mesoblast
the regenerative medicine company

Road to Commercialization for Mesenchymal Lineage Cells

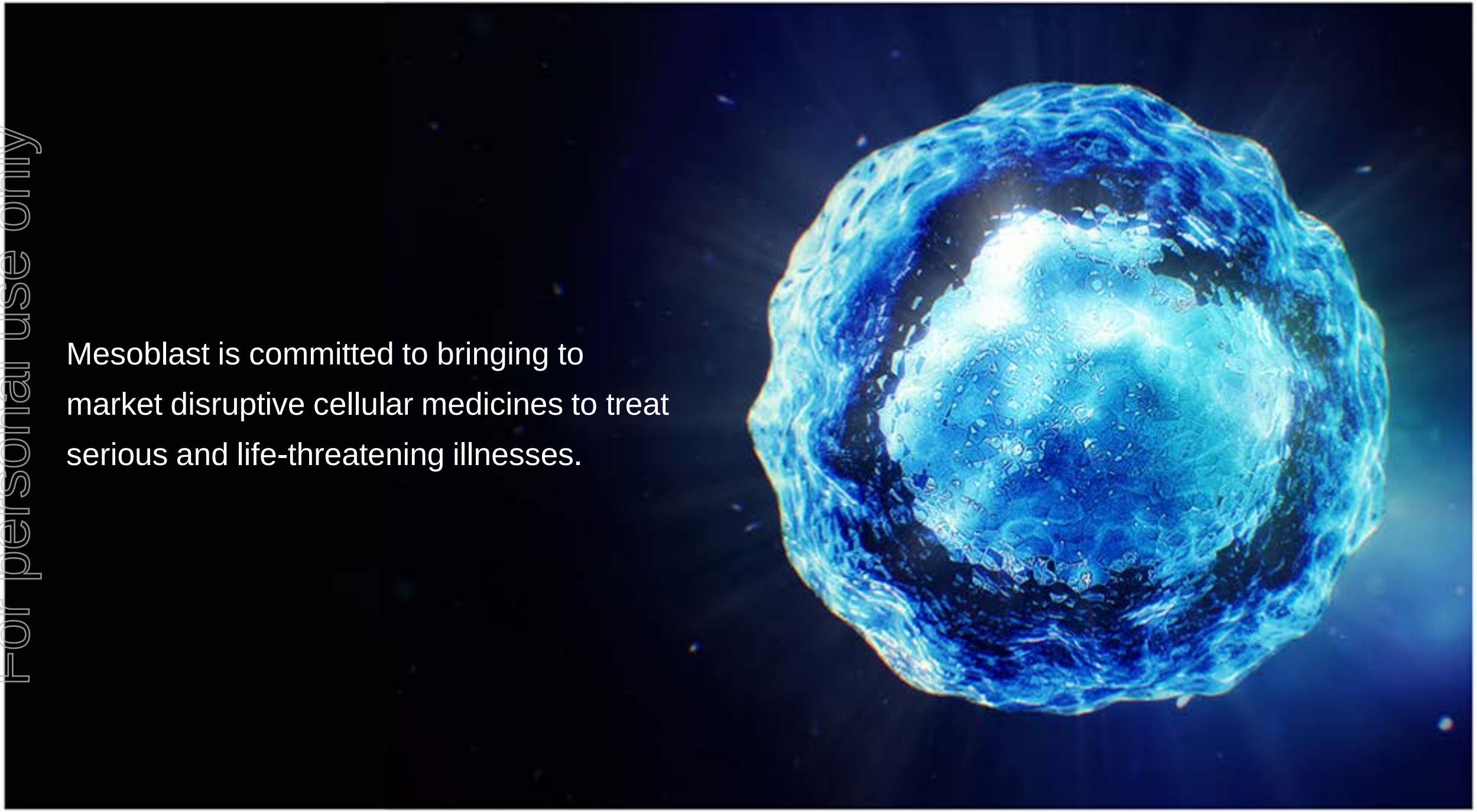
2018 ISSCR Annual Scientific Meeting

Melbourne June 21, 2018

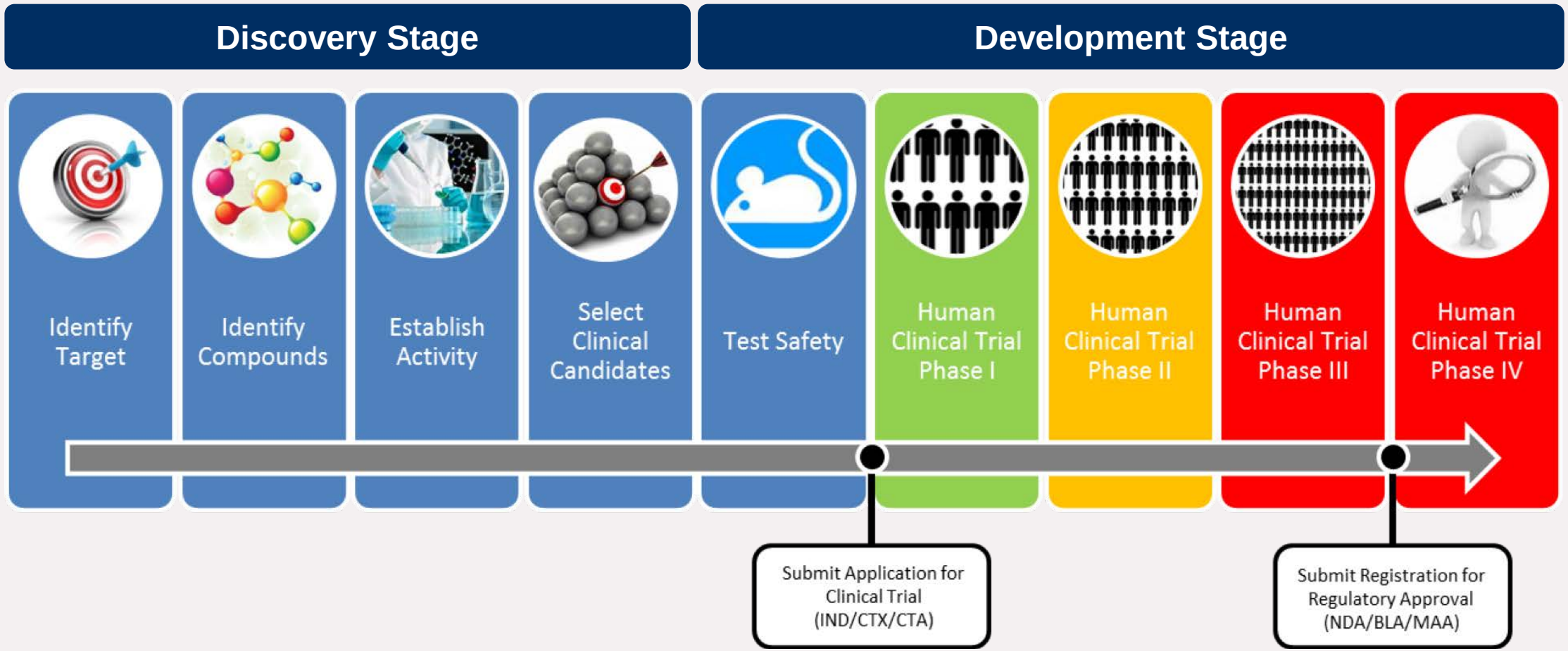
CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This presentation includes forward-looking statements that relate to future events or our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to differ materially from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this presentation are forward-looking statements. Words such as, but not limited to, "believe," "expect," "anticipate," "estimate," "intend," "plan," "targets," "likely," "will," "would," "could," and similar expressions or phrases identify forward-looking statements. We have based these forward-looking statements largely on our current expectations and future events, recent changes in regulatory laws, and financial trends that we believe may affect our financial condition, results of operation, business strategy and financial needs. These statements may relate to, but are not limited to: expectations regarding the safety or efficacy of, or potential applications for, Mesoblast's adult stem cell technologies; expectations regarding the strength of Mesoblast's intellectual property, the timeline for Mesoblast's regulatory approval process, and the scalability and efficiency of manufacturing processes; expectations about Mesoblast's ability to grow its business and statements regarding its relationships with current and potential future business partners and future benefits of those relationships; statements concerning Mesoblast's share price or potential market capitalization; and statements concerning Mesoblast's capital requirements and ability to raise future capital, among others. Forward-looking statements should not be read as a guarantee of future performance or results, and actual results may differ from the results anticipated in these forward-looking statements, and the differences may be material and adverse. You should read this presentation together with our financial statements and the notes related thereto, as well as the risk factors, in our most recently filed reports with the SEC or on our website. Uncertainties and risks that may cause Mesoblast's actual results, performance or achievements to be materially different from those which may be expressed or implied by such statements, include, without limitation: risks inherent in the development and commercialization of potential products; uncertainty of clinical trial results or regulatory approvals or clearances; government regulation; the need for future capital; dependence upon collaborators; and protection of our intellectual property rights, among others. Accordingly, you should not place undue reliance on these forward-looking statements. We do not undertake any obligations to publicly update or revise any forward-looking statements, whether as a result of new information, future developments or otherwise.

