaccination</li> </ol>	
0.6 mg/kg	RAG1 RAG1 Artemis	Wk 78 Wk 52 Wk 12	<ul> <li>Continues on IVIG, Improvement in chronic URI</li> <li>IVIG/SCIG dependent, Generating naïve B cells</li> <li>IVIG dependent, Generating naïve B cells</li> </ul>		
1.0 mg/kg	Artemis Artemis	Wk 104 Wk 104	<ul> <li>Off Study at 140 weeks – Deceased</li> <li>Continues on IVIG, Persistent Chronic URI, Improvement in chronic norovirus enteritis</li> </ul>		



# Potential near-term BLA and PRV opportunity for JSP191 in SCID

Severe Combined Immunodeficiency (SCID) is a lethal genetic immune disorder where HCT is the only proven cure

### **Potential FDA filing strategy**

#### Ultra orphan, high unmet need population

 SCID patients who failed primary transplant do not have the option for a second transplant with current toxic conditioning agents

#### Focus on current clinical data

• JSP191 safety and efficacy in 10 SCID re-transplant T-B- patients

#### Additional supportive clinical data that can be generated

- Historical clinical data of patients currently in the JSP191 SCID study
- Natural history study of SCID patients who have failed their first transplant

JSP191 may be eligible for Priority Review Voucher (PRV) with SCID approval JSP191 has been granted Rare Pediatric Disease Designation in SCID





# AML/MDS

# Study NCT04429191: JSP191+Flu/TBI in AML/ MDS patients ineligible for myeloablative conditioning

- Due to toxicity concerns, 45% of AML/ MDS patients receive reduced intensity (RIC) or non-myeloablative (NMA) conditioning<sup>1</sup>
- Busulfan & melphalan RIC regimens still have substantial toxicity with 25+ day average hospitalizations<sup>2</sup> and 20%+ 100-day transplant related mortality<sup>3</sup>



Goal: Create a safe and substantially more effective regimen by adding JSP191 on to current NMA (Flu/TBI)

### JSP191 Ph1b Study



Presented as late-breaking oral presentation at the 2022 Transplant & Cellular Therapy (TCT) conference



[1] CIBMTR Final 2021 Transplant Center-Specific Survival Report, 2021
[2] Broder MS, et al. Am Health Drug Benefits. 2017;10(7):366-374.
[3] Oran B, et al. Transplantation and Cellular Therapy. 2021; 921.e1-921.e10.
ClinicalTrials.gov NCT04429191

# AML/ MDS Study NCT04429191: Single agent JSP191 depletes diseased stem & progenitor cells in bone marrow in 5 to 7 days





Muffly L et al. Tandem Meetings Transplantation and Cellular Therapy (TCT) 2022 April 23-26; Salt Lake City, UT



[1] Paras G, Morsink LM, Othus M, et al. Conditioning intensity and peritransplant flow cytometric MRD dynamics in adult AML. Blood.

2022;139(11):1694-1706

JSP191 is an investigative drug and is not approved for any indication

# AML/ MDS Study NCT04429191: No JSP19 related SAEs, no 100-day transplant related mortality and proof of concept for outpatient stem cell transplant

### **Clinical Safety**

- No JSP191 related SAEs
- No significant JSP191 infusion reactions
- One subject with refractory late onset grade 3 acute GI GVHD
- One subject with secondary graft failure
- No 100-day transplant-related mortality
- No significant mucositis, hypersensitivity, hepatotoxicity, or other organ damage

### **Clinical Setting**

- Protocol allows for outpatient conditioning
- 11 patients given outpatient JSP191 along with outpatient transplant



# Proposed registrational study of JSP191 in MDS/AML – Randomized, double-blind, placebo-controlled, event-driven trial



#### Endpoints

#### Primary

 AML: Event Free Survival (relapse or death, event driven)

• MDS: CR, Durable CR

#### Secondary

- OS, NRM, graft failure, engraftment
- GVHD and TRM
- MRD

### Additional

- Chimerism
- Depletion of HSCs



MDS/AML: Myelodysplastic syndromes/ Acute Myeloid Leukemia; CR: Complete Response; OS: Overall Survival, NRM: Non-Relapse Mortality; TRM: Transplant-Related Mortality; HCT: Hematopoietic Cell Transplantation : GVHD: Gastrointestinal Graft vs. Host Disease Hematopoietic Cell Transplantation; MRD: Measurable Residual Disease

JSP191 is an investigative drug (16) and is not approved for any indication



# **LR-MDS** Therapeutic

# JSP191's ability to directly deplete cancerous stem cells may be leveraged as a disease-modifying therapeutic in lower-risk MDS



Shift of HSCs towards normal hematopoiesis



LR-MDS patients are currently managed with supportive therapies, including transfusion and erythropoietin-stimulating agents meant to address symptoms but not the underlying disease...

" There is a tremendous unmet need for new treatments for MDS; rates of relapse are high, and many patients are not eligible for existing approved therapies..."

