mesoblast
the regenerative medicine company

Global Leader in Cellular Medicines for Inflammatory Diseases

Investor and Analyst Event

Acute Graft Versus Host Disease KOL Symposium

June 2019

Nasdaq: MESO ASX: MSB

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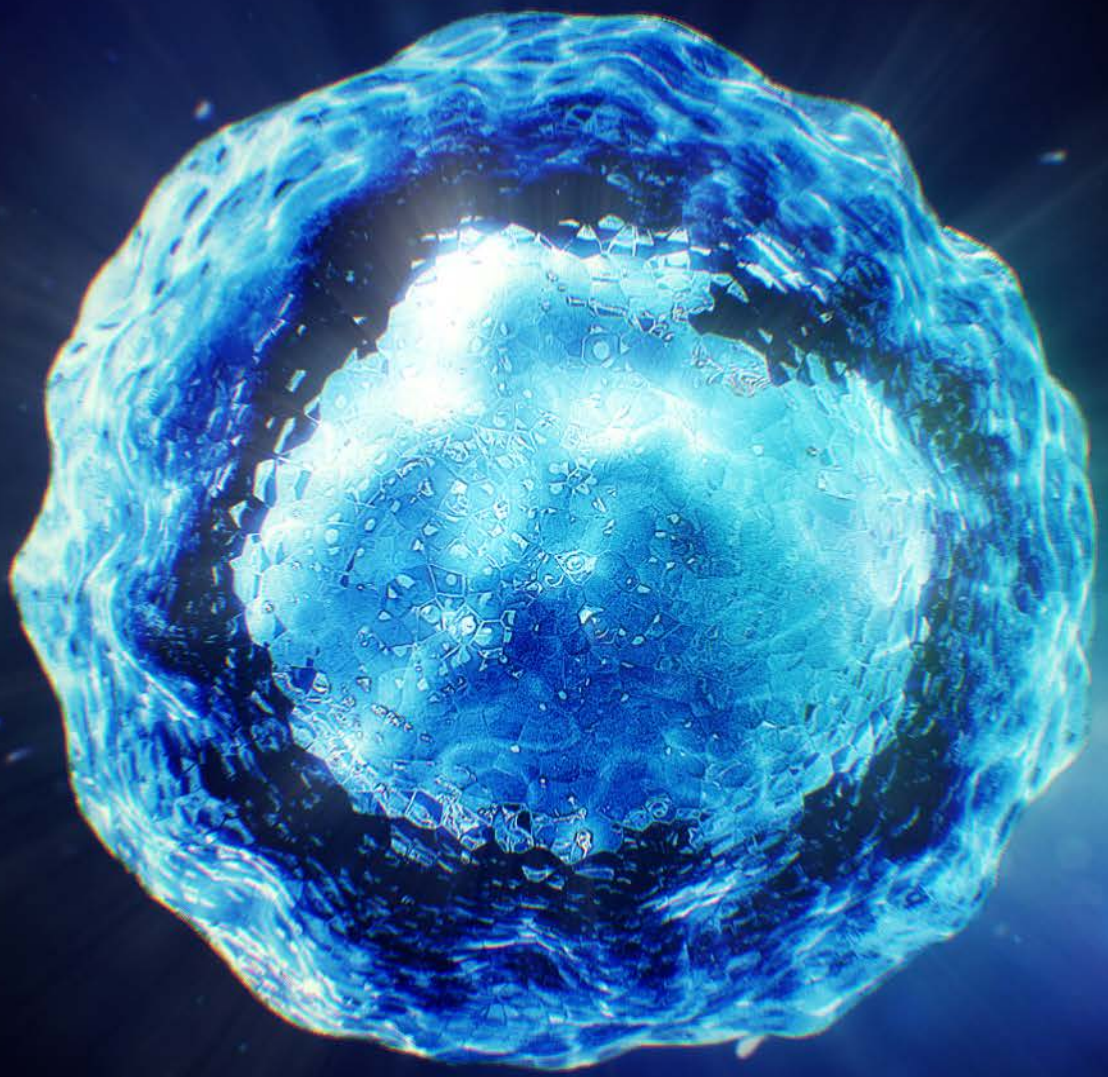
Agenda for Today

1. **Brief Corporate Overview of Mesoblast** — **Josh Muntner (CFO)**
2. **Steroid Refractory Acute GVHD (SR-aGVHD):** — **Dr. Donna Skerrett (CMO)**
   - Significant Burden of Illness and Unmet Need
   - Properties of Remestemcel-L Relevant to Acute GVHD
   - Steroid Refractory Disease Outcomes Predicted by Organ Involvement
   - Summary of MESO's GVHD Clinical Program (Protocol 280, Expanded Access Program, Phase 3 Trial GVHD001)
3. **Real World aGVHD Clinical Experience** — **Dr. Susan E. Prockop (MSKCC)**
   - Current SR-aGVHD Treatment Paradigm and Prognosis
   - Limitations of Current Treatment Alternatives in Clinical Practice
   - Acute GVHD Patient Journey
   - Potential Role of Emerging Therapies in Clinical Development for aGVHD
   - Real World Clinical Experience - Experience using Remestemcel-L
4. **Maximizing Remestemcel-L** — **Eric Strati (SVP, Commercial)**
   - Overview of SR-aGVHD Market
   - Commercial Opportunity for Remestemcel-L
   - Ongoing Mesoblast Commercial Readiness Activities
5. **Closing and Q&A**

Our Mission

Mesoblast is committed to bring to market innovative cellular medicines to treat serious and life-threatening illnesses



Premier Global Cellular Medicines Company

Innovative Technology Platform[1]	Late Stage Pipeline	Commercialization
▪ Innovative technology targets the most severe disease states refractory to conventional therapies ▪ Well characterized multimodal mechanisms of action ▪ Underpinned by extensive, global IP estate	▪ Upcoming BLA submission for steroid-refractory acute GVHD ▪ 2 blockbuster product candidates completed Phase 3 trial enrollment - heart failure and back pain ▪ China cardiovascular partnership established	▪ Building focused US sales force for acute GVHD product launch ▪ Industrial-scale manufacturing to meet commercial demand ▪ First approved products commercialized by licensees in Japan[2] and Europe[3] ▪ Increasing revenues and milestone payments

1. Mesenchymal precursor cells (MPCs) and their culture-expanded progeny mesenchymal stem cells (MSCs).
2. Licensee JCR Pharmaceuticals Co., Ltd. received the first full PMDA approval for an allogeneic cellular medicine in Japan and markets this product under its trademark, TEMCELL® Hs Inj.
3. Licensee Takeda received first central marketing authorization approval from the European Commission for an allogeneic stem cell therapy and markets this product under its trademark, Alofisel®.

Corporate History

Over a decade of scientific, manufacturing, clinical development and corporate transaction experience targeted at bringing to market, cellular medicines for inflammatory diseases

2004:
Mesoblast is founded in Melbourne, Australia and listed on the ASX

2010:
Entered into strategic alliance to develop and commercialize MPC therapeutics

2011:
Entered into manufacturing partnership with Lonza Group in Singapore for MPC medicines

2013:
Acquired MSC business from Osiris Therapeutics with trailing earn-out and milestone payments on the MSC business

2014:
Granted manufacturing pioneer status by Economic Development Board of Singapore

2015:
Dual listed on the Nasdaq

2016:
TEMCELL® HS Inj (MSC medicine) launched in Japan by Mesoblast licensee JCR

2017:
Entered licensing agreement with Takeda for the treatment of certain fistulae; Alofisel® approved in EU

2018:
Entered into partnership agreement with Tasly for cardiovascular assets in China

2019:
Smith & Nephew acquires Osiris Therapeutics including rights to the trailing earn-out and milestone payments on the MSC business

2019:
Initiates first Biologics License Application (BLA) submission to US FDA: remestemcel-L (MSC) for steroid refractory acute graft versus host disease

Global IP Estate Provides Substantial Competitive Advantage

- ~800 Patents and patent applications (69 Patent families) across all major jurisdictions
- Covers composition of matter, manufacturing, and therapeutic applications of mesenchymal lineage cells
- Enables licensing to third parties for different indications, when in alignment with our corporate strategy, e.g.TiGenix (subsequently acquired by Takeda)
- Provides strong global protection against competitors seeking to develop products in areas of core commercial focus

Markets
U.S., Europe, China, and Japan

Sources
Allogeneic, Autologous, (Bone Marrow, Adipose, Dental Pulp, Placenta), Pluripotent (iPS)

Diseases
All Tier 1 & Tier 2 Indications, and multiple additional conditions

Commercial-Scale Manufacturing Capability

- Immune privileged nature of mesenchymal lineage cells enables allogeneic “off the shelf” product candidates
- Culture expansion scalable to produce anticipated commercial quantities
- Management know-how in regulatory activities necessary for product approval and commercial launch

Lonza contract manufacturing facility in Singapore

We believe remestemcel-L will be the first commercially produced allogeneic mesenchymal lineage cell product registered for sale in the U.S.

Commercial and Late-Stage Product Pipeline

MARKETED

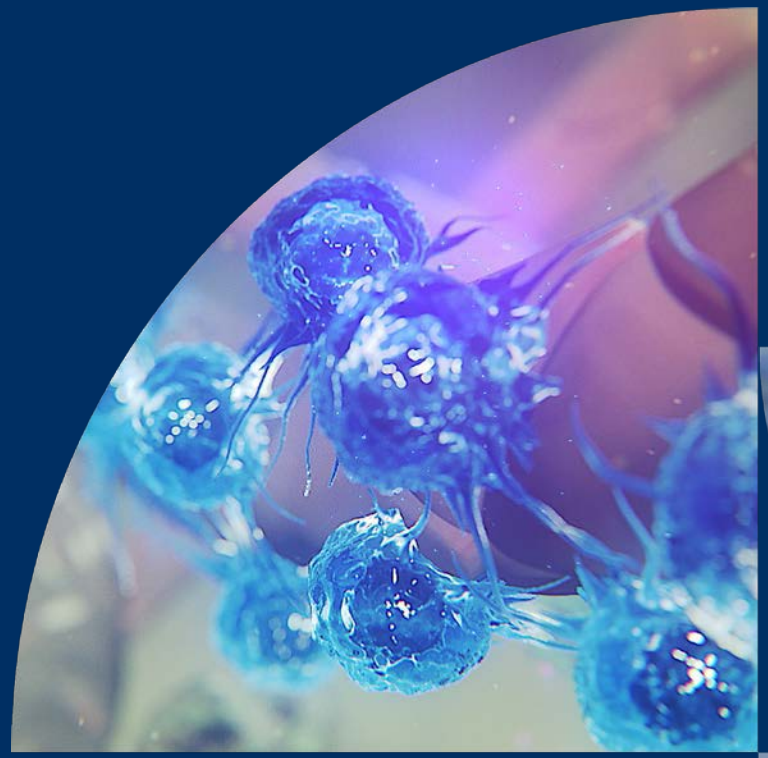
PLATFORM	PRODUCT	THERAPEUTIC AREA		APPROVAL	COMMERCIAL RIGHTS
MSC (Bone Marrow)	TEMCELL® HS Inj[1]	Acute Graft Versus Host Disease	1st allogeneic regen med approved in Japan	✓	JCR Japan
MSC (Adipose)	Alofisel®[2]	Perianal Fistula	1st allogeneic regen med approved in Europe	✓	Takeda Global

IN DEVELOPMENT

PLATFORM	PRODUCT CANDIDATE	THERAPEUTIC AREA	PRE-CLINICAL / PHASE 2 / PHASE 3	COMMERCIAL RIGHTS
MSC suite	Remestemcel-L	Acute Graft Versus Host Disease		mesoblast
	Remestemcel-L	Crohn's Disease		
	Remestemcel-L	Osteoarthritis/Cartilage Repair		
MPC suite	Revascor	Advanced HF (Class II/III) End-Stage HF (Class III/IV)[3]		TASLY China
	MPC-06-ID	Chronic Low Back Pain		mesoblast
	MPC-300-IV	Rheumatoid Arthritis Diabetic Nephropathy		

1 Mesoblast receives royalty income from its licensee JCR Pharmaceuticals Co Ltd on sales of JCR's TEMCELL® Hs. Inj. product in Japan.
2 Mesoblast will receive royalty income from its licensee Takeda Pharmaceuticals on Takeda's worldwide sales of its product Alofisel® in the local treatment of perianal fistulae.
3 Study funded by the United States National Institutes of Health (NIH) and the Canadian Health Research Institute; conducted by the NIH-funded Cardiothoracic Surgical Trials Network.

This chart is figurative and does not purport to show individual trial progress within a clinical program.



Steroid Refractory Acute GVHD (SR-aGVHD):
Dr. Donna Skerrett (Mesoblast Chief Medical Officer)

Acute Graft vs Host Disease

Remestemcel-L for Steroid-Refractory aGVHD

Acute Graft Versus Host Disease (aGVHD)

Significant Burden of Illness and Unmet Need

Burden of Illness

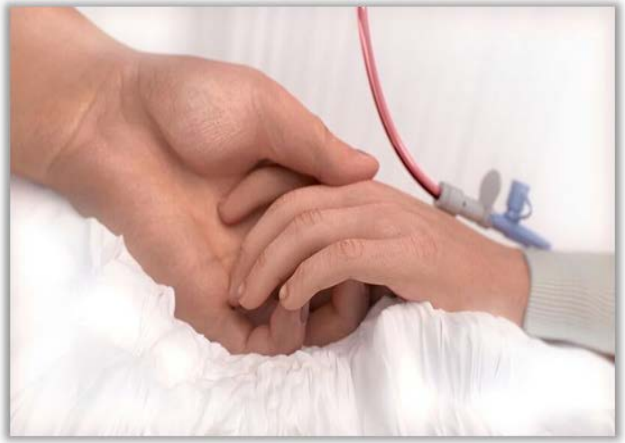
- aGVHD is a life-threatening complication that occurs in ~50% of patients receiving allogeneic bone marrow transplants (BMT)[1]
- Steroid-refractory aGVHD is associated with **mortality rates as high as 90%[1,7] and significant extended hospital stay costs[2]**

Minimal Treatment Options

- There is only one approved treatment for SR-GVHD in the U.S. and **no approved treatment for children under 12 years old, outside Japan**
- In Japan, Mesoblast's licensee has received the only product approval for SR - aGVHD in both children and adults

Market Opportunity

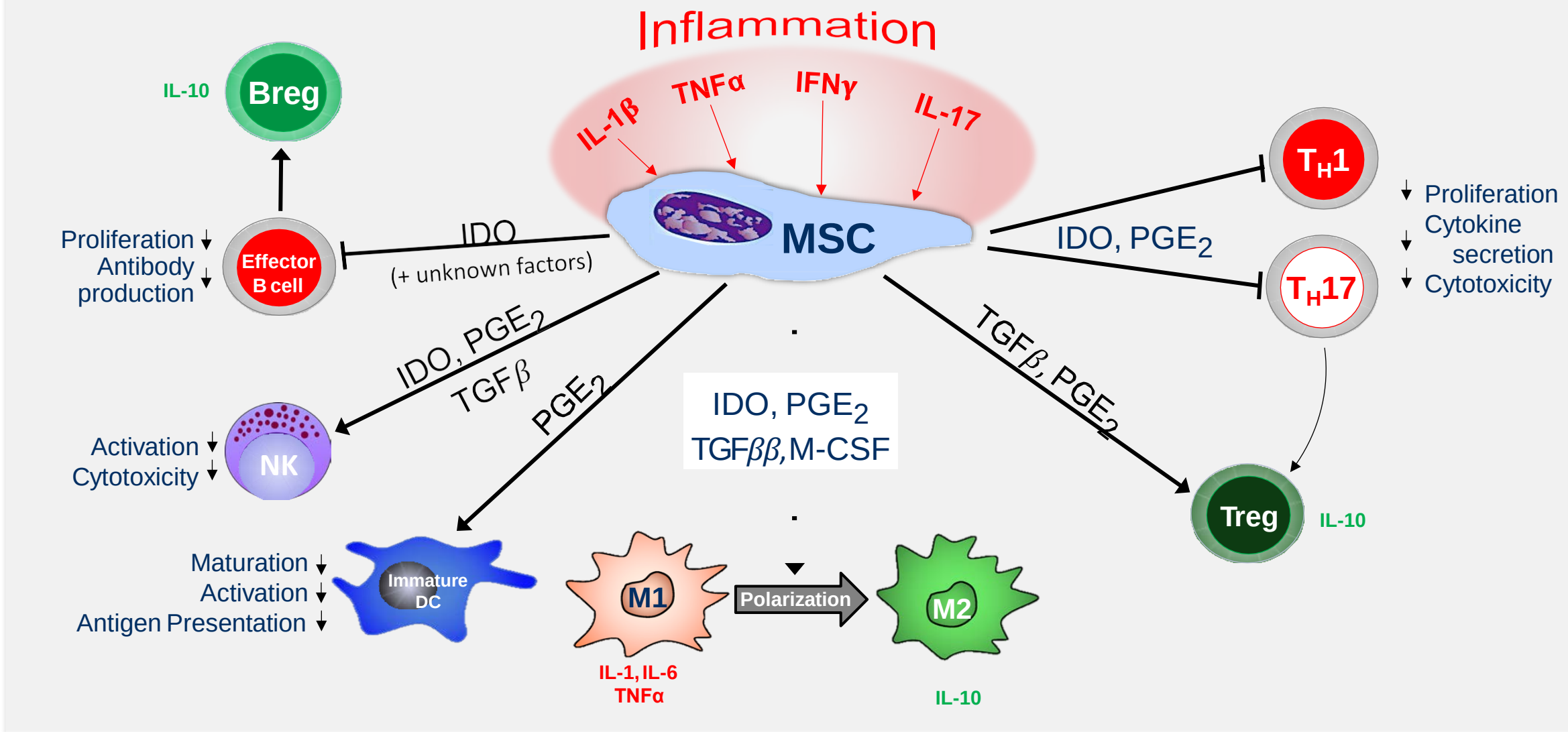
- >30,000 allogeneic BMTs performed annually worldwide (>20K US/EU) ~20% paediatric[3,4]
- Our licensee, JCR Pharmaceuticals Co., Ltd launched TEMCELL® HS Inj.[5] in Japan for SR-aGVHD in 2016; reimbursed up to ~US$195k[6]
- **SR-aGVHD represents US$ > 700m US/EU market opportunity[4,8]**