Mesoblast is committed to bringing to market disruptive cellular medicines to treat serious and life-threatening illnesses.



Lengthy, Complex Process to Bring a New Medicine to Patients Ethically and with Integrity



Source: Scientifist.com

Implementation of Regulatory Environment to Protect Patients

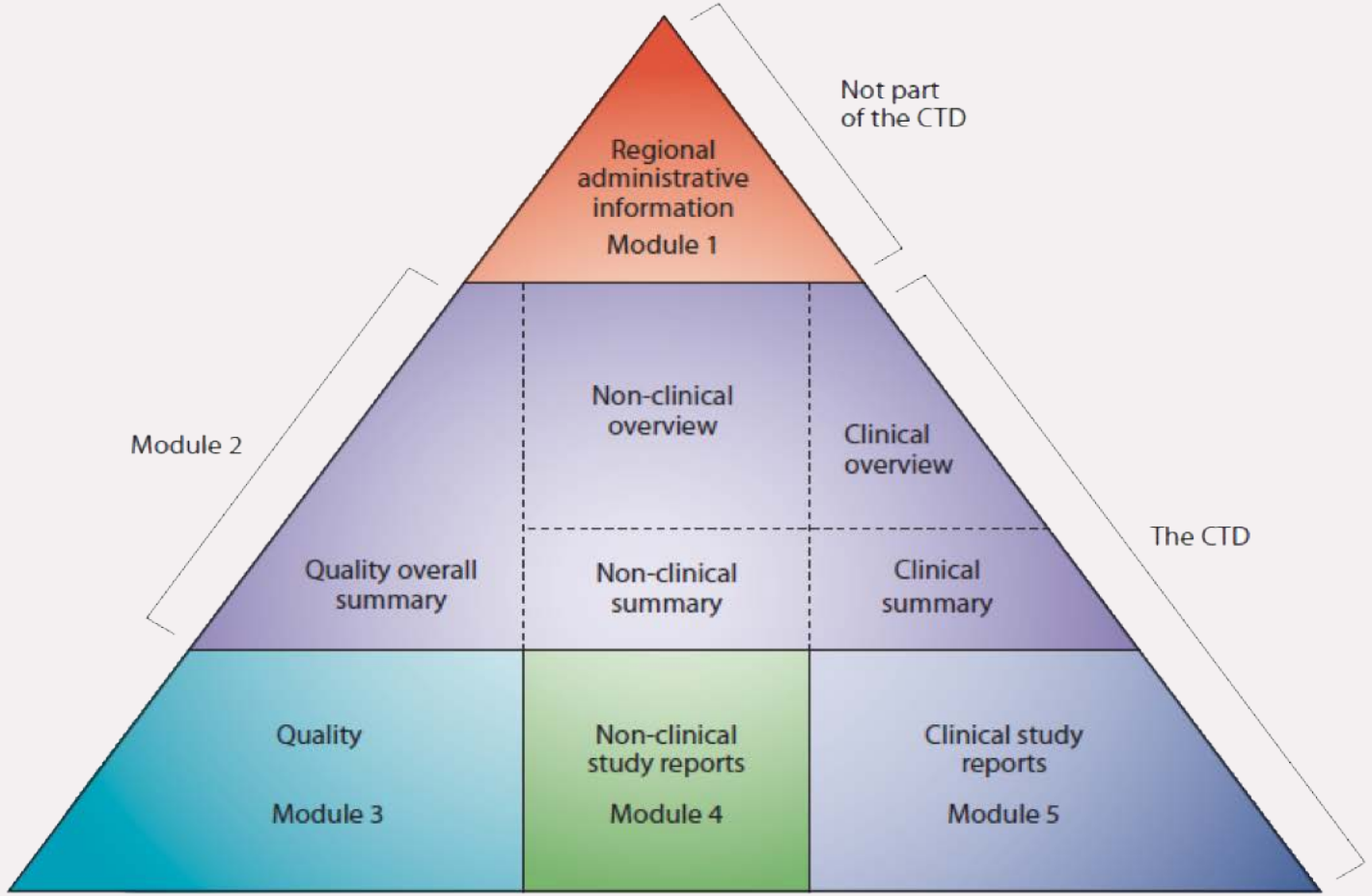
Section	What it covers
Quality	Demonstration that the proposed manufacturing process produces consistent quality product, controlled by in-process and finished product acceptance criteria; a controlled environment, GMP controls, and validated processes and testing
Safety	Research of the method of action – through a series of experiments, analytical, followed by animal studies: • Usually starting with rodents • Animal models that should be reflective of action in humans • Safety studies such as carcinogenicity and toxicity tests • Sufficient evidence to provide confidence before introducing the investigational product in to humans
Efficacy	Clinical studies, in a staged approach to manage risk: • Phase 1 – evaluation of safety in a small number of healthy patients (10-20) • Phase 2 – evaluation for efficacy in a small number of patients with the disease state • Phase 3 – evaluation of efficacy and safety in much larger groups, typically with two large pivotal or registration trials required for market approval

Regulatory Filing Requirements (FDA):

Common Technical Documents for a Biologics License Application

The CTD triangle.

The Common Technical Document is organized into five modules. Module 1 is region specific and modules 2, 3, 4 and 5 are intended to be common for all regions.



Mesoblast: A Leading Global Cellular Medicines Company

Disruptive Technology Platform[1]

- Immuno-selected, culture expanded cellular medicines
- Well characterized mechanisms of action targeting multiple pathways
- Extensive, robust IP estate
- Targeting the most severe disease states refractory to conventional therapies

Industrial Scale Manufacturing

- Unique cell properties enable large scale expansion and use in unrelated recipients
- Proprietary media formulations meet industrial scale needs
- 'Off the shelf' delineated products with batch to batch consistency and reproducibility