- Platzbecker et al., 2021 Leukemia

### JSP191 depletion may enable healthy HSCs to take over the bone marrow niche and restore functional hematopoiesis



JSP191 depletion and rebound of healthy HSCs<sup>2</sup>

JSP191 depletion of MDS cells<sup>1</sup>

70

80

60

# LR-MDS Study: Study of JSP191 as second line therapy in subjects with lower-risk myelodysplastic syndrome (LR-MDS)



#### Single Arm Trial Design

#### **Key Assessments**

- Safety
- Transfusion independence
- Hematologic improvement (hemoglobin, platelets, neutrophils)
- ORR (per 2006 IWG response criteria)
- Change in cellular population in blood and marrow
- MDS is a heterogeneous disorder of the bone marrow and hematopoietic stem cells that typically occurs in older patients and can progress to AML
- Low to intermediate risk MDS patients are not eligible for transplant and have few therapeutic options other than erythropoiesis-stimulating agents (ESAs) which do not affect the diseased stem cells
- > LR-MDS patients refractory to ESAs are dependent on routine transfusions which are associated with poor survival
- JSP191 will be studied as second line therapy in low to intermediate risk MDS patients first in a dose escalation phase (0.1 to 1.5 mg / kg, up to n=6 per cohort) and then dose expansion phase (up to 20 additional subjects)





# mRNA Cellular Programming

mRNA-based cell therapy reprograms HSCs with a transient advantage during the peri-engraftment period without requiring permanent DNA change



### Potential Jasper mRNA platform benefits

- Improved homing to bone marrow
- Improved engraftment
- Immune evasion
- Potential for pure CD34+ stem cell grafts

### Engraftment in the bone marrow niche



Sean Morrison, Nat Rev Immunol. (2017)



# JSP191 potential to significantly accelerate the use of transplant in major markets

Allogeneic Transplant Volume (2019): ~41,000 Transplants/Year





[1] Center for International Blood & Marrow Transplant Research (CIBMTR) US Summary Slides 2021; [2] European Society of Blood and Marrow Transplantations (EBMT) 2021 Transplant Activity Survey; [3] Asia-Pacific Blood and Marrow Transplantation Group (APBMT) Activity Survey 2020; [4] Japanese Data Center for Hematopoietic Cell Transplantation (JDCHCT) Nationwide Survey 2021 Summary Slide; [5] Xu L, et al. Nature (2021) 56:2940–2947.

JSP191 is an investigative drug (23) and is not approved for any indication

# The registrational study for JSP191 will start in AML/MDS, the largest indications for allogeneic transplant

		Allo-HCT	Incie	dence
		AML, MDS	AML	MDS
	US	4,400	21,500	38,500
* * * * * * *	EU <del>5</del>	9,250	22,000	38,000
*:	China	4,400	32,000	60,500
	Japan	2,000	9,500	18,000
	Total	20,050	85,000	155,000
		Today	Expansion Opportunity With Safer Conditioning	

30% of patients not currently transplanted may be newly eligible with approval of JSP191

Based on Jasper internal market research of US high-volume AML and MDS allogeneic transplant physicians when showed the JSP191 target product profile



[1] Center for International Blood & Marrow Transplant Research (CIBMTR) US Summary Slides 2021
[2] European Society of Blood and Marrow Transplantations (EBMT) 2021 Transplant Activity Survey
[3] Asia-Pacific Blood and Marrow Transplantation Group (APBMT) Activity Survey 2020
[4] Xu L, et al. Nature (2021) 56:2940–2947; GlobalData.

# Projected program timelines





# Anticipated upcoming milestones

### **JSP191**

- Pivotal AML/ MDS study launch (US & EU)
- Proof of concept LR-MDS therapeutic study
- CMC validation activities including manufacturing BLA qualification lots

#### mRNA Stem Cell Editing Platform

- Additional *in vivo* proof of concept experiments
- Manufacturing and toxicology to support IND







# Transforming the Field of Hematopoietic Stem Cell Therapies

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# JSP191 depletes diseased HSCs across the progression of MDS/AML patients





MDS/AML: Myelodysplastic syndromes/ Acute Myeloid LeukemiaHSC: Hematopoietic stem cells; LR-MDS: Low-Risk Myelodysplastic syndromes; HR-MDS: High-Risk Myelodysplastic syndromes

JSP191 is an investigative drug and is not approved for any indication

# Currently less than 1% of patients receive potentially curative HCT in non-malignant diseases

Non-malignant diseases that could be treated with hematopoietic stem cell transplantation



Primary immuno- deficiencies	SCID, Chronic Granulomatous Disease, Wiskott- Aldrich syndrome, Leukocyte Adhesion Deficiency, Hemophagocytic Lymphohistiocytosis
Bone marrow failures	Fanconi Anemia, Diamond Blackfan Anemia, Shwachman Diamond Syndrome, Paroxysmal Nocturnal Hemoglobinuria, Congenital Amegakaryocytic Thrombocytopenia, Aplastic Anemia
Metabolic disorders	Gaucher Disease, Fabry Disease, Cystinosis, Pompe Disease, Adrenoleukedystrophy, Mucopolysaccharidosis I-IV, Metachromatic Leukodystrophy
Bleeding disorders	Hemophilia A, Hemophilia B, von Willebrand Disease, Bernard-Soulier Syndrome
Hemoglobin- opathies	Sickle Cell Disease, Beta Thalassemia



Jasper mRNA technology can shift the paradigm for stem cell transplant and gene therapy