1. Westin, J., Saliba, RM., Lima, M. (2011) Steroid-refractory acute GVHD: predictors and outcomes. Advances in Hematology. **2**. Anthem-HealthCore/Mesoblast claims analysis (2016). Data on file **3.** Niederwieser D, Baldomero H, Szer J. (2016) Hematopoietic stem cell transplantation activity worldwide in 2012 and a SWOT analysis of the Worldwide Network for Blood and Marrow Transplantation Group including the global survey. **4.** Source: CIBMTR Current Uses and Outcomes of Hematopoietic Cell Transplantation 2017 Summary. Passweg JR, Baldomero, H (2016) Hematopoietic stem cell transplantation in Europe 2014: more than 40,000 transplants annually. **5.** TEMCELL is the registered trademark of JCR Pharmaceuticals Co. Ltd. **6.**Based on a JPY = USD 0.009375 spot exchange rate on market close on November 11, 2016. Amounts are rounded. Source: Bloomberg. 7. Axt L, Naumann A, Toennies J (2019) Retrospective single center analysis of outcome, risk factors and therapy in steroid refractory graft-versus-host disease after allogeneic hematopoietic cell transplantion. Bone Marrow Transplantation. 8.Data on file

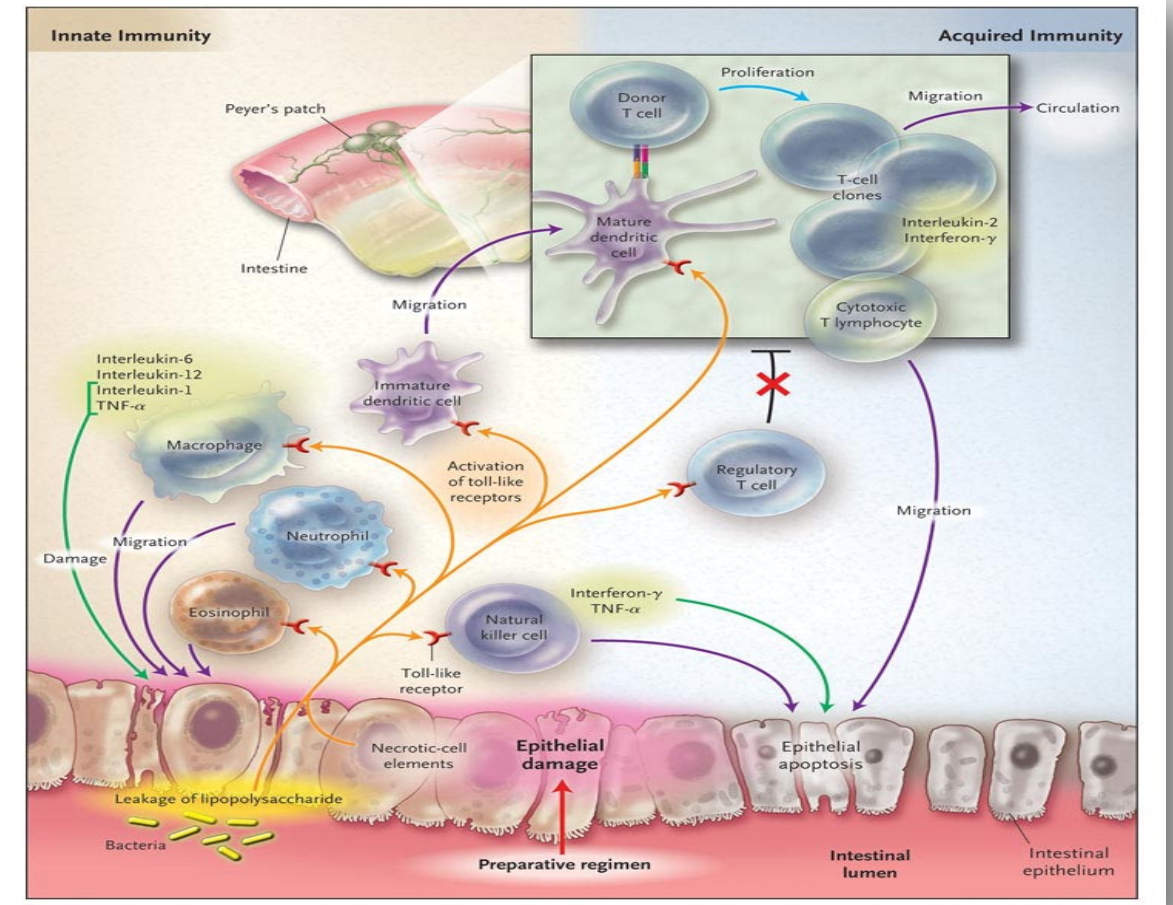
Immunomodulatory Actions of MSCs are Triggered by their Response to Inflammatory Cues:

Paracrine-mediated Alteration of the Function of Cellular Constituents of the Innate and Adaptive Immune Systems



Remestemcel-L: Properties of Remestemcel-L Relevant to aGVHD

BMT Conditioning Regimen Damage to Tissue Leads to Cellular and Cytokine Mediated Inflammatory Response; Alloreactive Donor T Cells Proliferate and Attack Multiple Host Tissues (i.e. Skin, GI, Liver)



Source: Copelan NEJM 354; 17-1813.

In vitro studies demonstrate that Remestemcel-L

- Inhibits alloantigen- and mitogen-driven T cell proliferation in vitro
- Decreases secretion of pro-inflammatory cytokines by immune cells, e.g. TNFα and IFNγ and increase secretion of anti-inflammatory factors, e.g. IL-10 and IL-4
- Induces expansion of regulatory T cells

In vivo, using animal homologs of product

- Inhibits T cell-mediated immune responses
- Distributes to areas of inflammation
- Multiple administrations did not increase B or T cell responses or generate adverse outcomes or rejection in animals

Remestemcel-L:

Summary Review of GVHD Programs in Support of Phase 3 Pediatric Trial (GVHD001)[1]

- Protocol 280 (260 patients) showed improved overall response at Day 28 and Day 100 to remestemcel-L over placebo for aGVHD grade C/D and visceral organ disease
- Protocol 280 (pediatric subgroup), the overall response rate was improved over controls and survival was improved for the cell-treated population compared to controls[1]
- Protocol 275 Expanded Access Program (241 patients) showed meaningful clinical response in pediatric patients across all grades and organ systems, with clinical response at Day 28 positively impacting survival to Day 100
- Combined post-hoc analysis of steroid-only pediatric patients (Protocol 275 and subset of Protocol 280) demonstrated significantly improved response by remestemcel-L treated patients over placebo
- A cumulative total of over 1,500 subjects have been enrolled across all ongoing or completed studies performed at present, of which approximately 638 subjects were treated with remestemcel-L and an additional 16 subjects under investigator initiated trials/EINDs; remestemcel-L was well tolerated in these subjects

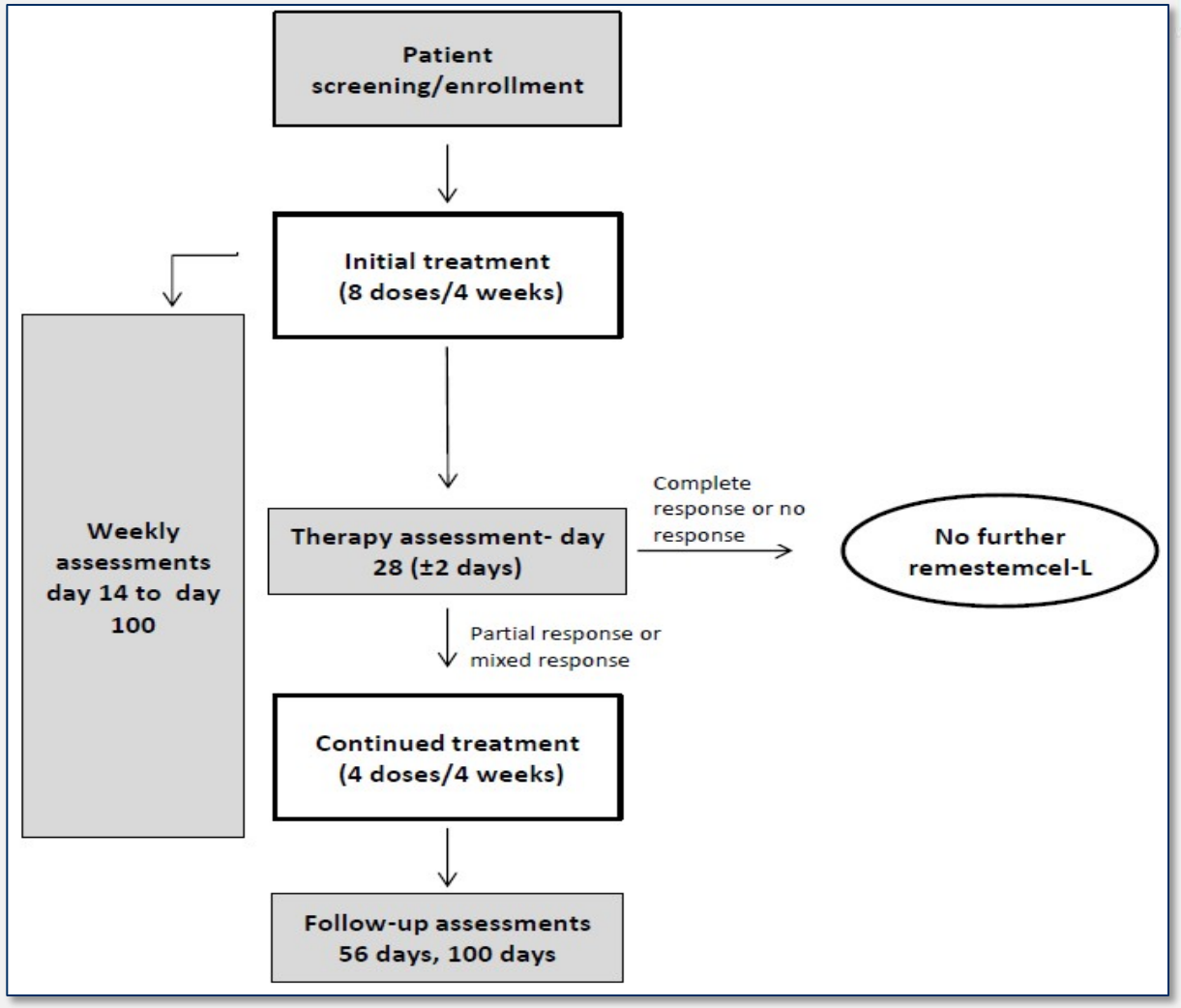
CONCLUSION: Protocol 275 and analysis of 280 support remestemcel-L's treatment effect on patients with aGVHD who failed steroid therapy. Remestemcel-L's treatment effect has been evaluated in aGVHD in pediatric patients and in patients with visceral organ involvement

1. Data on file.
2. NOTE: The subgroup was small and the p values are not significant due to the small numbers.

Remestemcel-L:

Phase 3 Pediatric Trial (GVHD001) - First-line Therapy in aGVHD After Failing Steroids[1]

- Multi-center, single-arm, open-label study to evaluate efficacy and safety to day 100 (GVHD001) and from day 100 to day 180 (GVHD002)
- 55 pediatric patients (2 months to 17 years)
- aGVHD following allogeneic HSCT failing systemic corticosteroid therapy
- Grade B aGVHD involving liver and/or GI tract with or without concomitant skin disease
- Grades C and D aGVHD involving skin, liver and/or GI tract
- Primary endpoint: **Overall response at Day 28**
- Key secondary endpoint: Survival at Day 100



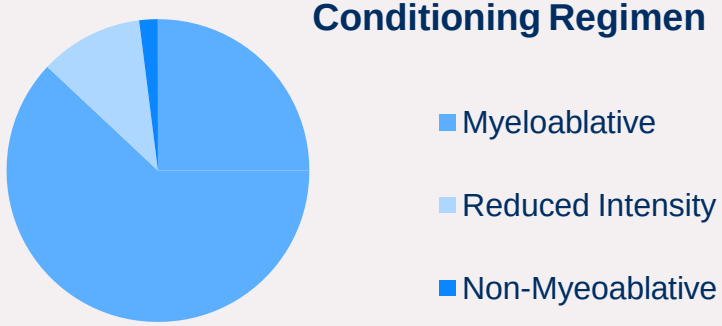
1. Data on file.

Remestemcel-L:
Protocol GVHD001 – Demographics[1]

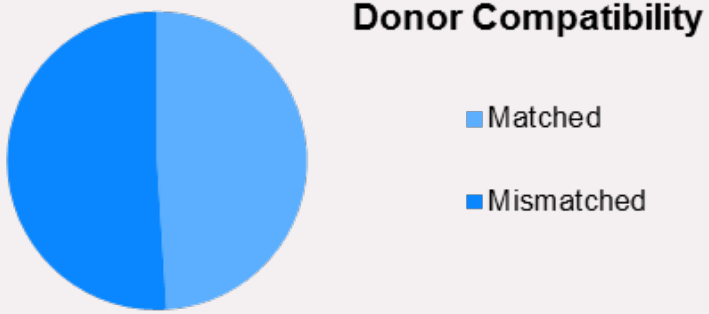
Subjects Enrolled	**55**
Age (years)	
Mean (SD)	**7.8 (5.44)**
Median (minimum, maximum)	**7.6 (0.6, 17.9)**
Gender	
Male	**35 (63.6%)**
Female	**20 (36.4%)**
Underlying Disease	
AML	**18 (32.7%)**
ALL	**12 (21.8%)**
Anemia	**5 (9.1%)**
CML	**4 (7.3%)**
Sickle Cell	**3 (5.5%)**
JML	**2 (3.6%)**
MDS	**2 (3.6%)**
Other	**9 (16.4%)**

1. Data on file.

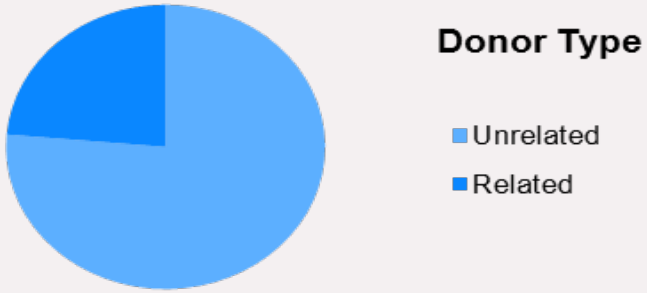
Remestemcel-L:
Protocol GVHD001 - Transplant Characteristics Reflect aGVHD Risk Factors[1]



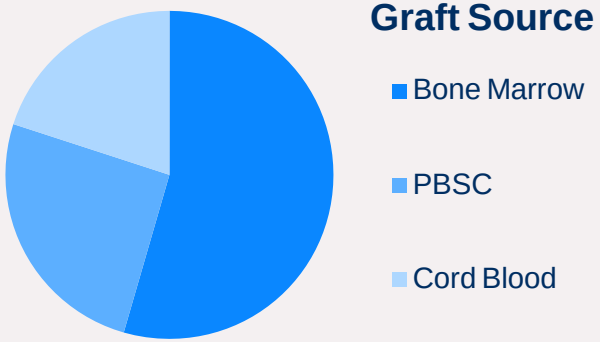
- 87% of subjects received myeloablative conditioning regimen



- 51% of subjects received an HLA-mismatched transplant



- 76% of subjects received an unrelated donor transplant

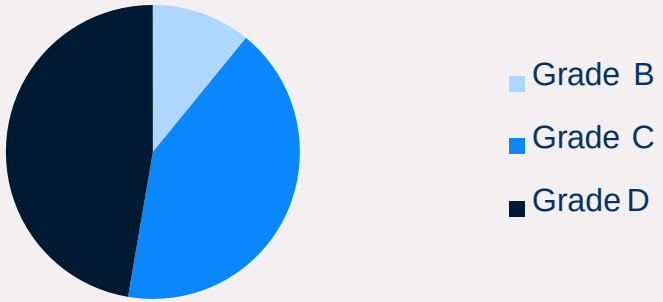


- 55% of subjects received a bone marrow transplant, 25% received PBSC, and 20% received CB