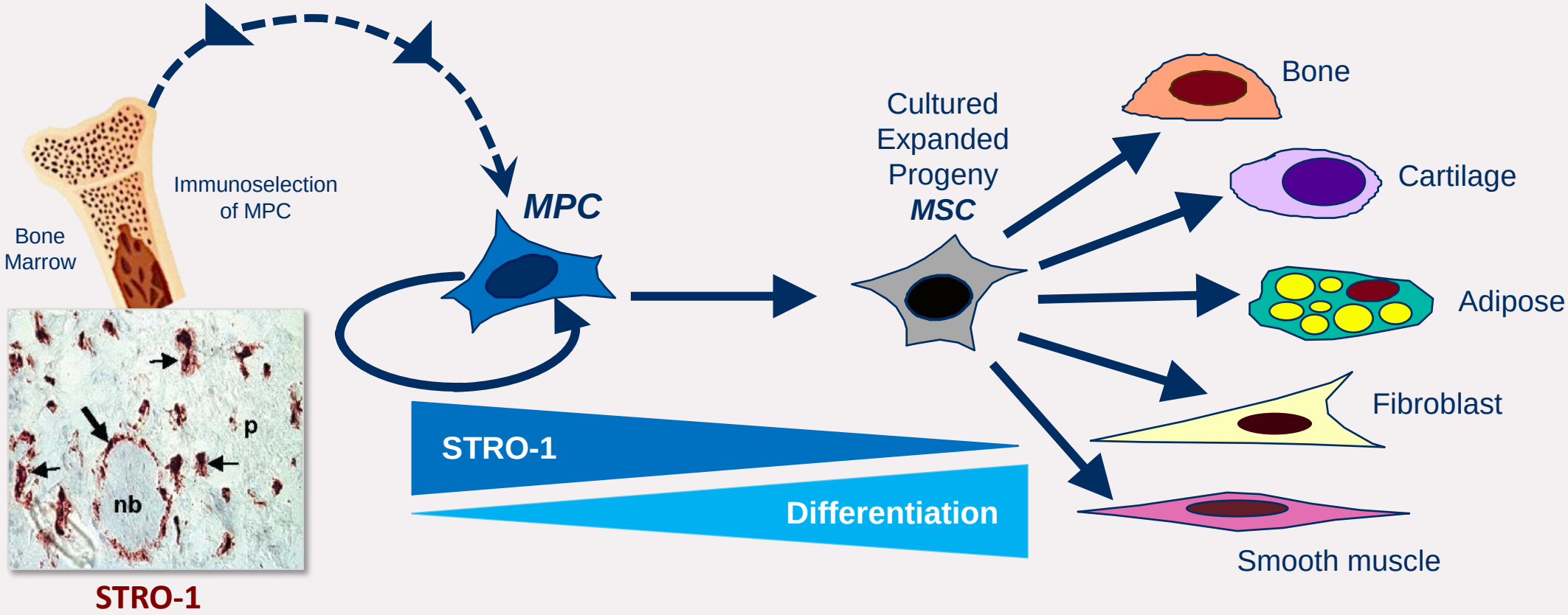
Multiple Revenue Generating Products & Phase 3 Assets

- 2 approved products commercialized by licensees in Japan[2] and Europe[3]
- 3 Phase 3 product candidates in U.S.
- Major near-term data readouts
- Revenue from approved and late-stage assets will help fund deep product pipeline

1. Mesenchymal precursor cells (MPCs) and their culture-expanded progeny mesenchymal stem cells (MSCs).
2. TEMCELL® Hs Inj licensee JCR Pharmaceuticals Co., Ltd. received the first full PMDA approval for an allogeneic cellular medicine in Japan.
3. Alofisel® licensee TiGenix NV/Takeda received first central marketing authorization (MA) approval in Europe for an allogeneic stem cell therapy.

STRO-1+ Mesenchymal Precursor Cells (MPCs)

At the apex of the entire mesenchymal lineage, irrespective of source of derivation

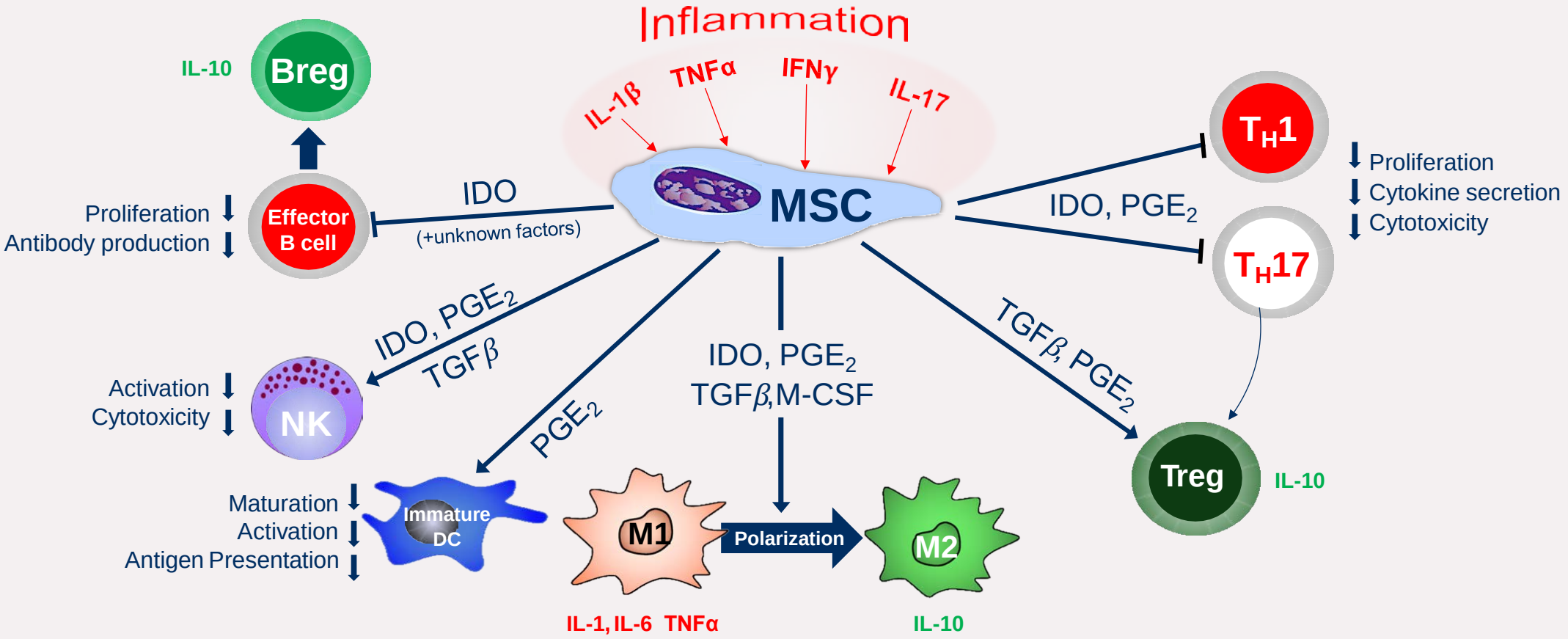


Simmons & Torok-Storb, Blood *78*: 55-62 (1991); Gronthos & Simmons, Blood *85*: 929-940 (1995); Gronthos *et al*., Blood 84:4164-4173 (1994); Gronthos *et al*., J. Bone Min. Res *14*:47-56 (1999); Gronthos *et al*., J Cell Sci. *116*: 1827-1835 (2003) ; Shi & Gronthos, J Bone Miner Res 18:696-704 (2003)

Barberi *et al*., PLoS Medicine *6*: e161 (2005); Hwang *et al*., PNAS 105:20641-20646 (2008); Brown *et al*., Cells Tissues Organs *189*:256–260 (2009); Whitworth *et al*., Stem Cells and Dev. *23*: 3021-3033 (2014); Zheng *et al*., PLoS ONE *10*: e0144226 (2015); Human mesenchymal stem cells (derived from hES cells) Merck Millipore *Cat# SCC036* (p.7)

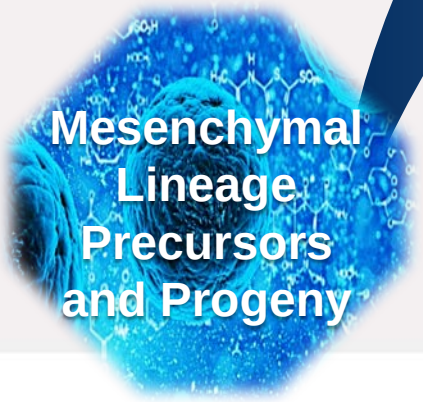
The Immunomodulatory Actions of MPCs and MSCs are Triggered by Their Receptor Initiated Responses to Inflammatory Cues:

Paracrine-mediated alteration of the function of multiple cellular constituents of the innate and adaptive immune systems



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
- Provides strong commercial protection for product candidates under development
- Enables licensing to third parties for indications, when in alignment with our corporate strategy



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

Industrial Scale Manufacturing

- Cellular technology platform enables immune privileged, allogeneic ‘off the shelf’ product candidates
- Delineated products with specific potency assays, batch to batch consistency and reproducibility
- Scalable culture expansion sufficient to produce anticipated commercial quantities
- Proprietary media formulations, advances in development of 3D bioreactor technology and automation to deliver step-changes in yield and significant COGS reductions

Clinical Pipeline and Products Commercialized by Licensees

MARKETED

PLATFORM	PRODUCT	THERAPEUTIC AREA	APPROVAL	COMMERCIAL RIGHTS
MSC (Bone Marrow)	TEMCELL® HS Inj[1]	Acute GVHD	✓	JCR — Japan Only
MSC (Adipose)	Alofisel[2]	Perianal Fistula	✓	TiGenix / Takeda — World Wide

IN DEVELOPMENT

	PLATFORM	PRODUCT CANDIDATE	THERAPEUTIC AREA	PRE-CLINICAL / PRE- IND	PHASE 2	PHASE 3	COMMERCIAL RIGHTS
TIER 1	MSC	MSC-100-IV	Acute GVHD	▬	▬	▬	mesoblast — the regenerative medicine company
TIER 1	MPC	MPC-150-IM	Advanced HF (Class II & III) End-Stage HF (Class III & IV)[3]	▬	▬	▬	mesoblast — the regenerative medicine company
TIER 1	MPC	MPC-06-ID	Chronic Low Back Pain	▬	▬	▬	mesoblast — the regenerative medicine company
TIER 1	MPC	MPC-300-IV	Rheumatoid Arthritis Diabetic Nephropathy	▬	▬	▬	mesoblast — the regenerative medicine company
TIER 2	Includes **MSC-100-IV** (Crohn's disease – biologic refractory), **MPC-25-IC** (Acute Cardiac Ischemia), **MPC-25-Osteo** (Spinal Fusion) and **MPC-75-IA** (Knee Osteoarthritis)						

1. Mesoblast receives royalty income on sales of TEMCELL® in Japan by its licensee JCR Pharmaceuticals Co Ltd.
2. Mesoblast will receive royalty income on world wide sales of Alofisel in the local treatment of perianal fistulae by its licensee TiGenix NV/Takeda Pharmaceuticals
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.

Acute Graft vs Host Disease

Remestemcel-L (MSC-100-IV) for Steroid-Refractory aGVHD

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
- Severe aGVHD (determined by grade C/D, visceral organ and multi-organ involvement, or high risk stratification) has the highest risk of failure to first-line corticosteroids and high transplant related mortality[1]
- Day 100 mortality can reach 70% in patients who fail to respond to initial steroid therapy, and 12 month mortality approaches 90%[2-5]
- 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. Aggarwal S, Pittenger MF. Human mesenchymal stem cells modulate allogeneic immune responses. Blood. 2005; 105:1815-22.

Visceral Organ Involvement Predicts High Mortality in aGVHD

Organ Involvement (n)	Univerate Analysis Hazard Ratio	P Value	Multiverate Analysis Hazard Ratio	P Value
Skin Only (1010)	1		1	
Gut Only (266)	1.11	0.448	0.80	0.139
Liver Only (28)	**4.11**	**<0.001**	**2.22**	**0.013**
Skin and Gut, No Liver (1083)	1.27	0.008	0.97	0.753
Skin and Liver, No Gut (160)	2.42	<0.001	1.54	0.006
Gut and Liver, No Skin (75)	**3.64**	**<0.001**	**1.88**	**0.001**
Skin and Gut, No Liver (448)	**4.82**	**<0.001**	**2.07**	**<0.001**

- Response rates to first-line corticosteroids are 20%-50% depending on organ involvement
- Steroid-refractory aGVHD patients have very high mortality rates
- Non-relapse mortality after failure of corticosteroids is predicted by visceral organ involvement[1]
- SR aGVHD associated with $200k - $500k additional healthcare costs[2]

1. Murata M et al 1083-8791 2013 American Society for Blood and Marrow Transplantation, 2. HealthCore® Claims Analysis July 2016.

MSC-100-IV (remestemcel-L):

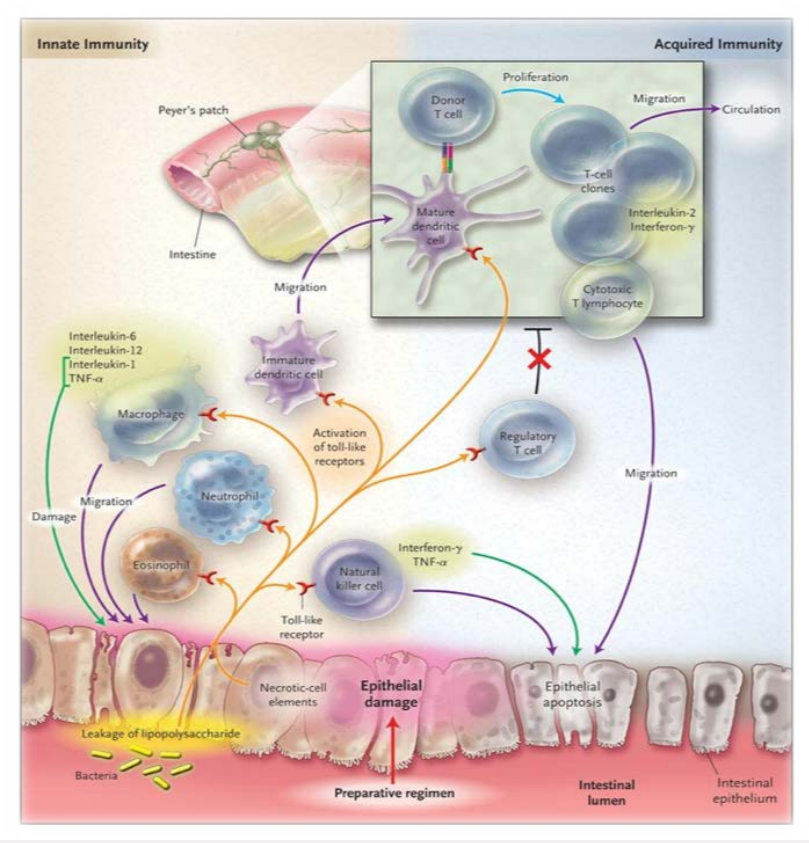
In vitro/in vivo studies demonstrate multiple MOA pathways addressing underlying inflammatory response in GVHD