1. Data on file.

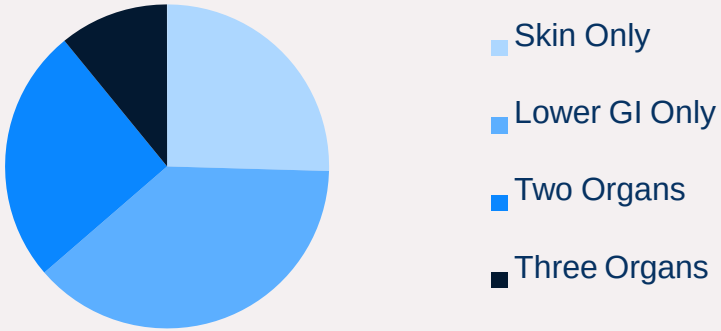
Remestemcel-L:
Protocol GVHD001 - Disease Characteristics Reflect aGVHD Severity[1]

GVHD Grade at Baseline



- 89% of subjects had Grade C/D disease at baseline
- 47% of subjects had Grade D disease at baseline

Baseline Organ Involvement

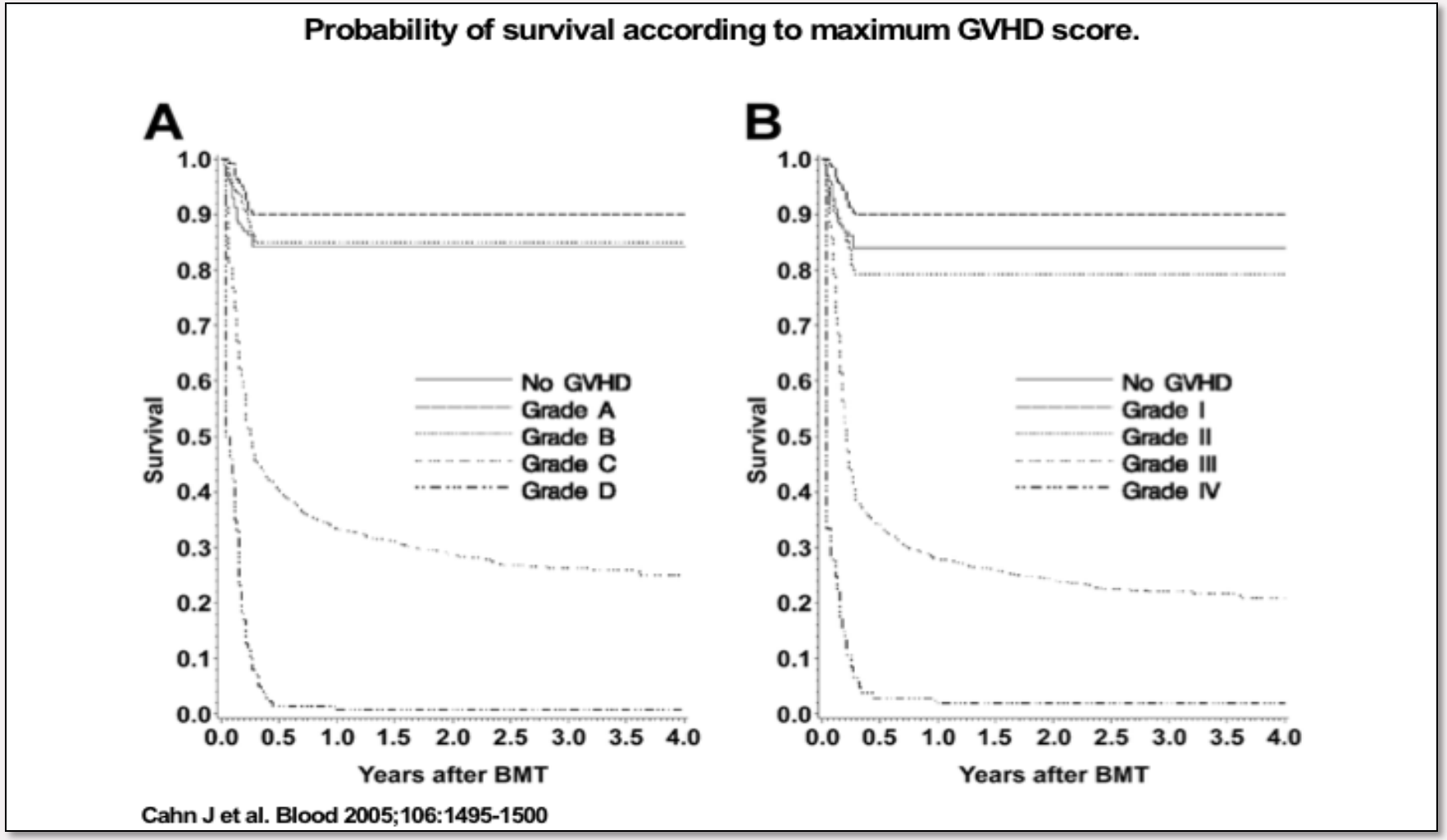


- 26% of subjects had Skin involvement only
  - All had stage 3 (n=10) or stage 4 (n=4) disease
- 38% of subjects had Lower GI involvement only
  - 16/21 had stage 3 (n=6) or stage 4 (n=10) disease
- 36% of subjects had multi-organ involvement, all with Lower GI
  - 6/20 had all three organs involved
  - 10/20 had Lower GI + Skin
  - 4/20 had Lower GI + Liver

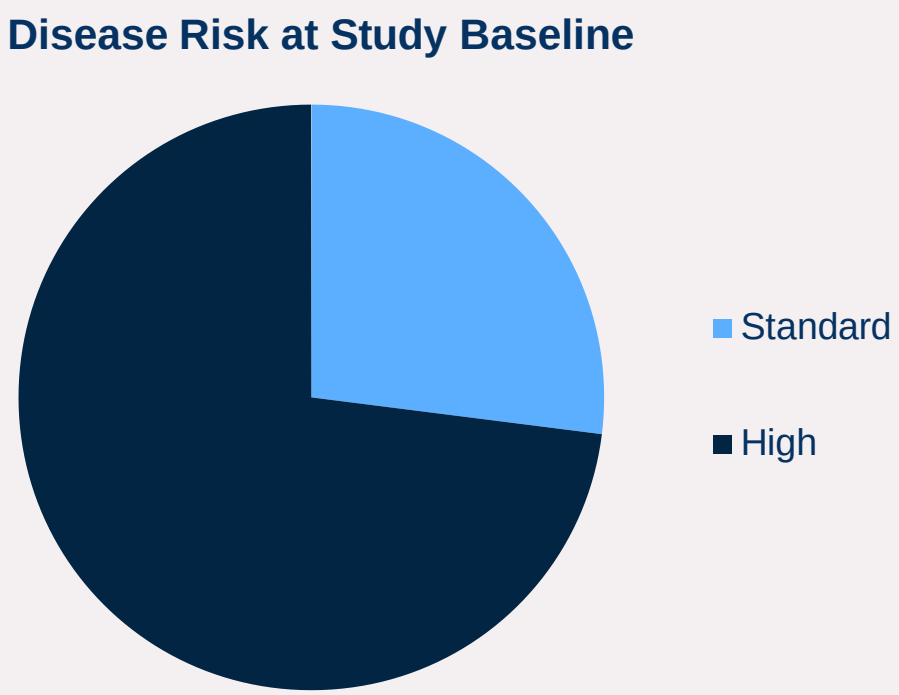
1. Data on file.

Remestemcel-L:

Grade C/D GVHD has Significantly Worse Survival than Grade A/B[1]



Remestemcel-L:
Protocol GVHD001 - Disease Characteristics (Risk)[1]

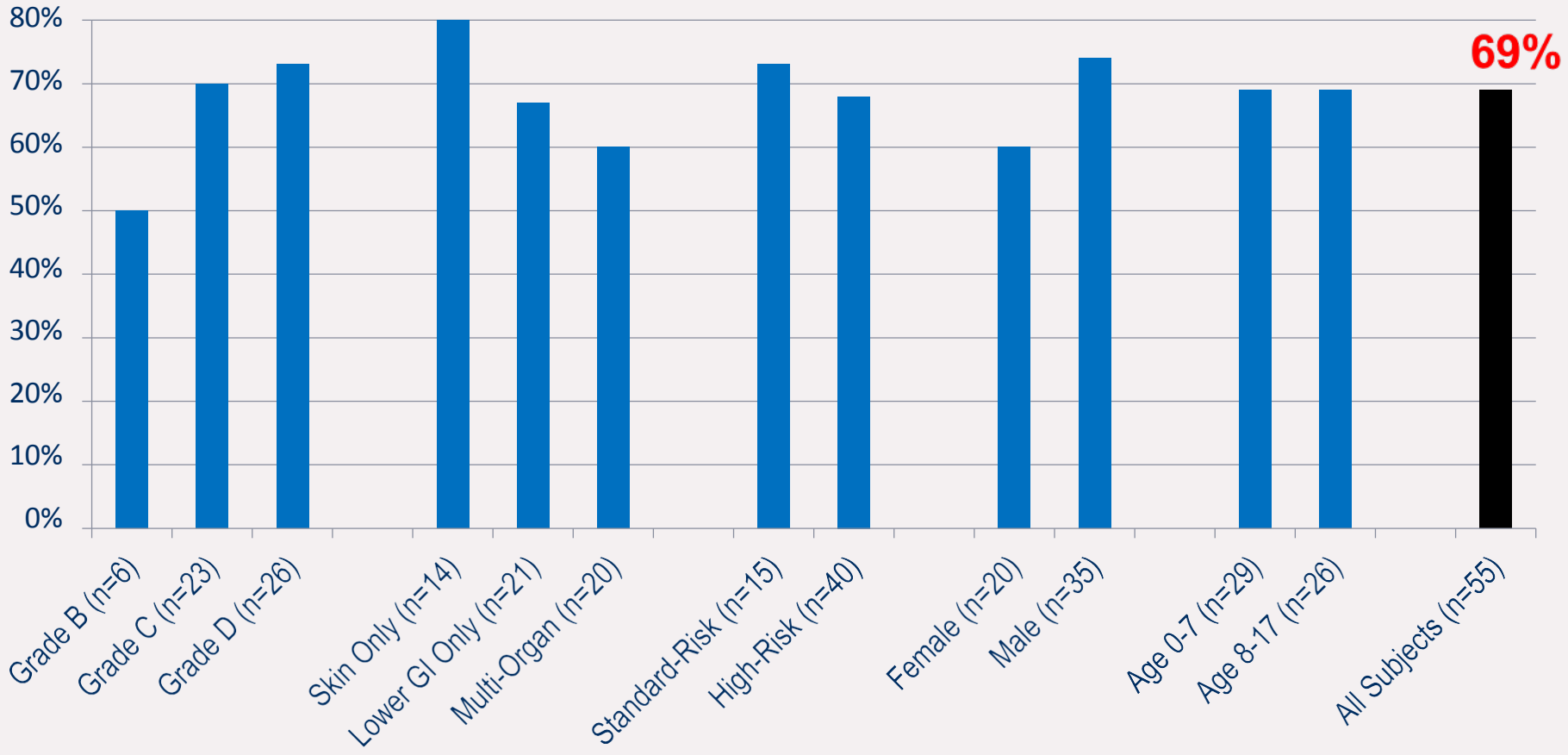


- 73% of subjects had high-risk disease at baseline
  - Stage 3 (n=6) or stage 4 (n=10) Lower GI only
  - Stage 4 Skin only (n=4)
  - Any stage Lower GI + any stage Liver (n=4)
  - Stage 2-4 Lower GI + any stage Skin (n=10)
  - All disease involving three organs (n=6)
- Standard risk disease was characterized by:
  - Stage 3 (n=10) Skin only
  - Stage 1 (n=1) or stage 2 (n=4) Lower GI only

1. Data on file.

Remestemcel-L:

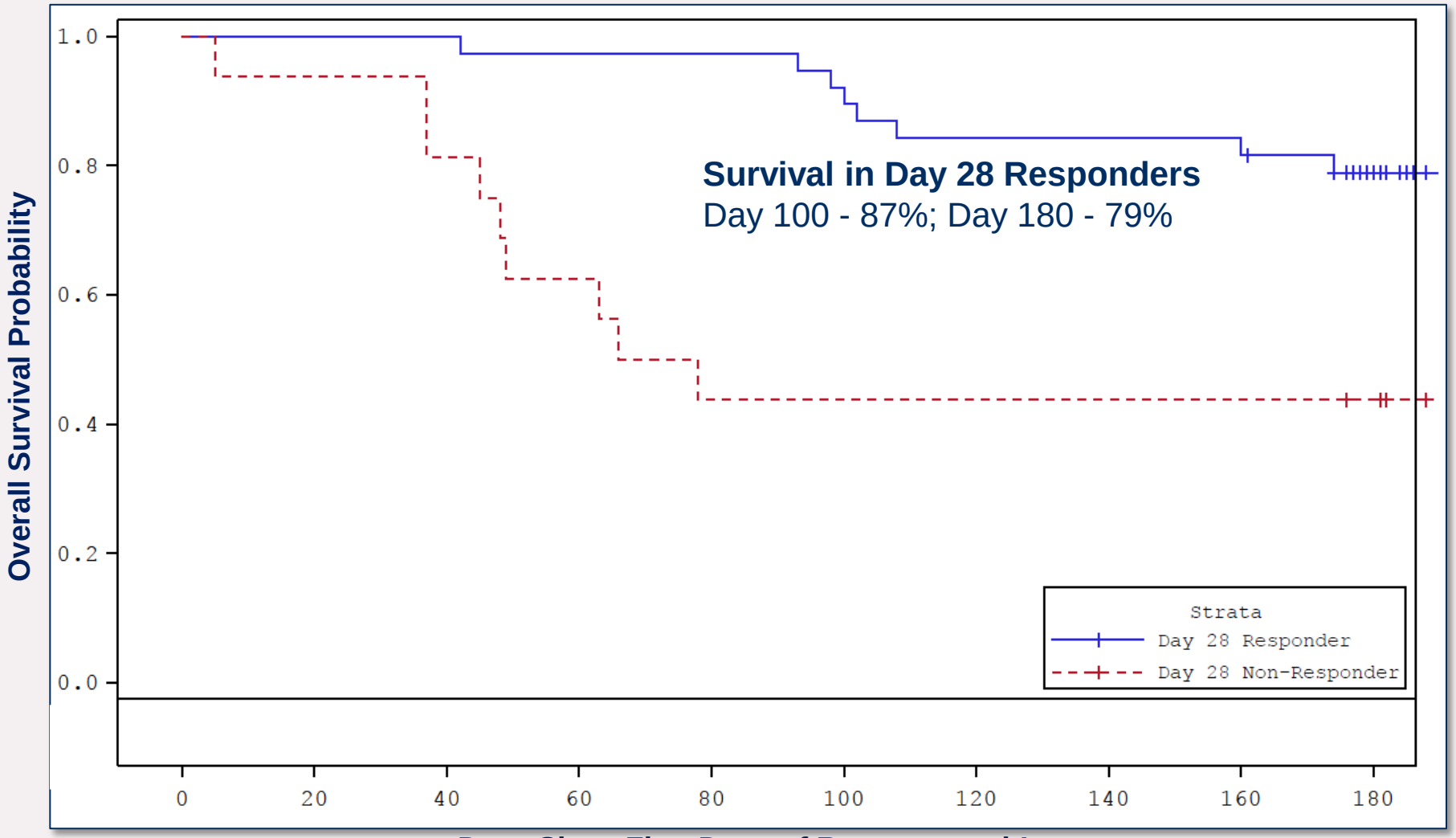
Protocol GVHD001 - Primary Efficacy Overall Response at Day 28 was 69%, p=0.0003[1]



- 69% Overall Response rate at Day 28 (29% CR + 40% PR); (95% CI: 55%, 81%)
- p-value calculated from the binomial distribution, under the assumption of a 0.45 success rate under the null hypothesis

1. Data on file.

Remestemcel-L: Protocol GVHD001/002 survival[1]



1. Data on file.

Remestemcel-L:
Phase 3 Trial (Protocol GVHD001) Successfully Completed[1]

- Phase 3 study evaluated remestemcel-L in 55 children to improve overall response rate and survival
  - 89% of children had grade C/D disease (the most severe form and historically associated with up to 90% mortality[2])
- Study successfully met the primary endpoint of improved Day 28 Overall Response (OR)
  - 69% vs 45% protocol-defined historical control rate (p=0.0003)
- Day 100 Overall Survival 75%, with 87% survival in Day 28 responders
- Day 180 Overall Survival 69%, with 79% survival in Day 28 responders
- Remestemcel-L infusions well tolerated
- Findings consistent with previous results in 241 SR-aGVHD children under expanded access program who failed to respond to multiple biologic agents[2]

1. Data on file.
2. Westin, J., Saliba, RM., Lima, M. (2011) Steroid-refractory acute GVHD: predictors and outcomes. Advances in Hematology; Axt L, Naumann A, Toennies J (2019) Retrospective single center analysis of outcome, risk factors and therapy in steroid refractory graft-versus-host disease after allogeneic hematopoietic cell transplantion. Bone Marrow Transplantation.
3. Kurtzberg J. et al. Effect of Human Mesenchymal Stem Cells (remestemcel-L) on Clinical Response and Survival Confirmed in a Large Cohort of Pediatric Patients with Severe High-Risk Steroid-Refractory Acute Graft Versus Host Disease. BBMT. 2016; 22.