In vitro studies demonstrate that remestemcel-L

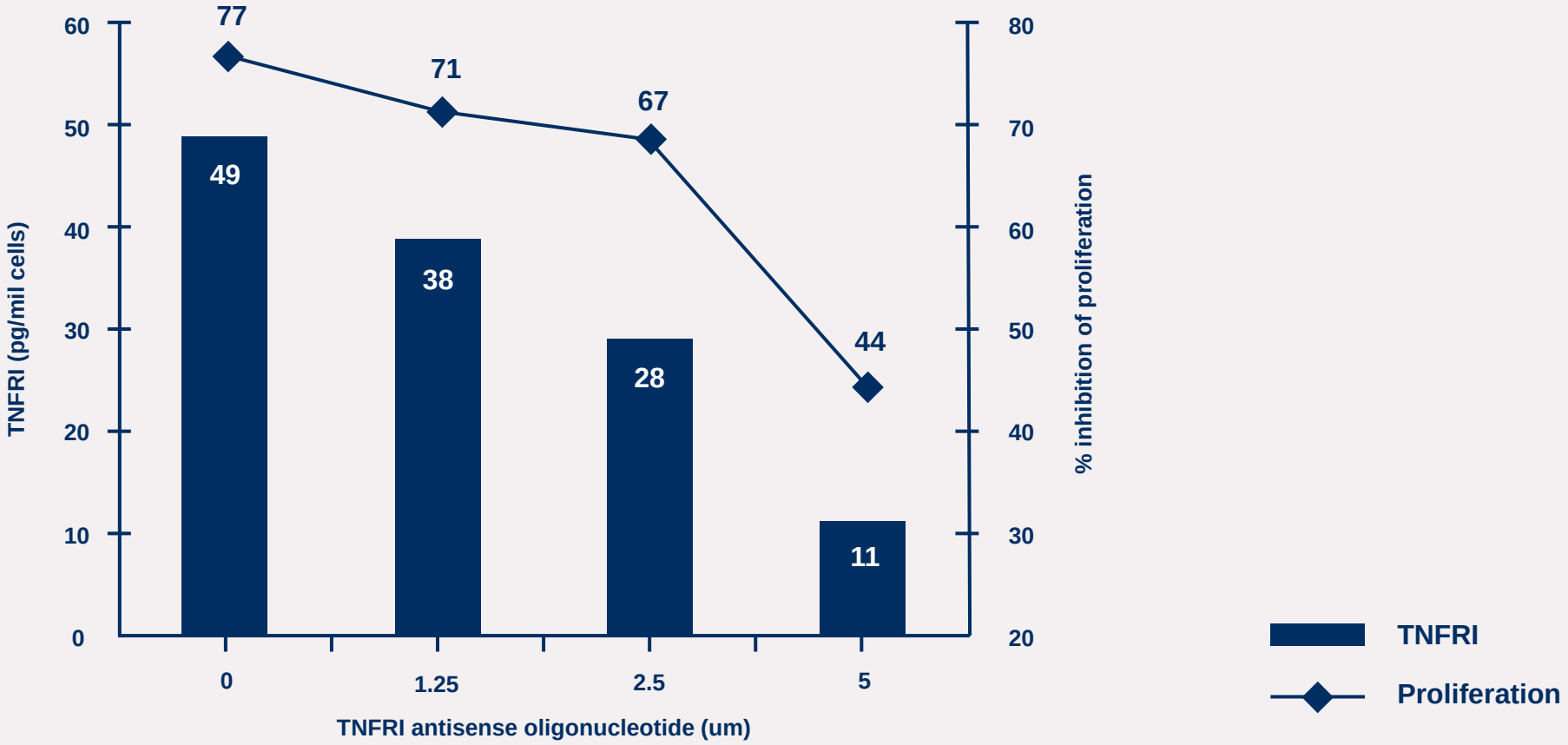
- Inhibits alloantigen- and mitogen-driven T cell proliferation in vitro
- Decreases secretion of pro-inflammatory cytokines by immune cells, e.g. TNFα and IFNγ and increase secretion of anti-inflammatory factors, e.g. IL-10 and IL-4
- Induces expansion of regulatory T cells

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



Relationship Between TNFR1 Expression on MSC and Inhibition of T Cell Proliferation[1]



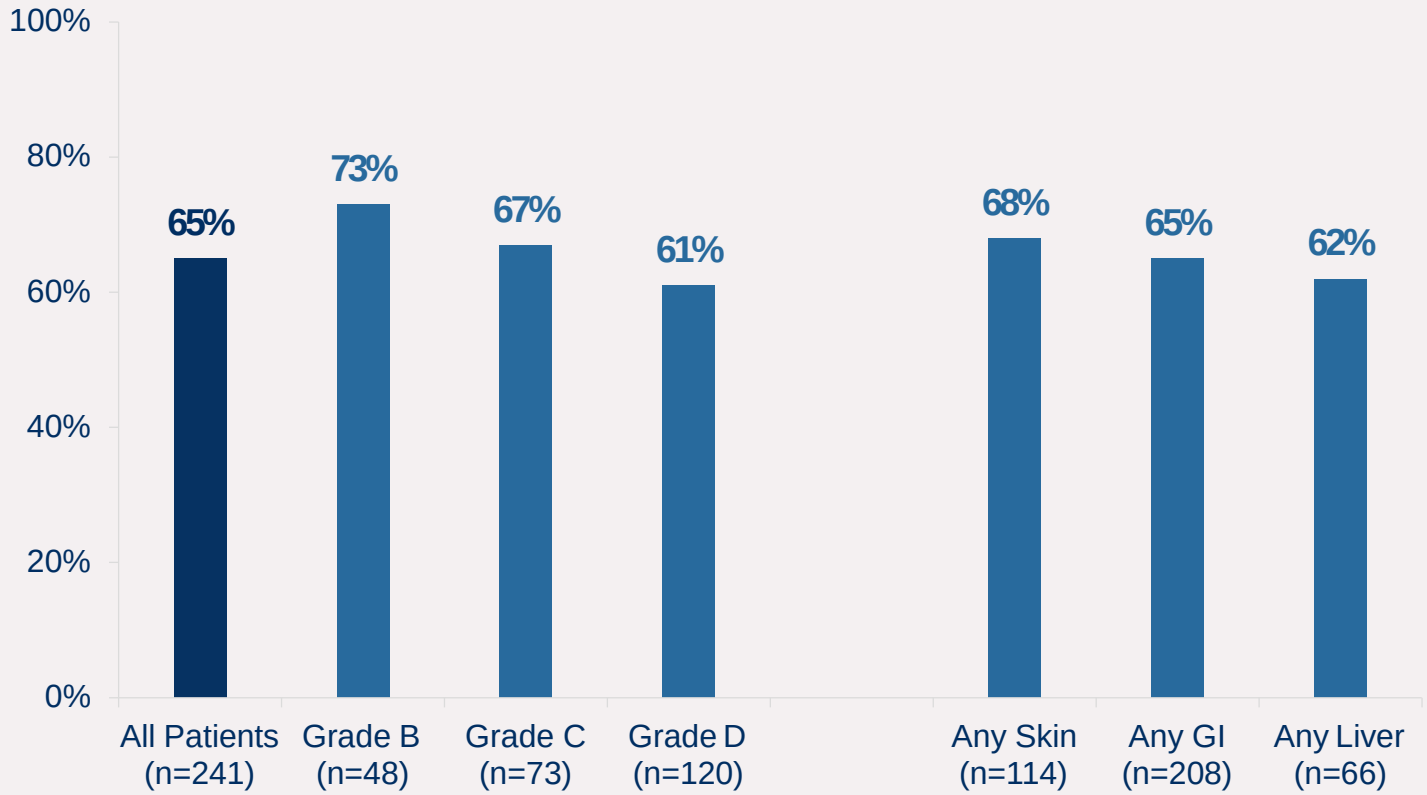
US PTO, Danilkovitch, A et. al. (2013) *US 8,486,695*

Remestemcel-L (MSC-100-IV):Expanded Access Program

Overall Day 28 response in pediatric aGVHD patients receiving remestemcel-L (MSC-100-IV) as first-line or salvage therapy after failing steroids

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 1mg/kg/day or equivalent)



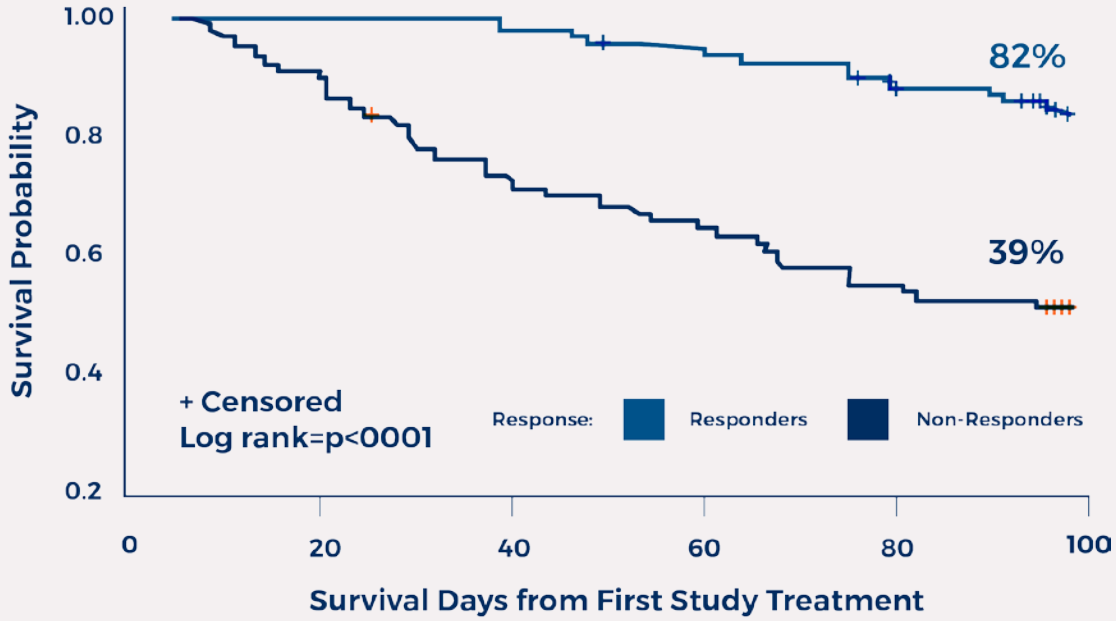
- **Complete Response was 14%, Partial Response was 51%**
- **Responses were observed for all GVHD grades and did not differ by baseline organ involvement**

Kurtzberg et al: Presentation Tandem Feb 2016

Remestemcel-L (MSC-100-IV):Expanded Access Program

Correlation of Day 28 overall response with Day 100 survival, using remestemcel-L (MSC-100-IV) as first-line or salvage therapy after failing steroids and/or additional treatments

MSC-100-IV in Children with SR-aGVHD who failed multiple other modalities
- Survival of Pediatric Patients Treated with MSC-100-IV 28-Day Responders vs Non-responders n=241



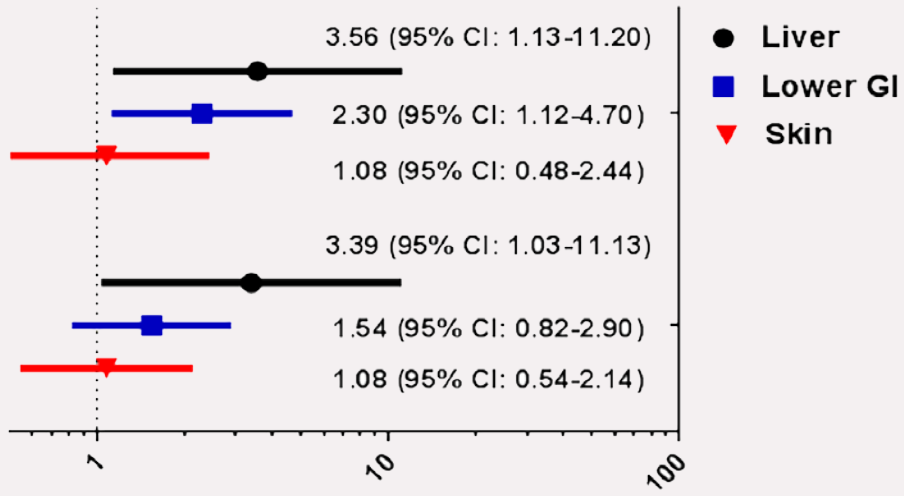
- In 241 Children under EAP, **Overall Response** (CR+PR) at Day 28 was **65%** (95% CI: 58.9%, 70.9%)
- **Day 100 survival** correlated with overall response, and was significantly improved in those who responded at Day 28 **(82% vs. 39%, p<0.0001)**

MSC-100-IV: Study 280 Adult Population

Randomized controlled data in patients who failed steroids and received no additional GVHD treatment prior to enrollment

Overall Response (CR + PR) by Organ Involvement – mITT population

		Remestemcel-L	Placebo	P Value
DAY 100	Liver	32/42 (76.2%)	9/19 (47.4%)	0.039
	GI	94/115 (81.7%)	39/59 (66.1%)	0.025
	Skin	72/92 (78.3%)	40/52 (76.9%)	0.838
	All	133/163 (81.6%)	59/81 (72.8%)	0.136
DAY 28	Liver	23/42 (54.8%)	5/19 (26.3%)	0.053
	GI	65/115 (56.5%)	27/59 (45.8%)	0.201
	Skin	53/92 (57.6%)	29/52 (55.8%)	0.862
	All	95/163 (58.3%)	44/81 (54.3%)	0.585



MSC-100-IV favorable responses in aGVHD cases involving the liver and GI

– *Response rates improve from Day 28 through Day 100*

Remestemcel-L for GVHD:

Mesoblast's product development strategy

1. Target ***pediatric*** patients with steroid refractory-aGVHD first

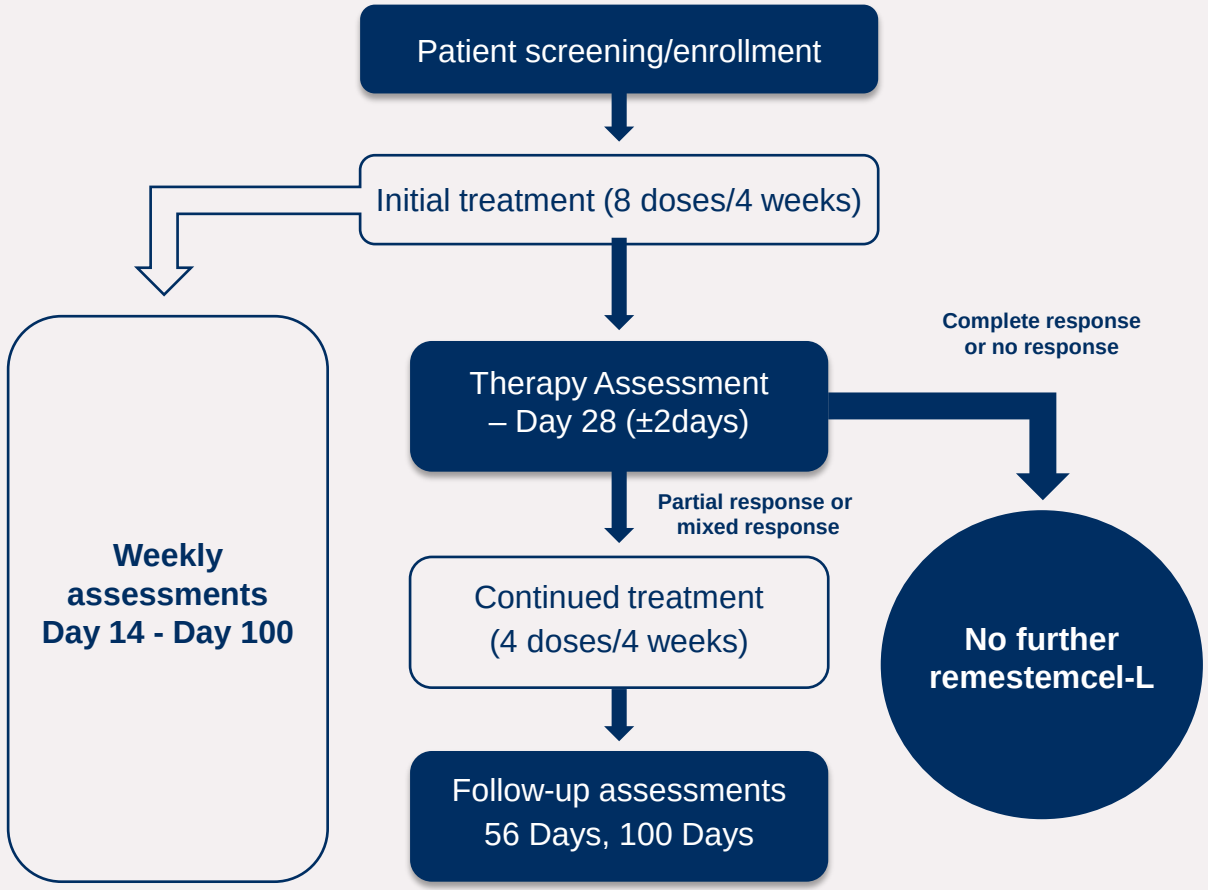
2. Seek label extension for high-risk ***adult*** patients with steroid refractory-aGVHD