Remestemcel-L:
Phase 3 Trial (Protocol GVHD001) Overall Safety Results[1]

- Remestemcel-L infusions well tolerated
  - 54 subjects were treated and received 535 infusions

- 13 subjects died during the initial 100 day follow-up period (24% mortality through Day 100):
  - None of the deaths was reported to be related to remestemcel-L by the investigators
  - The leading causes of death were: disease progression, infection, GVHD

- Four subjects terminated the study early (prior to Day 100):
  - 1 subject was not able to be dosed; 1 subject had a non-fatal AE (somnolence); 1 subject had parental consent withdrawn; and 1 subject was withdrawn by PI

- Adverse events were reported in 100% of the subjects:
  - 9 subjects(17%) experienced adverse events that were reported as related to the study drug
  - 8 subjects (15%) experienced adverse events that led to discontinuation of study drug
  - 3 subjects (6%) experienced an infusion reaction
  - Serious adverse events (SAEs) were reported in 35 subjects (65%):
    - The most commonly reported SAEs were infection in 17 subjects, (31%) and respiratory disorders in 11 subjects (20%)

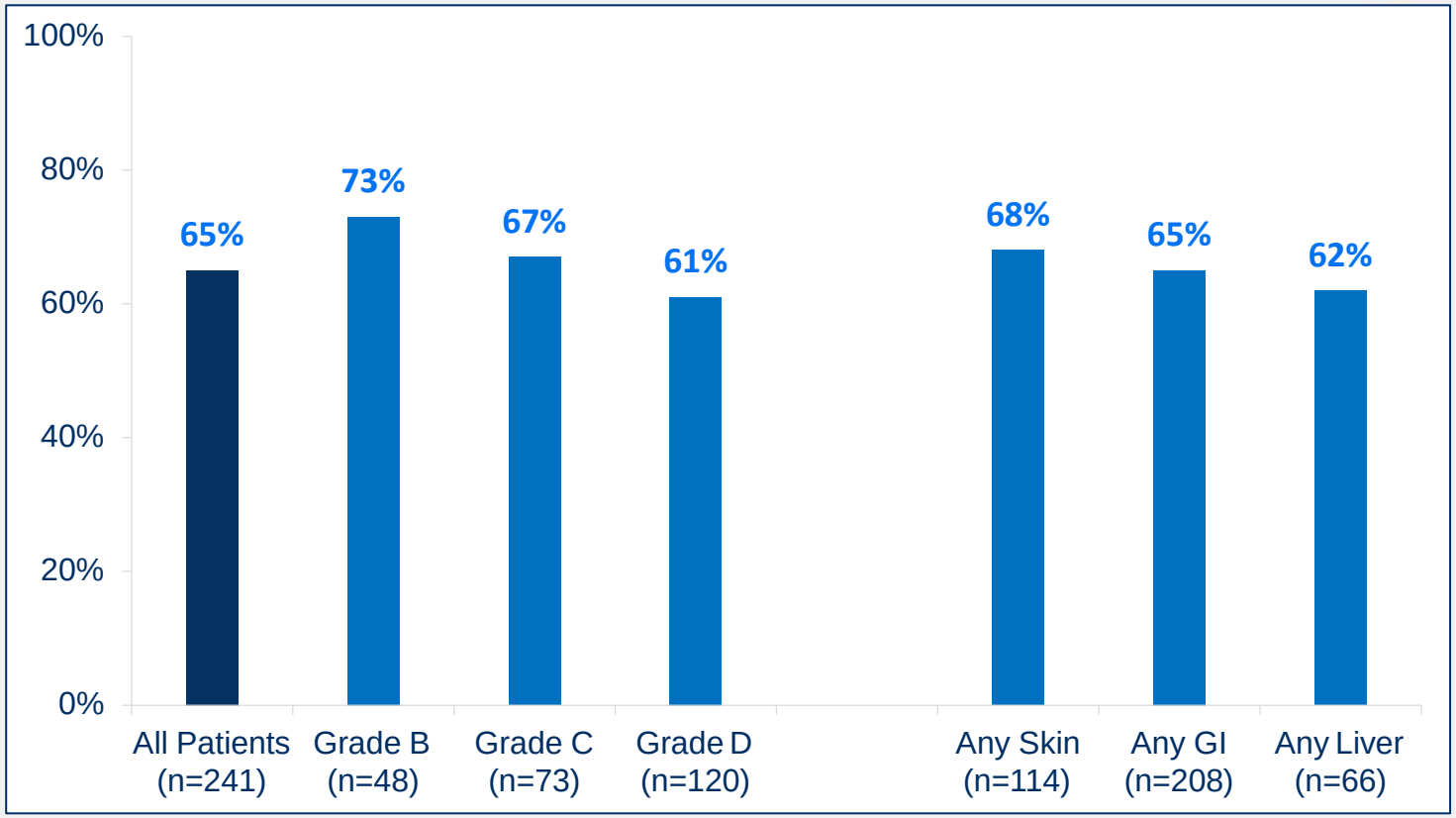
1. Data on file.

Remestemcel-L: Expanded Access Program (Protocol 275)

Overall Day 28 Response in Pediatric aGVHD Patients Receiving Remestemcel-L as First-line or Salvage Therapy After Failing Steroids[1]

Population: steroid-refractory aGVHD pediatric patients

- 241 pediatric patients undergoing HSCT were enrolled and treated at 50 sites in North America and Europe from 2007-2014
- Ages 2 months – 17 years
- Acute GVHD grades B-D (CIBMTR)
- Failed steroid treatment and multiple other agents
- aGVHD not improving after at least 3 days of methylprednisolone (at least 1 mg/kg/day or equivalent)



- Complete Response was 14%, Partial Response was 51%
- Responses were observed for all GVHD grades and did not differ by baseline organ involvement

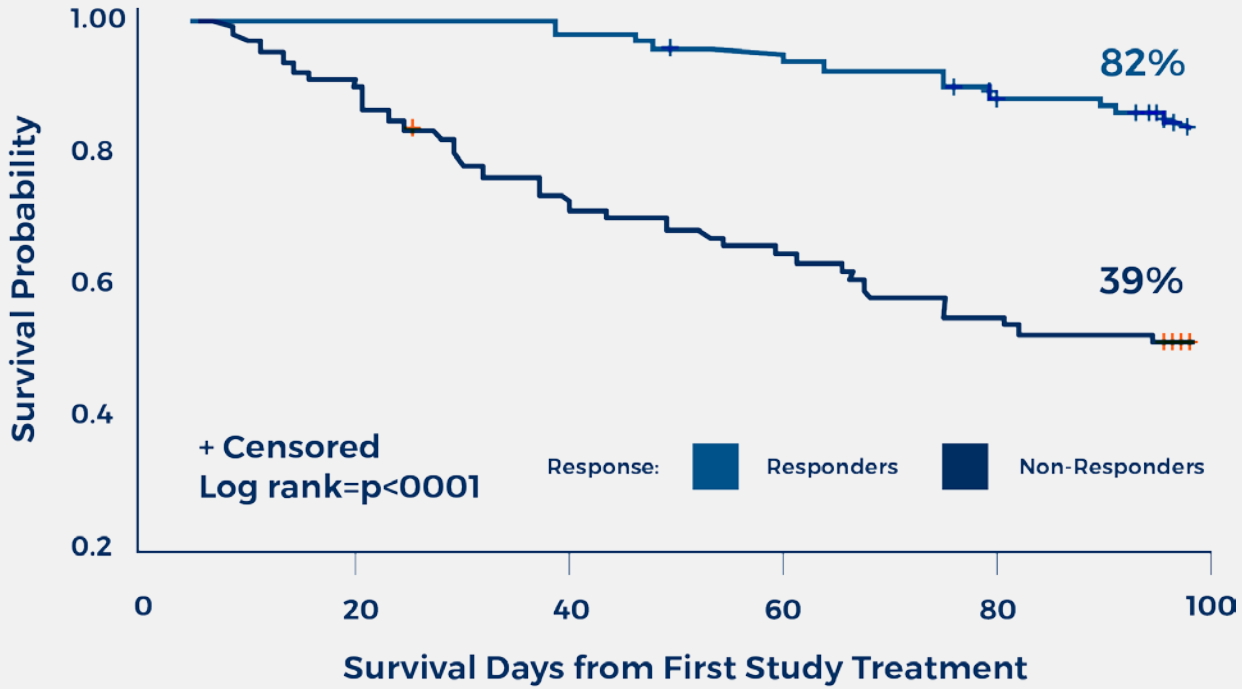
1. Kurtzberg et al: Presentation Tandem Feb 2016

Remestemcel-L: Expanded Access Program

Correlation of Day 28 Overall Response with Day 100 Survival, Using Remestemcel-L as First-line or Salvage Therapy After Failing Steroids and/or Additional Treatments[1]

Remestemcel-L in Children with SR-aGVHD who failed multiple other modalities

- Survival of Pediatric Patients Treated with Remestemcel-L 28-Day Responders vs Non-responders n=241



- In 241 Children under EAP, **Overall Response** (CR+PR) at Day 28 was **65%** (95% CI: 58.9%, 70.9%)
- **Day 100 survival** correlated with overall response, and was significantly improved in those who responded at Day 28 **(82% vs. 39%, p<0.0001)**

1. Kurtzberg et al: Presentation Tandem Feb 2016

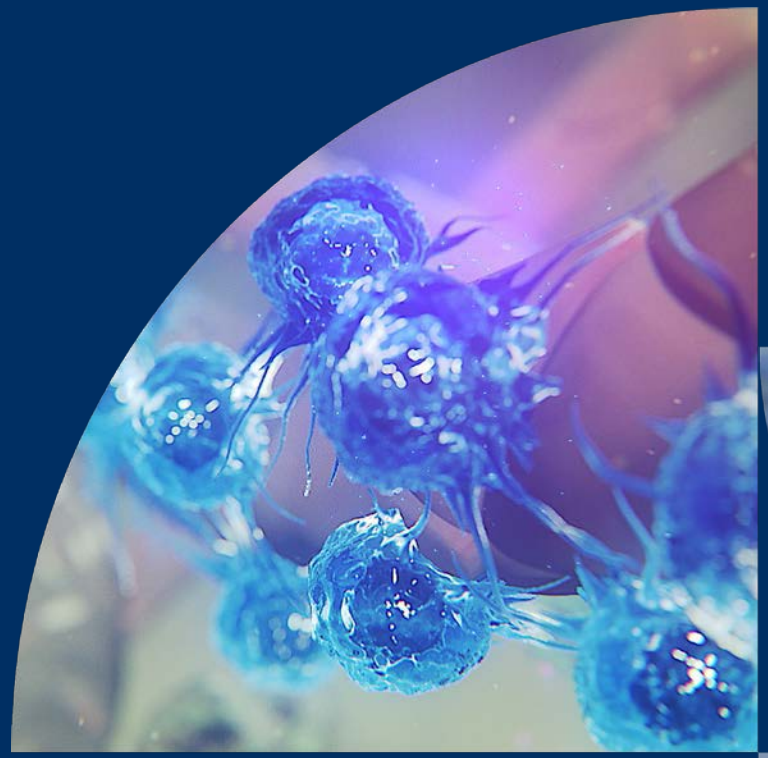
Remestemcel-L: Product Development Strategy

1. Target ***pediatric*** patients with SR-aGVHD first
   - Extensive safety and efficacy data generated and published in children with SR-aGVHD[1,2]
   - High economic burden in treatment of children with SR-aGVHD
   - Fast-track designation provides eligibility for priority review and rolling review process
   - Submit single, open-label Phase 3 trial seeking regulatory approval

2. Seek label extension for high-risk ***adult*** patients with SR-aGVHD
   - This adult subset has the highest mortality and greatest resistance to other treatment agents
   - High economic burden in treating this population subset
   - Remestemcel-L has shown efficacy signals in subgroup analyses of this population

3. Lifecycle potential in ***chronic*** GVHD (cGVHD)
   - Chronic GVHD represents a distinct GVHD patient population
   - Proof of concept data already published for MSC in cGVHD[3]

1. Allogeneic Human Mesenchymal Stem Cell Therapy (Remestemcel-L) as a Rescue Agent for Severe Refractory Acute Graft-versus-Host Disease in Pediatric Patients - Biology of Blood and Marrow Transplantation Journal, August 2013
2. Khandelwal P, Teusink-Cross A, Davies S (2017) Ruxolitinib as Salvage Therapy in Steroid-Refractory Acute Graft-versus-Host Disease in Pediatric Hematopoietic Stem Cell Transplant Patients. Biol Blood Marrow Transplant 23; 1122-1127
3. Weng JY, Du X, Geng SX, Peng YW, Wang Z, Lu ZS et al. Mesenchymal stem cell as salvage treatment for refractory chronic GVHD. Bone Marrow Transplant 45: 1732-1740 (2010).



Real World aGVHD Clinical Experience:
Dr. Susan E. Prockop (MSKCC)

Susan E. Prockop, MD

- New York-based pediatric oncology; clinical expertise in allogeneic and autologous bone marrow and peripheral blood stem cell transplantation; congenital and acquired diseases of hematopoiesis and immunity
- Associate Professor, Memorial Sloan Kettering Cancer Center
- Assistant Professor of Pediatrics, Pediatrics, Weill Cornell Medical College
- Fellow in Pediatric Hematology/Oncology (MSK Kids); Pediatric Hematology/Oncology (New York Presbyterian)
- Has been in practice for more than 20 years
- M.D., Columbia University College of Physicians and Surgeons
- B.A., Hamilton College
- Author of numerous scientific articles and publications

Acute Graft-versus-Host Disease (aGVHD) Background

- Acute graft-versus-host disease (aGVHD) is associated with significant morbidity and is a leading cause of mortality after allogeneic hematopoietic stem cell transplantation
- Although the incidence of aGVHD varies across transplant type and regimen, severe aGVHD (determined by grade C/D, visceral organ and multi-organ involvement, or high risk stratification) has the highest risk of primary treatment failure and high transplant related mortality[1]
- Day 100 mortality can reach 70% in patients who fail to respond to initial steroid therapy[2-4], and 12 month mortality approaches 90%[5]
- Mesenchymal stem cells have anti-inflammatory and immunomodulatory biological activity that supports their investigational use in aGVHD[6]

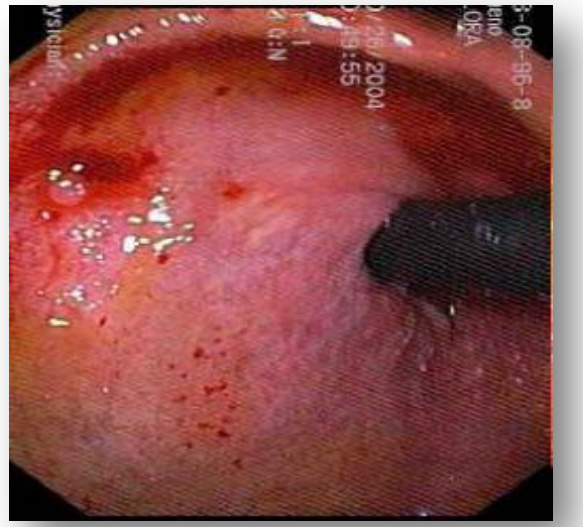
1. Jaqasia M, Arora M, Flowers ME, et al. Risk factors for acute GVHD and survival after hematopoietic cell transplantation. Blood. 2012; 119 (1): 296-307.
2. MacMillan ML, DeFor TE, Weisdorf DJ. The best endpoint for acute GVHD treatment trials. Blood. 2010; 115 (26): 5412-5417.
3. MacMillan ML, Couriel D, Weisdorf DJ, et al. A phase 2/3 multicenter randomized clinical trial of ABX-CBL versus ATG as secondary therapy for steroid-resistant acute graft-versus-host disease. Blood. 2007; 109 (6): 2657-2662.
4. Pidala J, Kim J, Field T, et al. Infliximab for managing steroid-refractory acute graft-versus-host disease. Biol Blood Marrow Transplant. 2009; 15 (9): 1116-1121.
5. Arai S et al, Poor outcome in steroid refractory graft verses host disease with anti-thymocyte globulin treatment. Biol Blood Marrow Transplant. 2002; 8: 155-160.
6. Mesenchymal Stem Cells: Mechanisms of Inflammation Mesenchymal Stem Cells: Mechanisms of Inflammation. Nora G. Singer and Arnold I. Caplan Annu Rev Pathol. 2011;6:457-78. doi: 10.1146/annurev-pathol-011110-130230.; Human mesenchymal stem cells modulate allogeneic immune cell responses. Sudeepta Aggarwal and Mark F. Pittenger Blood. 2005 Feb 15;105(4):1815-22. Epub 2004 Oct 19.

Acute Graft-versus-Host Disease:

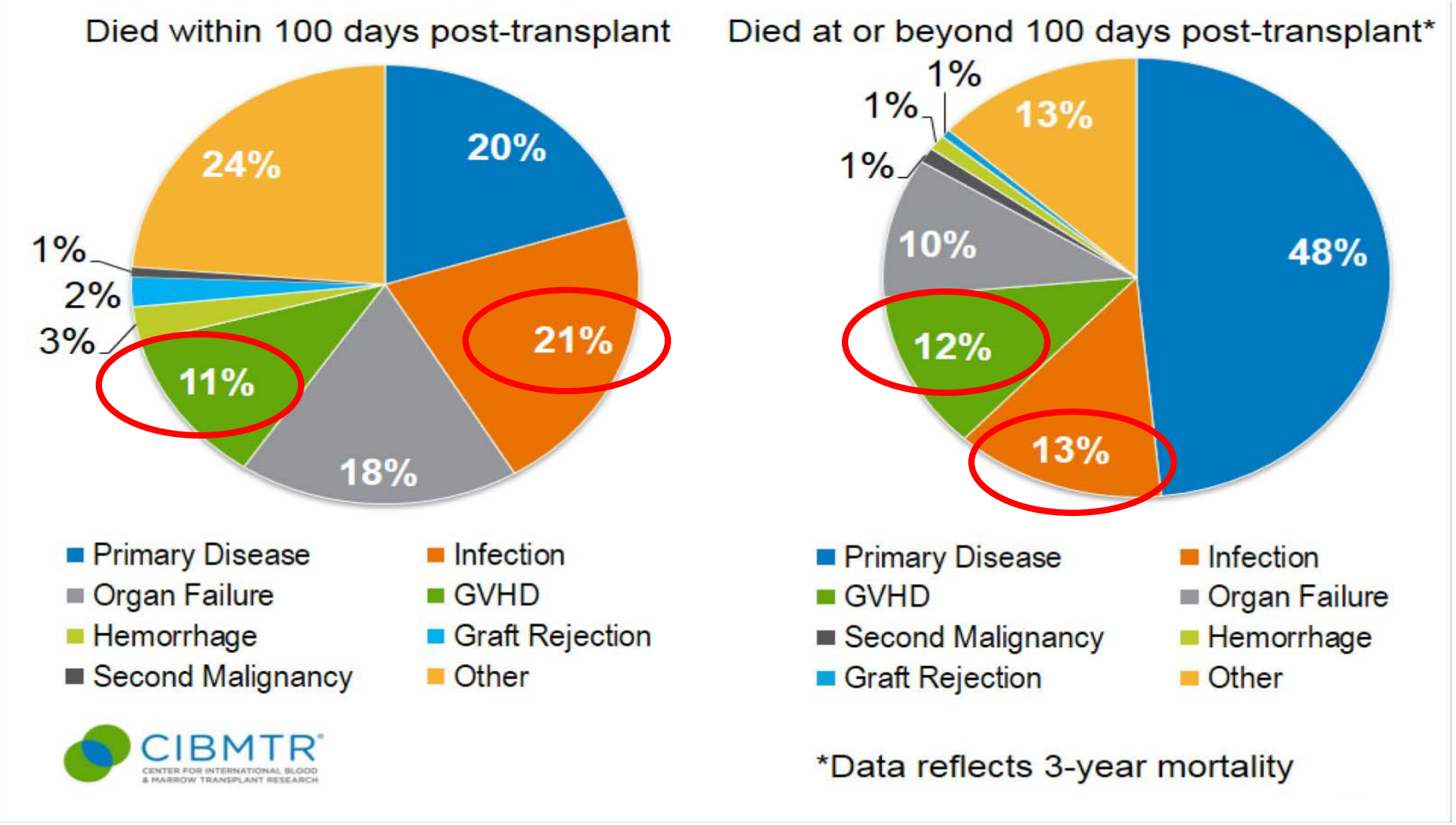
Limitations to Currently Used Treatments in Clinical Practice

- **First line therapy typically high dose steroids (2mg/kg/day)**
- **There is only one approved treatment for steroid-refractory acute GVHD in the U.S.**
  - Approved only for patients aged 12 and above
  - No consensus around second-line agents
  - Prior RCTs w/ significant risks and limited benefit
  - Increased immunosuppression balanced by increased infections
- **Need for new treatment modalities**
  - Poor prognosis for severe refractory GVHD
  - Spontaneous remission does not occur
  - High burden of morbidity in addition to mortality

GI GVHD

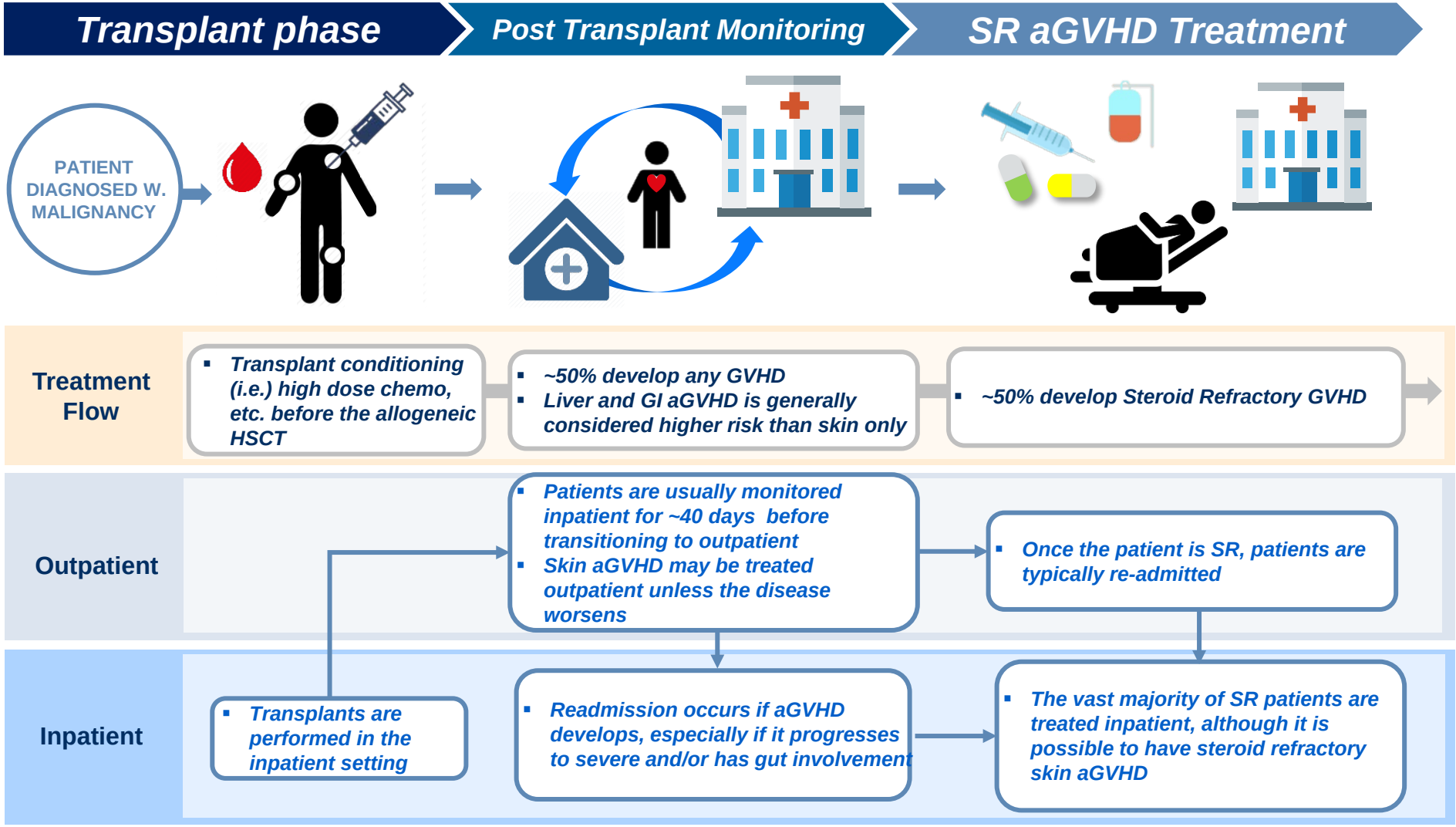


Causes of Death after Unrelated Donor HCT Done in 2015-2016



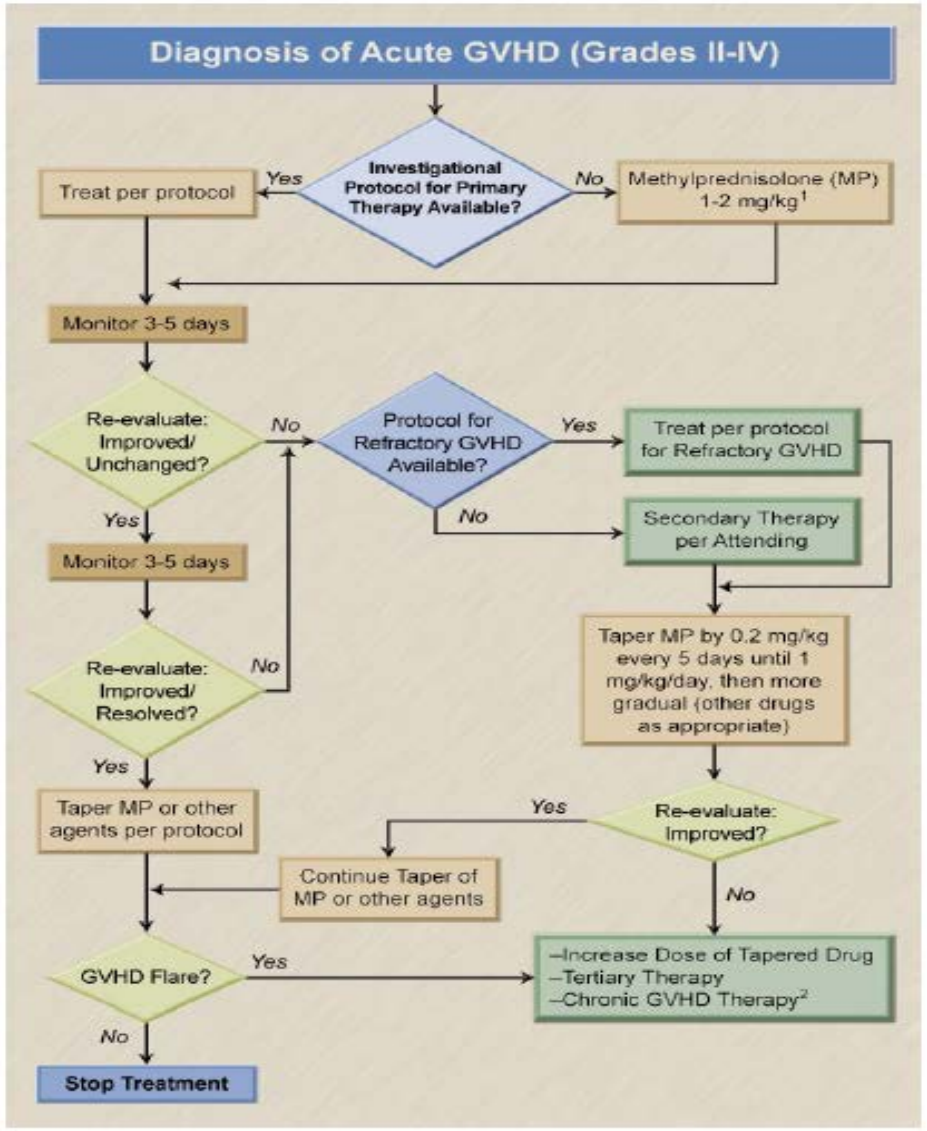
Source: CIBMTR 2018.

Acute Graft-versus-Host Disease Patient Journey[1]

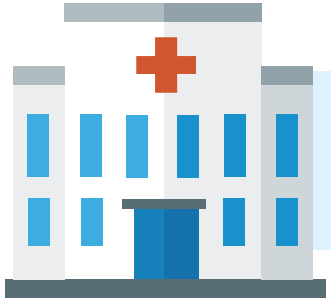


1. Qualitative Mesoblast market research conducted in 2018.

Acute Graft-versus-Host Disease: Diagnosis, Management and Treatment[1,2]



Management of aGVHD



- Most hospitals have protocols and/or formulary restrictions but these are seen as soft guidelines rather than strict controls
- Payers require PAs to be submitted in some cases for access / additional reimbursement associated with high cost treatments like ECP and some biologics

Most Common 1L Treatment

Immunosuppression followed by **infliximab (Remicade) /** and other anti TNFs

Other 1L & 2L+ Therapies

Jakafi, Orencia, Campath, and clinical trial enrollment

Enrollment in clinical trials is a viable option in all lines of therapy

Important Considerations

- Immune-suppressants increase risk of infection, a major mortality concern
- Gut involvement is a concern, eliminating most oral options

1. Qualitative Mesoblast market research conducted in 2018.
2. http://www.bloodjournal.org/content/bloodjournal/109/10/4119.full.pdf

Kinase Inhibitor Therapy for Acute GVHD:

JAK Inhibitors

The Janus kinase (JAK) family is composed of four tyrosine kinases

Activation of JAK -> phosphorylation of STAT family proteins, act as TFs for pro-inflammatory genes.

Inhibition of JAK1/2 significantly reduces T-cell function & impairs APCs (DCs)

Ruxolitinib (JAK1/JAK2)

FDA Approval (Adults and Children ≥ 12 years of age) based on results from REACH 1 (Jagasia et al BBMT 2019)

Treated 71 patients; Median age was 58 years,

Day 28, ORR 54.9% (CR, 26.8%) Best ORR 73.2%

Side Effects

REACH 1

Infections (55%) edema (51%) cytopenias (65%)

CMV (12.7%) Sepsis (12.7%) fBacteremia (9.9%)

Pulmonary Hemorrhage (N=1) Fatal Sepsis (N=1)

MSK Practice

Cautious use in patients with Stage III/IV GI GvHD

Consideration for other trials

Evaluation for pneumatosis

Kinase Inhibitor Therapy for Acute GVHD:

JAK Inhibitors in Pediatrics

Pediatrics

Retrospective cohort Cincinnati Childrens – (Khandelwal et al, BBMT 2017)

13 patients – 11 w/ response assessment w/ ORR 45% (1 CR and 4 PR)

All PRs required additional IS

Side Effects

"High rate of reversible SAEs"

Elevated ALT (N=5)

Grade 3 (N=2) and 4 (N=3)Neutropenia – all patients required G-CSF support

Grade 3 Thrombocytopenia (N=3) – all patients required platelet transfusion

InfectionsViral EBV (N=2) adenovirus (N=2) BK (N=3)

Bacterial (6) Fungal (1)

Off Label Use in Pediatric Patients at MSK

3 patients treated – 1 PR

Grade 3 and 4 cytopenias (N=3), Infection (N=3): EBV (N=1) adeno (N=2) CMV (N=2) nocardia (N=1)

Pneumatosis

Ongoing trial for pediatric patients

Real World Clinical Experience:

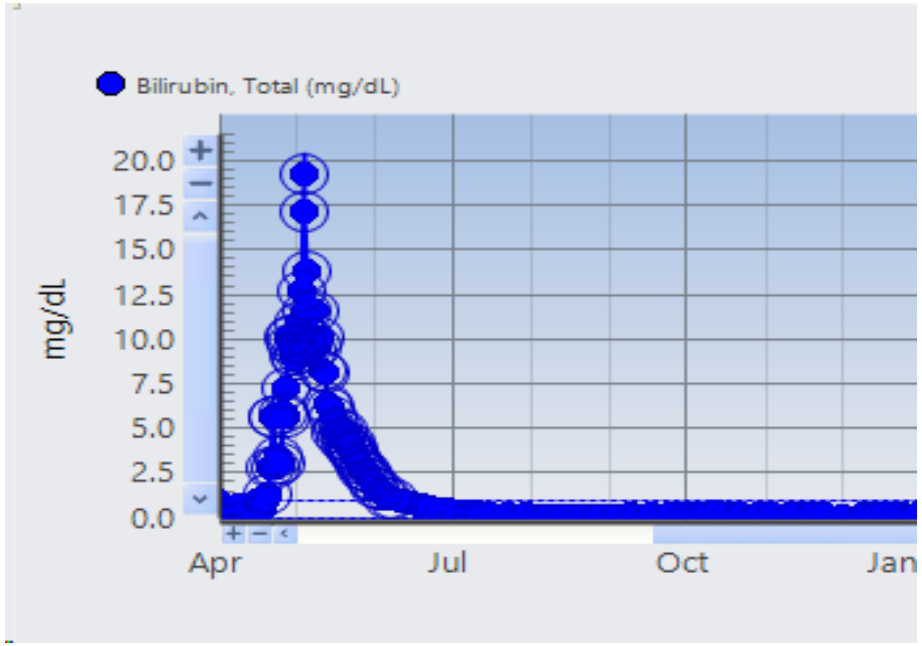
Clinical Experience using Remestemcel-L

Real World Clinical Experience:
Clinical Experience using Remestemcel-L

27 month old male transplanted for MDS w/ monosomy 7
double UCBT Clo/Mel/Thio GvHD prophylaxis with MMF and tacrolimus