3. Lifecycle potential in ***chronic*** GVHD (cGVHD)

Remestemcel-L (MSC-100-IV): Phase 3

Phase 3 pediatric trial GVHD001 as first-line therapy in aGVHD after failing steroids

- Multi-center, single-Arm, open-label 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 only
- 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



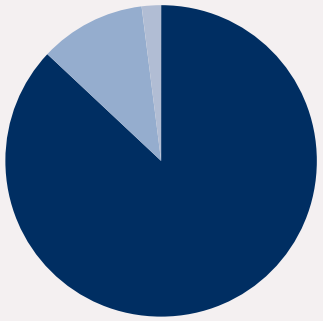
Protocol GVHD001: Demographics

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%)

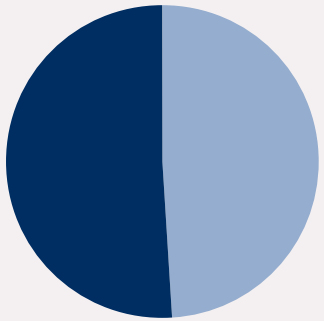
Protocol GVHD001:Transplant Characteristics Reflect aGVHD Risk Factors



Conditioning Regimen

- Myeloablative
- Reduced Intensity
- Non-Myeoablative

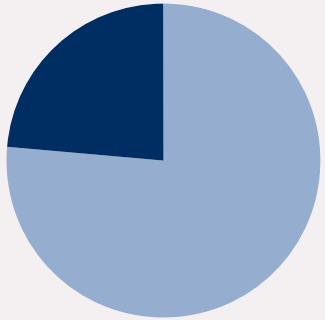
87% of subjects received myeloablative conditioning regimen



Donor Compatibility

- Matched
- Mismatched

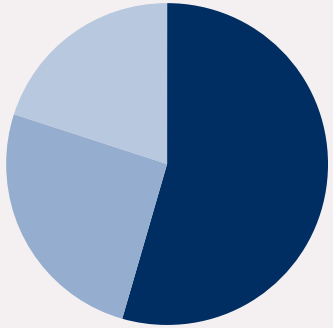
51% of subjects received an HLA-mismatched transplant



Donor Type

- Unrelated
- Related

76% of subjects received an unrelated donor transplant

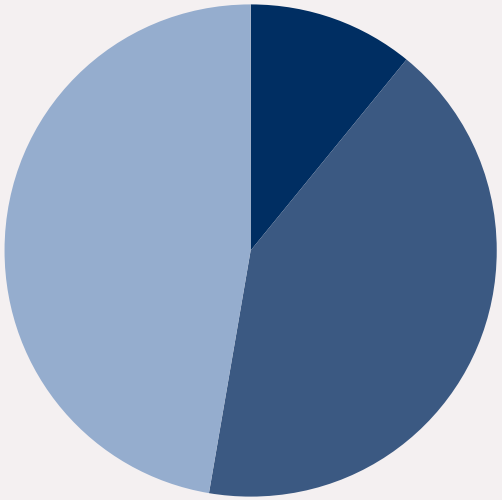


Graft Source

- Bone Marrow
- PBSC
- Cord Blood

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

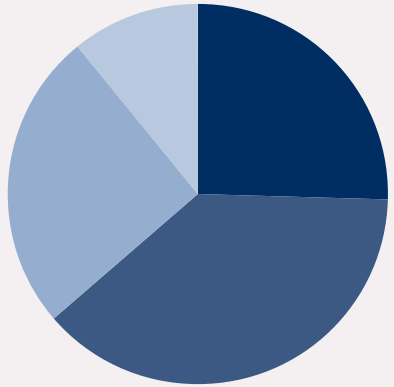
Protocol GVHD001: Disease Characteristics Reflect aGVHD Severity



GVHD Grade at Baseline

- Grade B
- Grade C
- Grade D

Baseline Organ Involvement



- Skin Only
- Lower GI Only
- Two Organs
- Three Organs

47% of subjects had Grade D disease at baseline

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

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

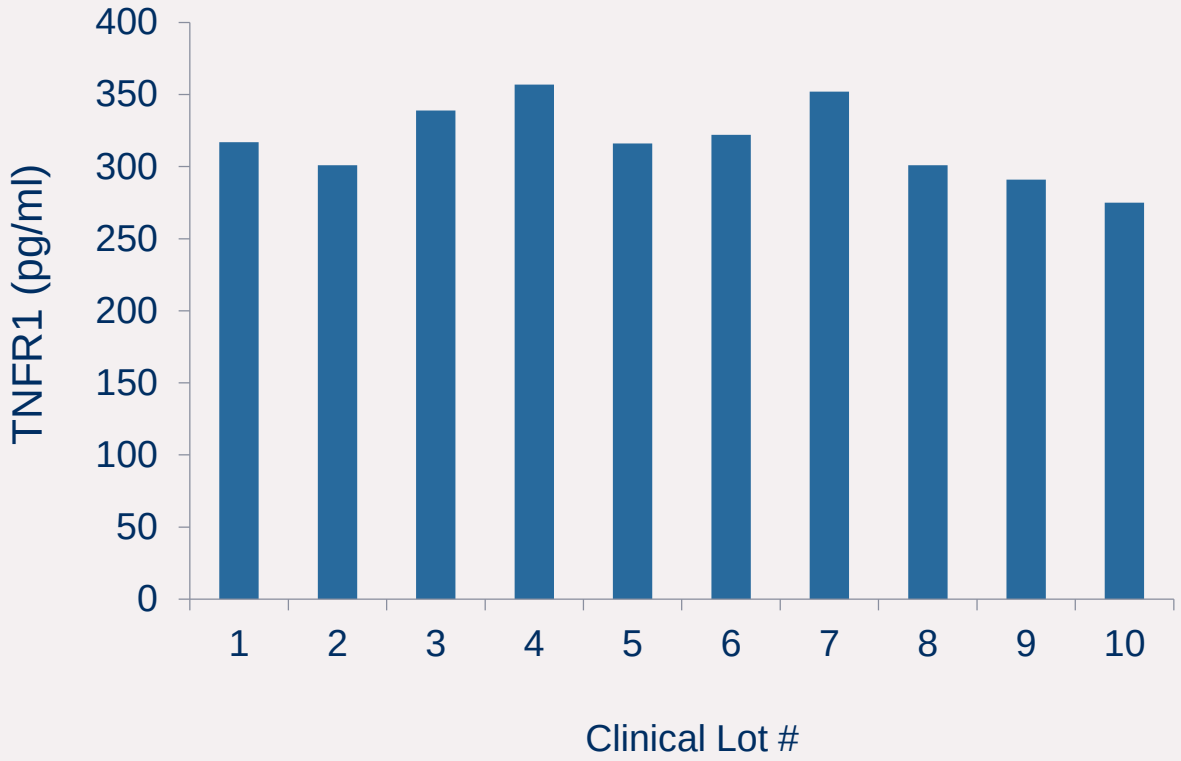
16/21 stage 3 (n=6) or stage 4 (n=10) disease