GvHD diagnosed Day +21 post-transplant
Progression with 2mg/kg/day steroids – Overall Grade IV
Stage IV GI GvHD
Stage IV Hepatic GvHD
Upper GI GvHD
No nutritional support and requiring opiate infusion

Received MSCs 2 x 10e6/kg 2x/week x 8 doses
Day 12 w/ Stage II Hepatic GvHD -> TPN
Day 28 w/ Stage II GI GvHD, resolution of Hepatic GvHD
Received extension therapy
Complete response by Day 64



Real World Clinical Experience:
Clinical Experience using Remestemcel-L

17 year old patient transplanted at an outside center for CML
- Haploidentical TCD transplant from sister w/Mel/Thio/Flu
- Haploidentical TCD transplant from father w/ Flu/Cy/TLI
  - EBV PTLD -> multiple doses of DLI -> GvHD

Acute GvHD Diagnosed Day + 128 (Day + 30 after DLI) - Overall Grade IV GvHD
- Stage IV Skin
- Stage IV GI GvHD

Treatment w/ 2mg/kg/day methylprednisolone, Beclomethasone/Budesonide
- Infliximab, Sirolimus/Tacrolimus

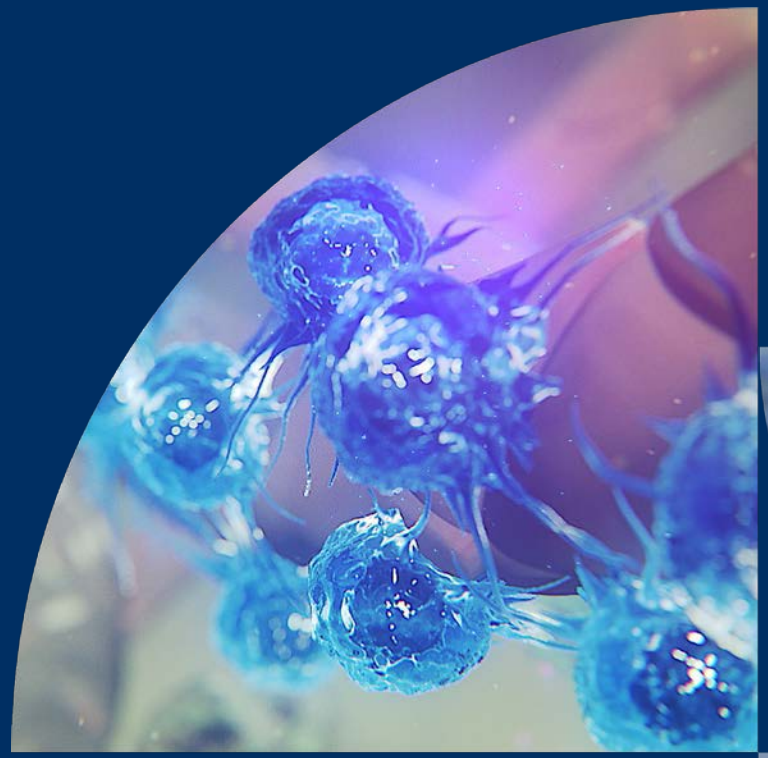
Biopsy with ongoing severe acute GvHD 11 months after diagnosis on ongoing therapy

On steroids w/ AVN, hyperglycemia, adenovirus, recurrent bacteremia and renal insufficiency from cidofovir
- Stage II GI GvHD
- Stage II Hepatic GvHD

Received MSCs 2 x 10e6/kg 2x/week x 8 doses
- Day 28 w/ Stage I GI GvHD, resolution of Hepatic GvHD
- Received extension therapy w/ complete response by Day 42.

Real World Clinical Experience:
Clinical Experience using Remestemcel-L

- Effective early and late in patients with severe acute GvHD
- Rapid response – especially of hepatic GvHD
- Impressive safety profile
- Treatment with Remestemcel-L in patients with history of
  CMV/adenovirus/EBV PTLD
  w/o flares of those infections



Maximizing Remestemcel-L:
Eric Strati (SVP, Commercial)

Remestemcel-L:

Steroid Refractory Acute GVHD Represents a Compelling Commercial Opportunity

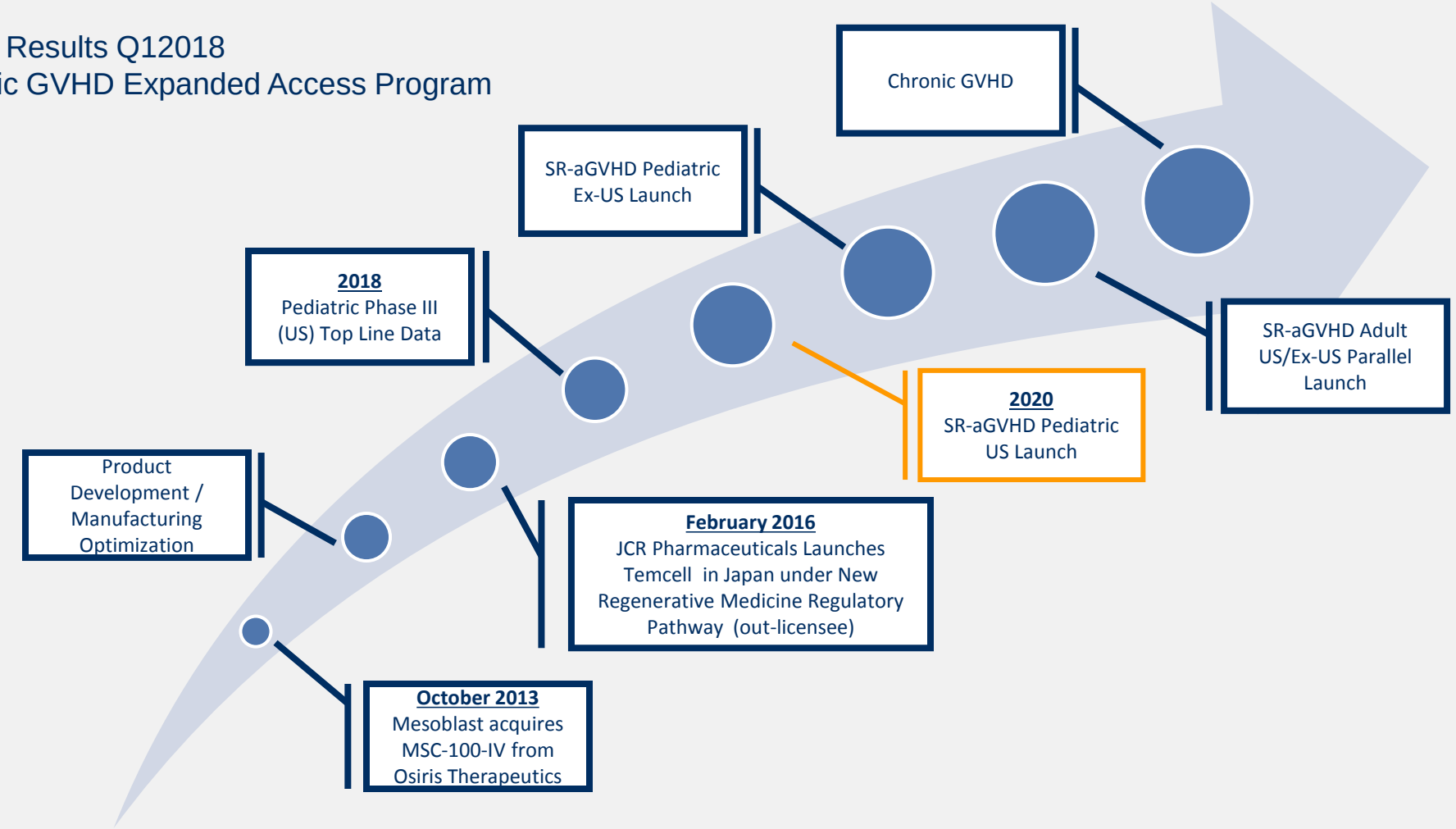
Market Opportunity	• Overview of GVHD Lifecycle Management Strategy • Target Populations for SR-aGVHD North America / Europe
Maximizing Patient Access & Providing Product Education	• Developing a Price for Remestemcel-L Reflective of Value • Product / Disease State Education Strategy
US Commercial Model for 2020 Launch	• Field Structure Overview • Commercial Priorities Pre-Launch / Launch

Remestemcel-L:

Comprehensive Global GVHD Program Underway

- **Mesoblast has over 10 years experience in hematology-oncology space**

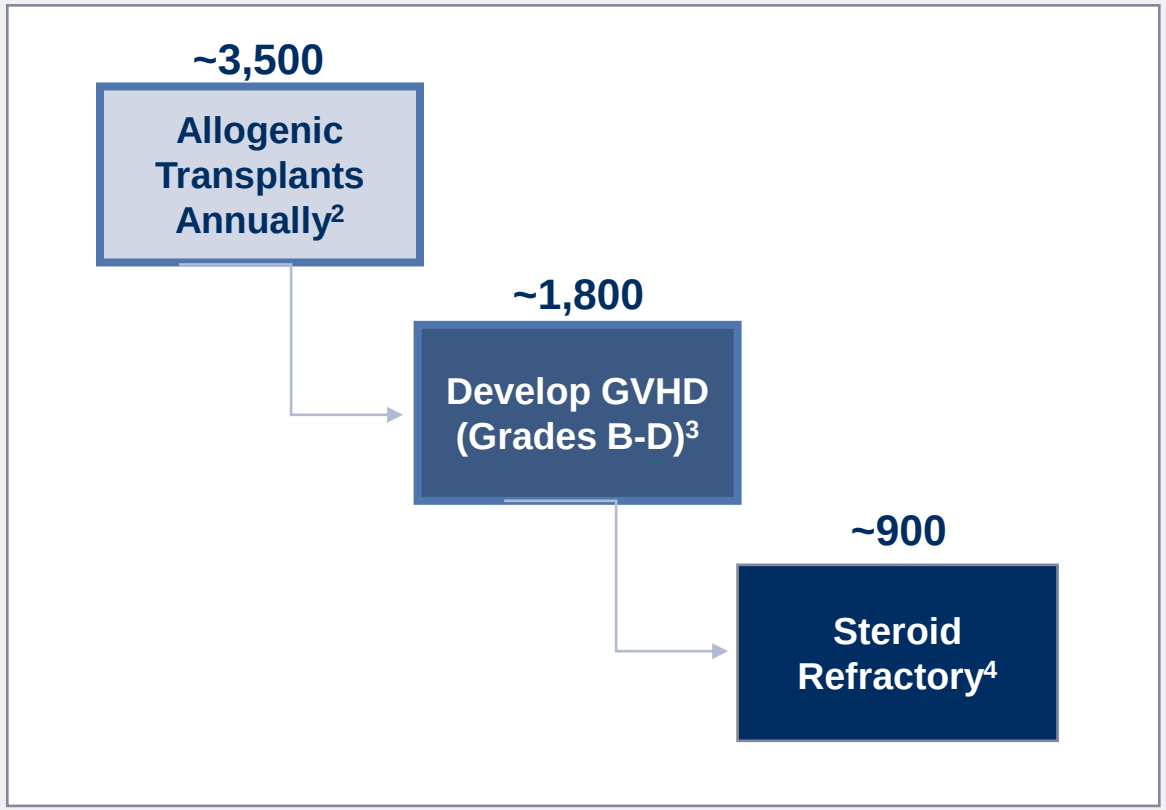
- **Remestemcel-L:**
  - Positive Phase III Results Q12018
  - Large US Pediatric GVHD Expanded Access Program (>240 patients)



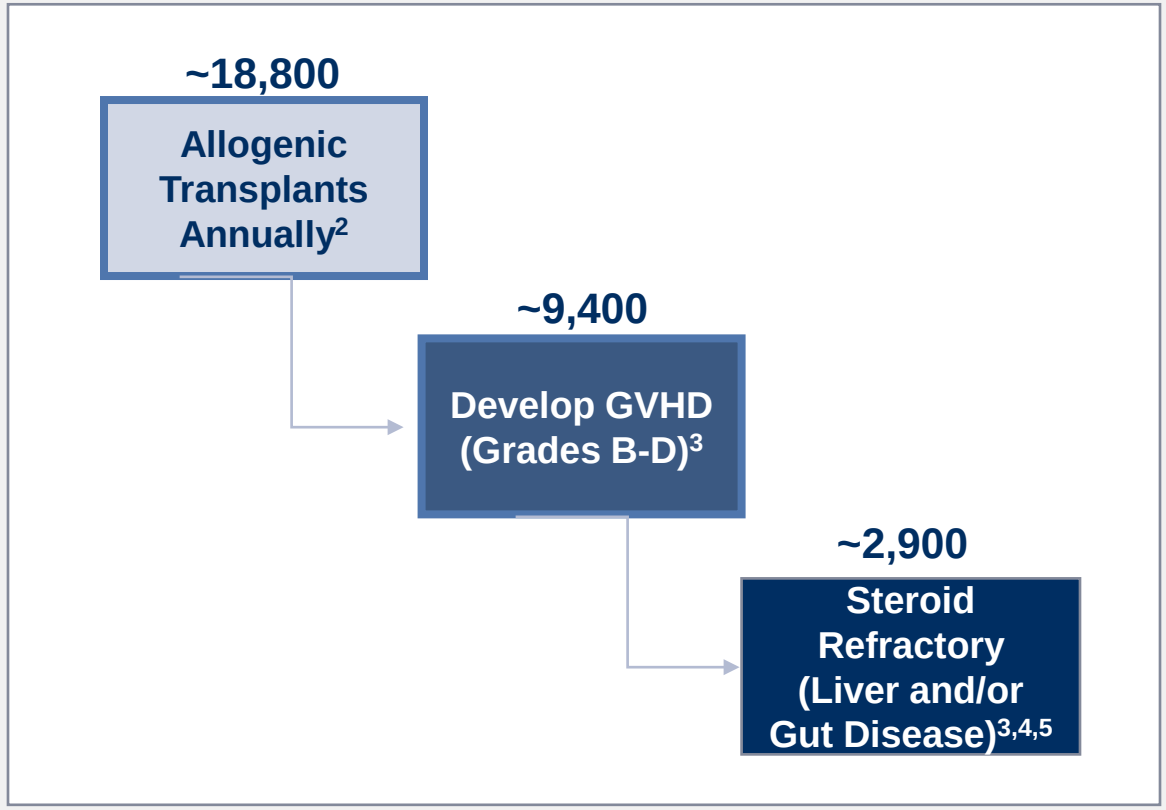
Remestemcel-L:

Target Steroid Refractory GVHD Population (North America/EU; excl. Japan) Estimated at ~3,800 Patients Annually[1]

Estimated Pediatric Target Population (2019)



Estimated Adult Target Population (2019)

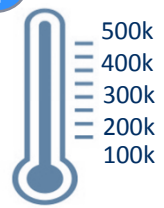


1. Figures are rounded up to the nearest values.
2. U.S. - D'Souza A, Fretham C. Current Uses and Outcomes of Hematopoietic Cell Transplantation (HCT): CIBMTR Summary Slides, 2018; Canada - Based on general population size and US transplant activity per 10m from D'Souza A, Fretham C. Current Uses and Outcomes of Hematopoietic Cell Transplantation (HCT): CIBMTR Summary Slides, 2018; EU - Passweg JR, Baldomero H, Peters C (2014) Hematopoietic SCT in Europe: Data and Trends in 2012 with Special Consideration of Pediatric Transplantation.
3. Jagasia, M., Arora, M., Flowers, M. (2012) Risk Factors for acute GVHD and Survival after Hematopoietic Cell Transplantation. Blood, 5 January (119):296-307,
4. West, J., Saliba, RM., Alousi, A. (2011) Steroid Refractory Acute GVHD: Predictors and Outcomes. Advances in Hematology (2011); 1-8.
5. Figures presented exclude adult patients with skin only GVHD disease.

Remestemcel-L:

Multi-Pronged Approach to Developing Launch Price & Optimizing Patient Access

1. **Value Proposition:** Cost-offsets
2. **Market Research:** Stakeholder Perception
3. **US Payer Landscape:** Payer Mix, Healthcare Policy, etc.
4. **Market Pricing**

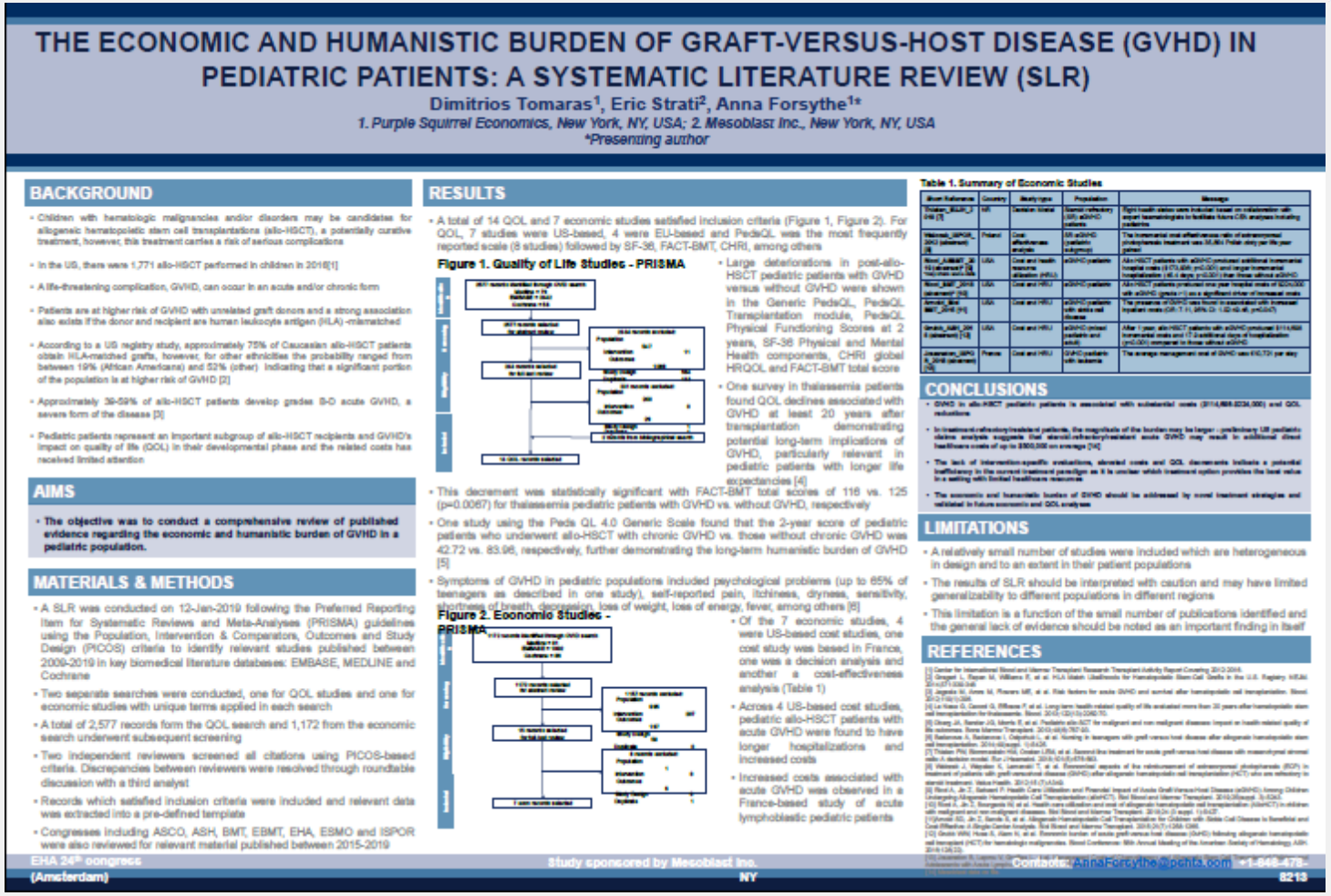


Remestemcel-L:

SR-aGVHD is Associated with Significant Burden of Illness in the Adult Population[1]

Conclusions:

- GVHD in allo-HSCT pediatric patients is associated with substantial costs ($114,698-$224,000) and QOL reductions
- In treatment-refractory/resistant patients, the magnitude of the burden may be larger - *preliminary US pediatric claims analysis suggests that steroid-refractory/resistant acute GVHD may result in additional direct healthcare costs of up to $500,000 on average*
- The lack of intervention-specific evaluations, elevated costs and QOL decrements indicate a potential inefficiency in the current treatment paradigm as it is unclear which treatment option provides the best value in a setting with limited healthcare resources
- The economic and humanistic burden of GVHD should be addressed by novel treatment strategies and validated in future economic and QOL analyses



THE ECONOMIC AND HUMANISTIC BURDEN OF GRAFT-VERSUS-HOST DISEASE (GVHD) IN PEDIATRIC PATIENTS: A SYSTEMATIC LITERATURE REVIEW (SLR)

Dimitrios Tomaras[1], Eric Strati[2], Anna Forsythe[1]*

1. Purple Squirrel Economics, New York, NY, USA; 2. Mesoblast Inc., New York, NY, USA

*Presenting author

BACKGROUND

- Children with hematologic malignancies and/or disorders may be candidates for allogeneic hematopoietic stem cell transplantations (allo-HSCT), a potentially curative treatment; however, this treatment carries a risk of serious complications
- In the US, there were 1,771 allo-HSCT performed in children in 2016[1]
- A life-threatening complication, GVHD, can occur in an acute and/or chronic form
- Patients are at higher risk of GVHD with unrelated graft donors and a strong association also exists if the donor and recipient are human leukocyte antigen (HLA) -mismatched
- According to a US registry study, approximately 75% of Caucasian allo-HSCT patients obtain HLA-matched grafts, however, for other ethnicities the probability ranged from between 19% (African Americans) and 52% (other). Indicating that a significant portion of the population is at higher risk of GVHD [2]
- Approximately 30-50% of allo-HSCT patients develop grades II-D acute GVHD, a severe form of the disease [3]
- Pediatric patients represent an important subgroup of allo-HSCT recipients and GVHD's impact on quality of life (QOL) in their developmental phase and the related costs has received limited attention

AIMS

- **The objective was to conduct a comprehensive review of published evidence regarding the economic and humanistic burden of GVHD in a pediatric population.**

MATERIALS & METHODS

- A SLR was conducted on 12-Jan-2019 following the Preferred Reporting Item for Systematic Reviews and Meta-Analyses (PRISMA) guidelines using the Population, Intervention & Comparators, Outcomes and Study Design (PICOS) criteria to identify relevant studies published between 2009-2019 in key biomedical literature databases: EMBASE, MEDLINE and Cochrane
- Two separate searches were conducted, one for QOL studies and one for economic studies with unique terms applied in each search
- A total of 2,577 records form the QOL search and 1,172 from the economic search underwent subsequent screening
- Two independent reviewers screened all citations using PICOS-based criteria. Discrepancies between reviewers were resolved through roundtable discussion with a third analyst
- Records which satisfied inclusion criteria were included and relevant data was extracted into a pre-defined template
- Congresses including ASCO, ASH, BMT, EBMT, EHA, ESMO and ISPOR were also reviewed for relevant material published between 2015-2019

RESULTS

- A total of 14 QOL and 7 economic studies satisfied inclusion criteria (Figure 1, Figure 2). For QOL, 7 studies were US-based, 4 were EU-based and PedsQL was the most frequently reported scale (8 studies) followed by SF-36, FACT-BMT, CHRI, among others

Figure 1. Quality of Life Studies - PRISMA

- Large deteriorations in post-allo-HSCT pediatric patients with GVHD versus without GVHD were shown in the Generic PedsQL, PedsQL Transplantation module, PedsQL Physical Functioning Scores at 2 years, SF-36 Physical and Mental Health components, CHRI global HRQOL and FACT-BMT total score
- One survey in thalassemia patients found QOL declines associated with GVHD at least 20 years after transplantation demonstrating potential long-term implications of GVHD, particularly relevant in pediatric patients with longer life expectancies [4]
- This decrement was statistically significant with FACT-BMT total scores of 116 vs. 125 (p=0.0067) for thalassemia pediatric patients with GVHD vs. without GVHD, respectively
- One study using the Peds QL 4.0 Generic Scale found that the 2-year score of pediatric patients who underwent allo-HSCT with chronic GVHD vs. those without chronic GVHD was 42.72 vs. 83.96, respectively, further demonstrating the long-term humanistic burden of GVHD [5]
- Symptoms of GVHD in pediatric populations included psychological problems (up to 65% of teenagers as described in one study), self-reported pain, itchiness, dryness, sensitivity, shortness of breath, depression, loss of weight, loss of energy, fever, among others [6]

Figure 2. Economic Studies - PRISMA

- Of the 7 economic studies, 4 were US-based cost studies, one cost study was based in France, one was a decision analysis and another a cost-effectiveness analysis (Table 1)
- Across 4 US-based cost studies, pediatric allo-HSCT patients with acute GVHD were found to have longer hospitalizations and increased costs
- Increased costs associated with acute GVHD was observed in a France-based study of acute lymphoblastic pediatric patients

Table 1. Summary of Economic Studies

CONCLUSIONS

- GVHD in allo-HSCT pediatric patients is associated with substantial costs ($114,698-$224,000) and QOL reductions
- In treatment-refractory/resistant patients, the magnitude of the burden may be larger - preliminary US pediatric claims analysis suggests that steroid-refractory/resistant acute GVHD may result in additional direct healthcare costs of up to $500,000 on average [7,8]
- The lack of intervention-specific evaluations, elevated costs and QOL decrements indicate a potential inefficiency in the current treatment paradigm as it is unclear which treatment option provides the best value in a setting with limited healthcare resources
- The economic and humanistic burden of GVHD should be addressed by novel treatment strategies and validated in future economic and QOL analyses

LIMITATIONS

- A relatively small number of studies were included which are heterogeneous in design and to an extent in their patient populations
- The results of SLR should be interpreted with caution and may have limited generalizability to different populations in different regions
- This limitation is a function of the small number of publications identified and the general lack of evidence should be noted as an important finding in itself

REFERENCES

EHA 24th congress (Amsterdam)

Study sponsored by Mesoblast Inc. NY

Contact: AnnaForsythe@pchts.com +1-646-479-8213

1. The Economic And Humanistic Burden Of Graft-Versus-Host Disease (Gvhd) In Pediatric Patients: A Systematic Literature Review (Slr) - 24th European Hematology Association Congress.

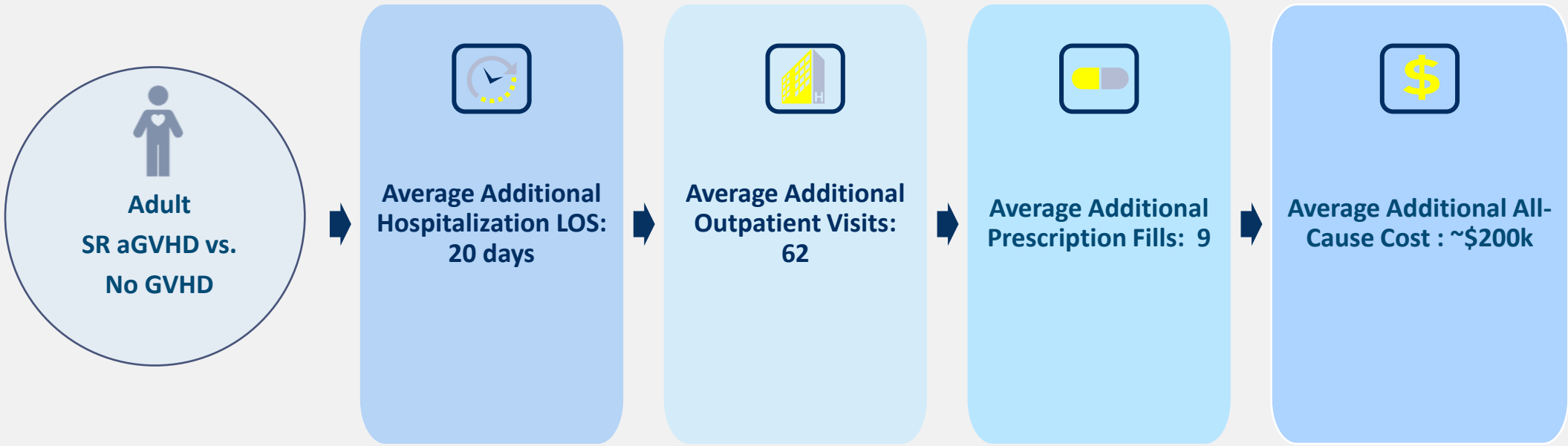
Remestemcel-L:

SR-aGVHD is Associated with Significant Burden of Illness in the Pediatric Population (US)[1]

1. Data on File: HealthCore® Claims Analysis

Remestemcel-L:

SR-aGVHD is Associated with Significant Burden of Illness in the Adult Population (US)[1]



1. Data on File: HealthCore® Claims Analysis

Remestemcel-L:

Results from Providers/Payers Qualitative US Market Research[1]

(n=20)

Median Response

Reaction to Tested Target Profile[2]

0 — 6 — 7

Most Significant Value Drivers for Remestemcel-L

- Day 100 Survival rate
- Day 28 overall response rate
- No increase in infections
- Large clinical data set (n ~300)
- Ability to administer the drug outpatient

Max Rating Product Attributes

"Remestemcel-L is Expected to Become Standard of Care"

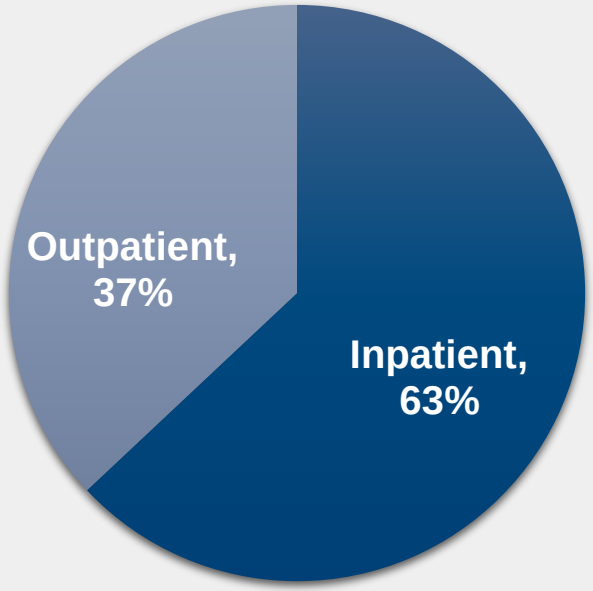
- Multiple Respondents[1]

1. ZS Associates June 2018 Qualitative Market Research: MCO Medical Directors n=5, Transplant Center Directors n= 5, Hospital Pharmacy Directors n=5, AMC-based Hem/Oncs / KOLs n=3.
2. Data on file.

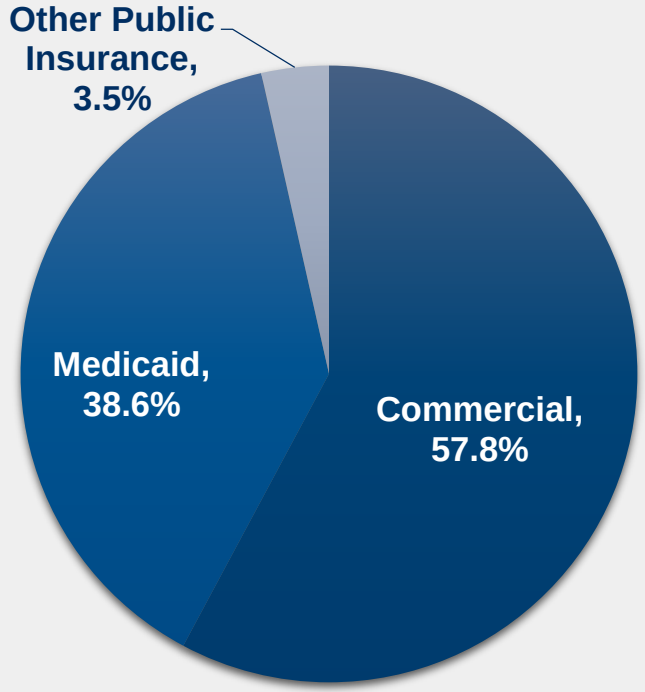
Remestemcel-L:

Overview of US Reimbursement Landscape

Projected Inpatient vs Outpatient Infusions by Patient Volume[1]



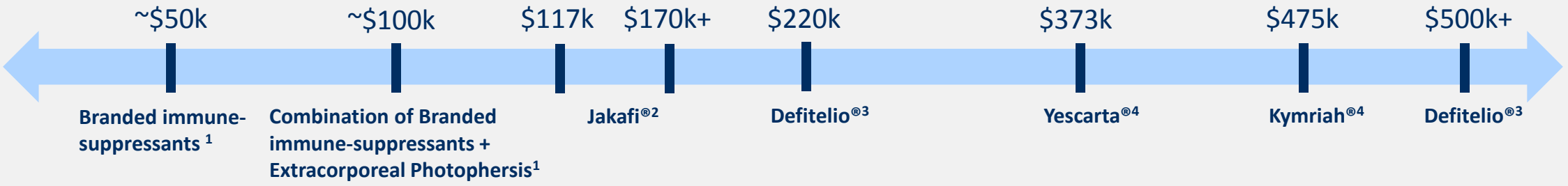
Preliminary Estimated Payer Mix[2,3]



1. Manufacture Data of File
2. HCUPnet Healthcare Cost and Utilization Project
3. Kaiser Family Foundation Health Insurance Coverage of Children 0-18

Remestemcel-L:

Overview of US Product Acquisition Pricing of Relevant Agents in the Refractory Hematology / Oncology Setting[1,2]

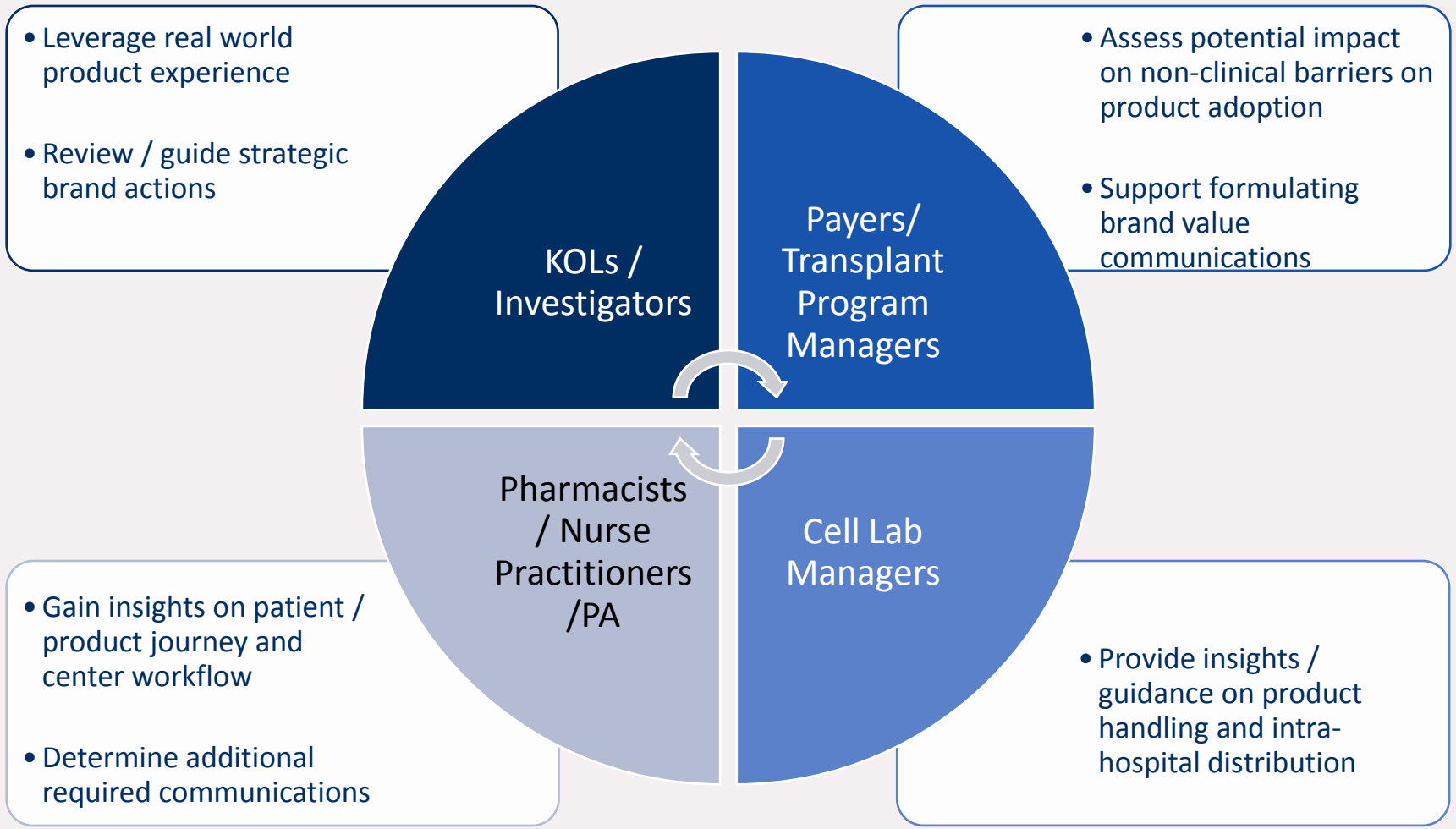


Treatment	Jakafi (ruxolitinib)	Defitelio (defibrotide sodium)	Yescarta (axicabtagene cilloleucel)	Kymriah (tisagenlecleucel)
Relevant Indication(s)	▪ Steroid-refractory acute graft-versus-host disease in adult and pediatric patients 12 years and older	▪ Treatment of adult and pediatric patients with hepatic veno-occlusive disease (VOD), with renal or pulmonary dysfunction following hematopoietic stem-cell transplantation (HSCT)	▪ Treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma(DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma	▪ Patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse ▪ Adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma and DLBCL arising from follicular lymphoma

1. Manufacture Data on File.
2. Redbook June 2019 (wholesale acquisition cost) – Dosing derived from Jakafi package insert with minimum SR acute GVHD treatment of 6 months followed by two 8 week tapering periods (9, 60 count package) and estimated costs for 1 year of treatment (13, 60 count package). Cost could exceed estimates if longer duration of therapy is required.
3. Redbook June 2019 (wholesale acquisition cost) –Dosing derived from Defitelio package insert with minimum treatment days of 21 and maximum 60 treatment days as defined in label, 75Kg average weight data from CDC.
4. https://www.reuters.com/article/us-gilead-sciences-fda/fda-approves-gilead-cancer-gene-therapy-price-set-at-373000-idUSKBN1CN35H.

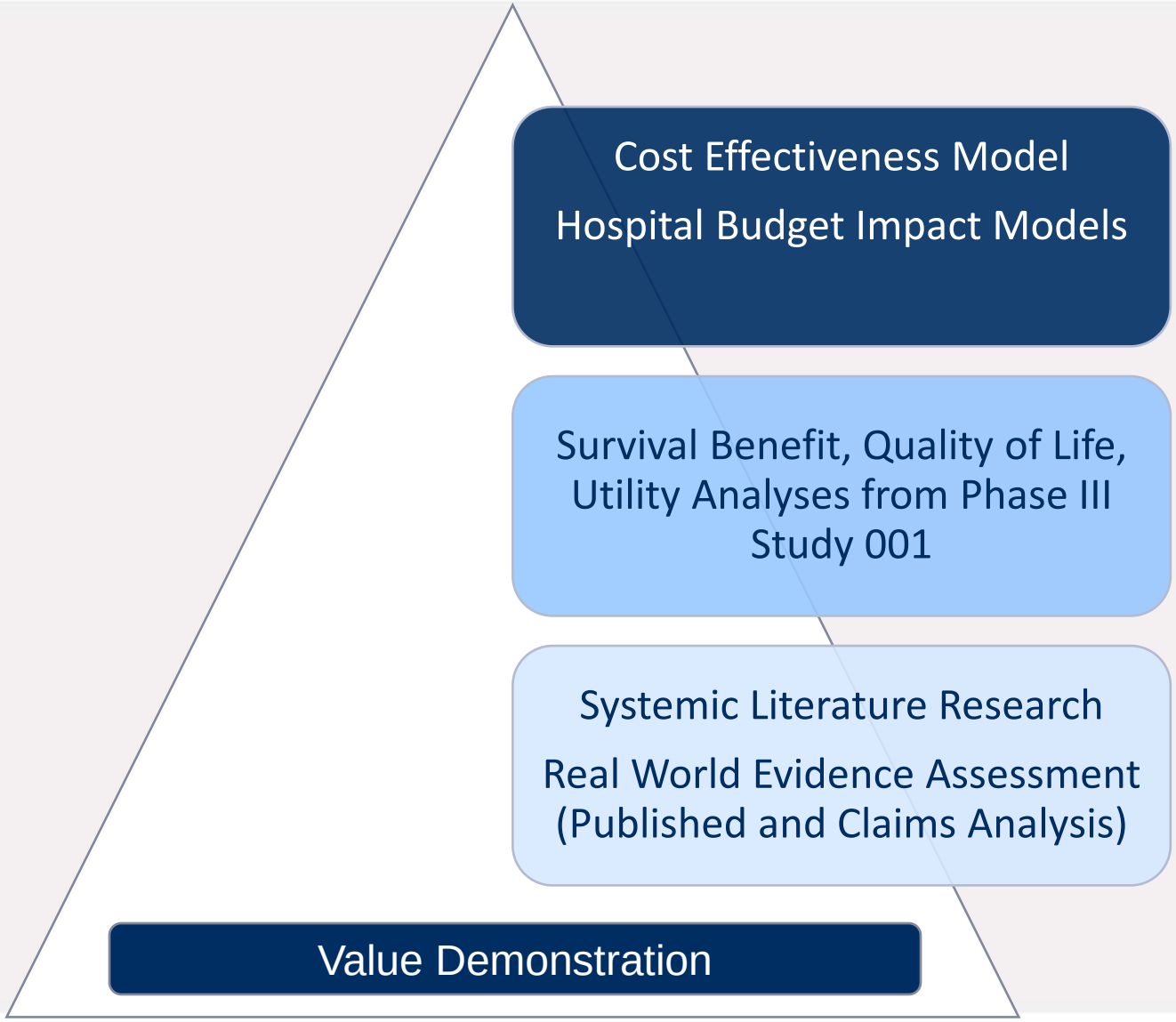
Remestemcel-L:

Developing a Nationally Diverse Strategic Council to Shape Scientific & Value Messaging



Remestemcel-L:

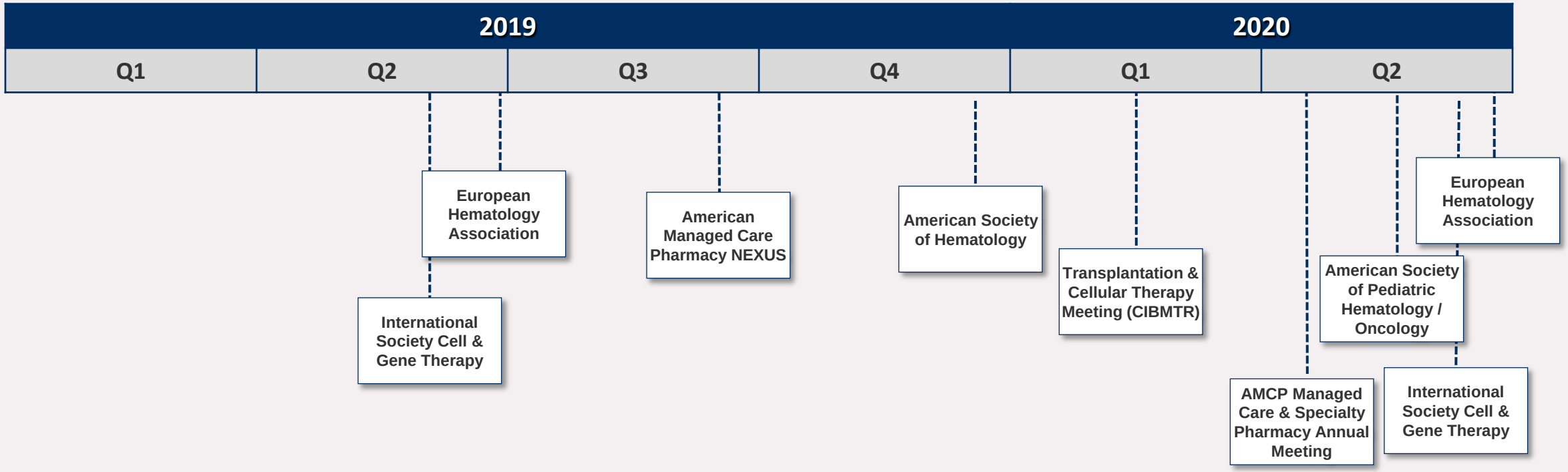
Comprehensive Health Economic Data Generation and Communication Strategy



Remestemcel-L:

Pre-Launch/Launch Planned Engagements at Target Medical/Payer Conferences

Data Presentations, Exhibits, Product Theaters & Sponsorship



Remestemcel-L: Hiring of Commercial Team Underway

Targeting Major Pediatric Transplant Centers and National / Regional Payers at Launch

Remestemcel-L: Hiring of Commercial Team Underway

Building a Highly Experienced Account Management Team Focused on Achieving Early Patient Access

Pre-Launch Priorities

- Provide economic burden of SR aGVHD education to national and target regional payers
- Profile target institutions for reimbursement processes and ordering / storage logistics for cryopreserved products
- Finalize distribution pathway with distributor and Rx-Hub support services

Launch Priorities

- Leverage developed reimbursement tools to secure coverage with Payers and patient access at Hospitals
- Hospital resource as a field extension of designated Rx-Hub
- Support Hospitals with product ordering logistics
- Execute product education events

Remestemcel-L: Hiring of Commercial Team Underway

Field Medical Science Liaisons Drive Scientific Exchange and Support Account Management Achieving Early Market Access

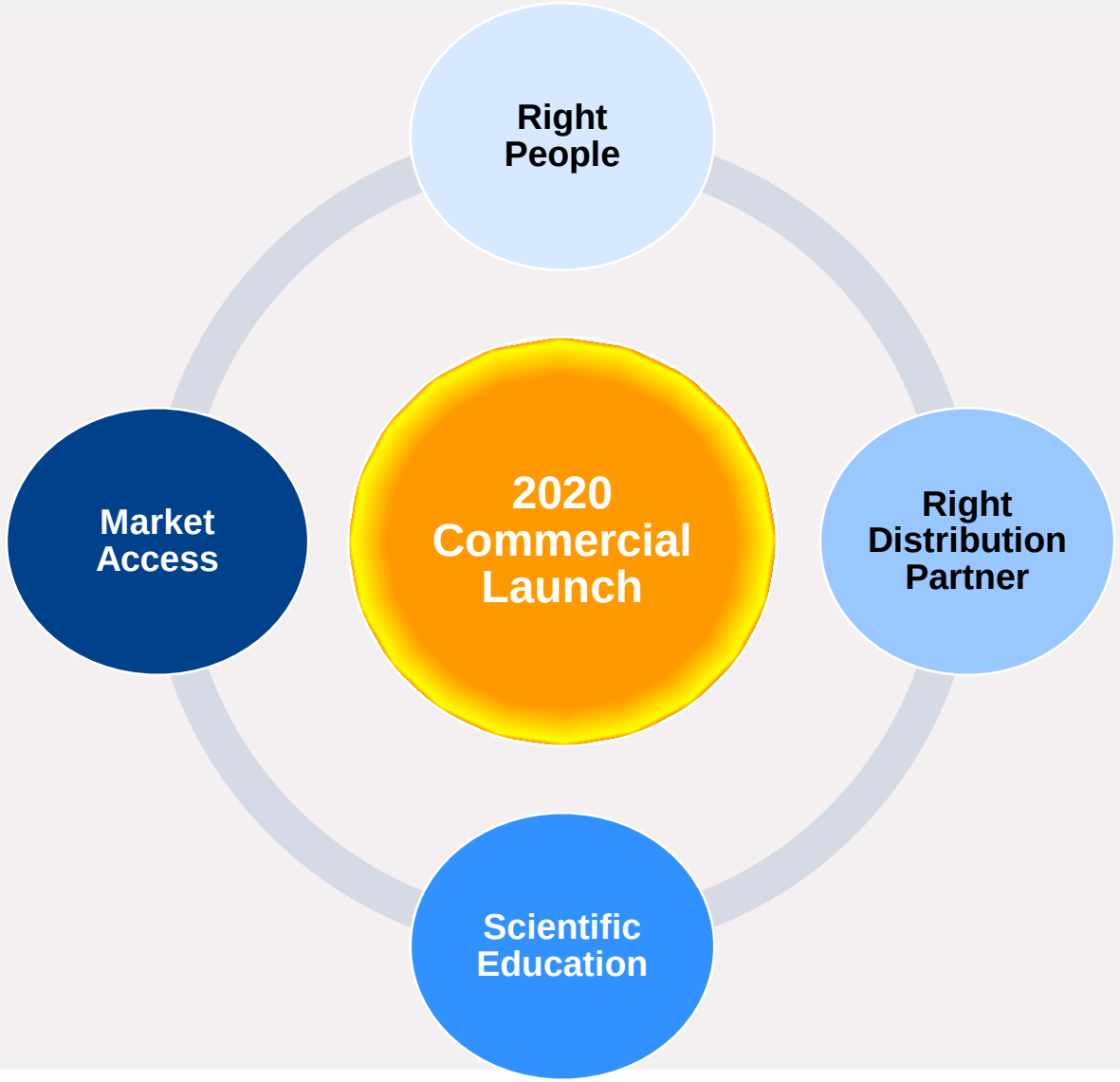
Pre-Launch Priorities

- KOL and Hospital profiling along with gathering relevant disease state management insights
- Scientific resource to payers as needed
- Scientific exchange
- National, regional and local congress coverage

Launch Priorities

- Scientific Exchange with KOLs, payers, IDNs/Hospitals
- Ongoing scientific resource to payers / Health Care Organizations
- Respond to unsolicited requests
- Gain insights on evolving treatment paradigms and medical developments
- Assist and Evaluate potential customer collaborators
- Ongoing national, regional, and local congress coverage

Delivering an Optimal Remestemcel-L Launch for 2020



Closing Remarks:
Josh Muntner (Chief Financial Officer)

Questions and Answer Session