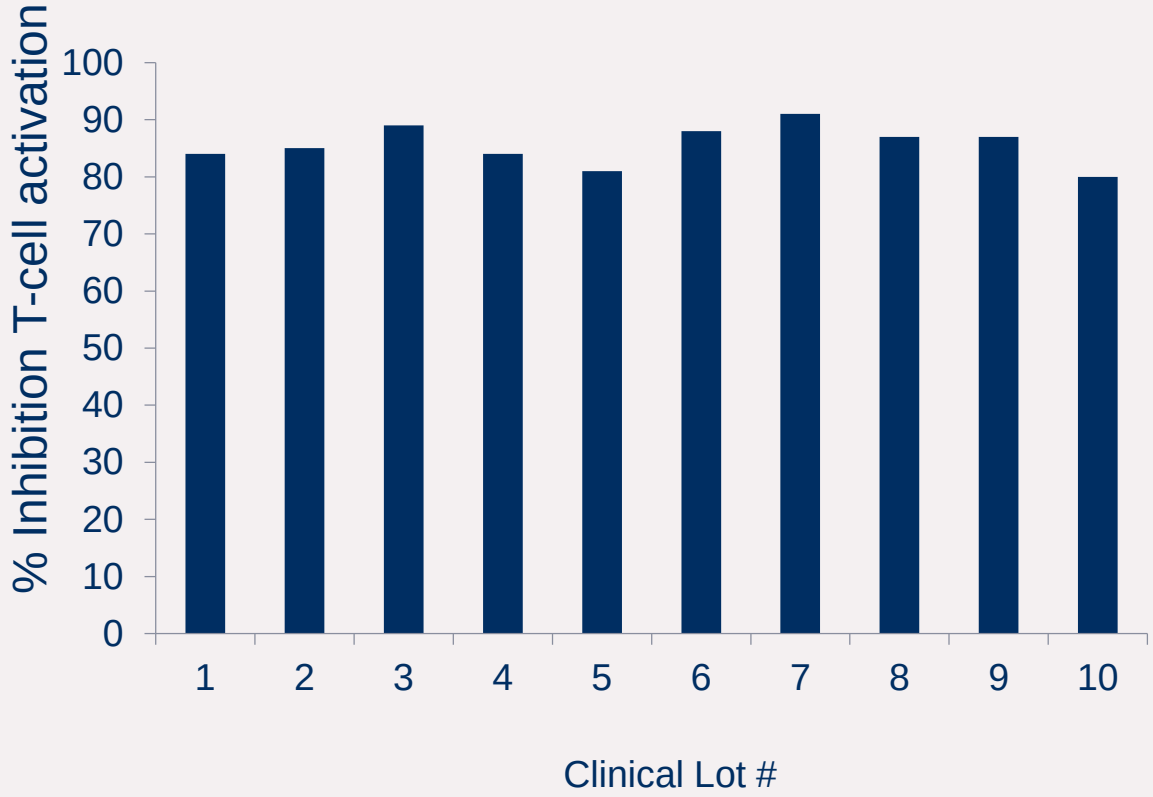
36% of subjects had multi-organ-involvement, all with Lower GI

6/20 had all three organs involved
10/20 had Lower GI + Skin
4/20 had Lower GI + Liver

Consistency of the Manufacturing Process in Phase 3:

Remestemcel-L demonstrates consistent lot to lot expression of TNFR1 and high level inhibition of T cell activation

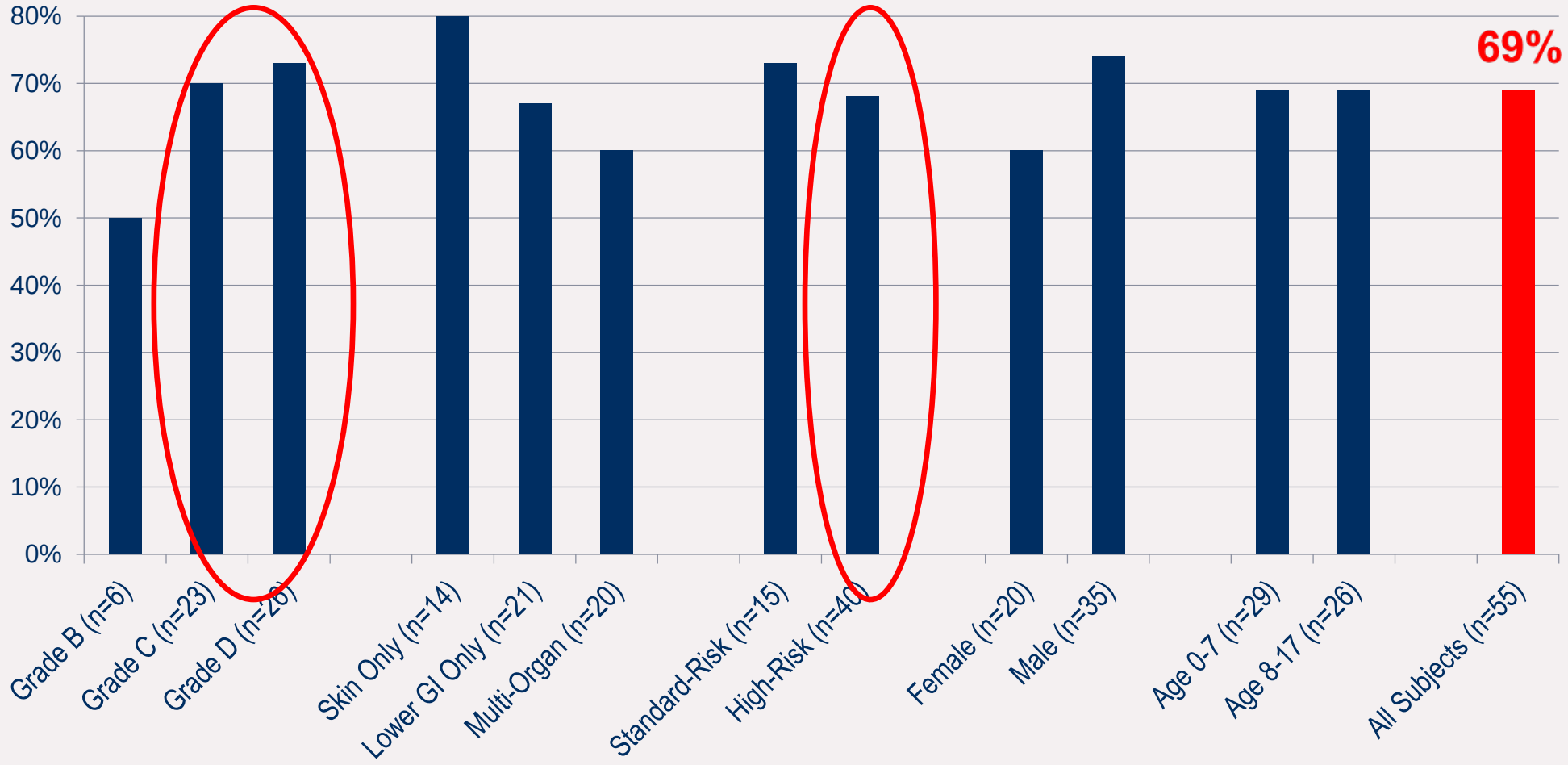




Source: Internal Mesoblast Data

Protocol GVHD001:Primary Efficacy Outcome

Overall response at Day 28 was 69%, p=0.0003



Protocol GVHD001: Summary of Phase 3 Trial Results

- Multi-dose regimen of remestemcel-L infusions was well tolerated

- Day 28 Overall Response was 69%
- Day 28 Overall Response was significantly greater than theoretical control rate of 45% (p=0.0003)

- **Overall survival at Day 100 was 75%**
- **Survival at Day 100 for responders at Day 28 was 87%**

Remestemcel-L as First Line in Steroid Refractory Acute GVHD

Phase 3 Conclusions

- Multi-dose regimen of remestemcel-L infusions was well tolerated
- Remestemcel-L successfully achieved the pre-specified primary endpoint of Day 28 Overall Response
- Remestemcel-L demonstrated substantial Day 100 survival benefits
- Results are consistent with the overall response, safety, and survival in the previous report of remestemcel-L (MSC-100-IV) in a 241 subject expanded access protocol of pediatric subjects with Steroid Refractory aGVHD who failed to respond to steroids as well as to multiple additional therapies

Next Steps

- Day 180 survival results **e**xpected in CY Q3, 2018
- BLA filing targeted for CYQ4 2018 / Q1 2019
- Potential for label extension to high-risk ***adult*** patients with steroid refractory-aGVHD

Thank you

mesoblast

the regenerative medicine company

Questions?