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SER-155 Phase 1b Cohort 1 Day 100 Data

May 2023

SER-155 May Represent a Novel Solution to Reduce GI Pathogen Abundance and Infection & GvHD in Allogeneic HSCT

- SER-155 is an **oral**, **cultivated consortium**, designed to reduce abundance of pathogens linked to infections and GvHD in allogeneic HSCT recipients*
- SER-155 Phase 1b study Cohort 1
  - **SER-155 was well-tolerated** through 100 Days post HSCT
  - SER-155 bacterial strain **engraftment was as expected**
  - **GI pathogen domination was rare and transient** in patients after SER-155 treatment compared to expected rates from prior cohort studies

Enrollment ongoing in SER-155 Phase 1b Cohort 2 a randomized, double-blind, placebo-controlled study

Expect to release topline results in mid-2024

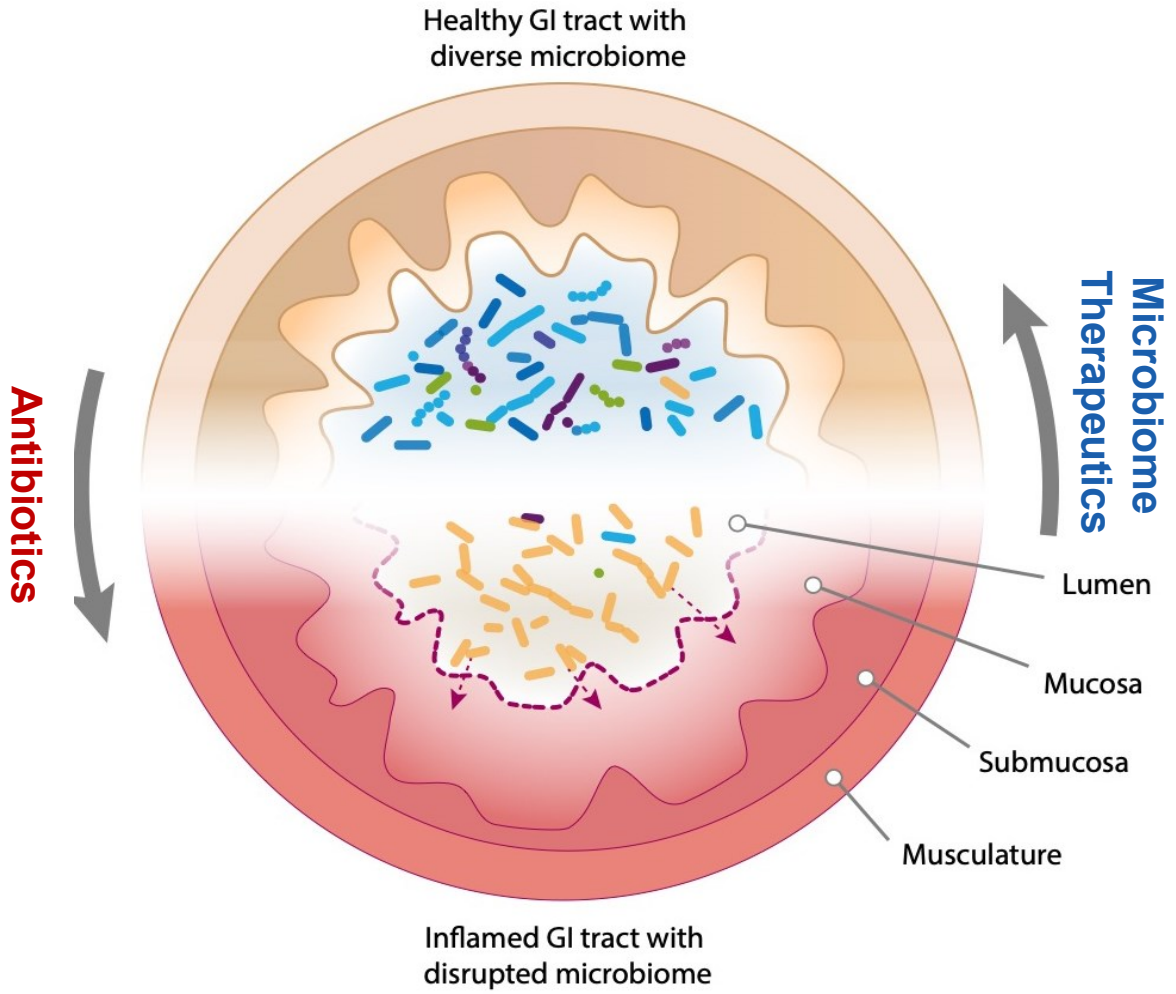
*Note: SER-155 is an investigational therapeutic and has not been approved by any regulatory authority, including the US Food & Drug Administration

Beneficial Bacteria Protect the GI Tract from Potential Microbial Pathogens

A healthy, diverse microbiome is **essential to preventing colonization and infection with pathogens**

Antibiotics and other insults can drive the loss of beneficial microbes, **enabling pathogens and drug-resistant bacteria to rapidly expand and dominate in GI tract**

Domination with pathogens and drug-resistant bacteria in patients **can increase intestinal permeability and is associated with increased risk of blood stream infections and other medical complications**



Sources: Pamer, E., Science 2016; Kim et al, Nature, 2019; McGovern et al, CID 2020, Ubeda et al, J.Clin Invest 2010; Taur et al, Clin Infect Dis, 2012, Tamburini et al, Nat Med 2018

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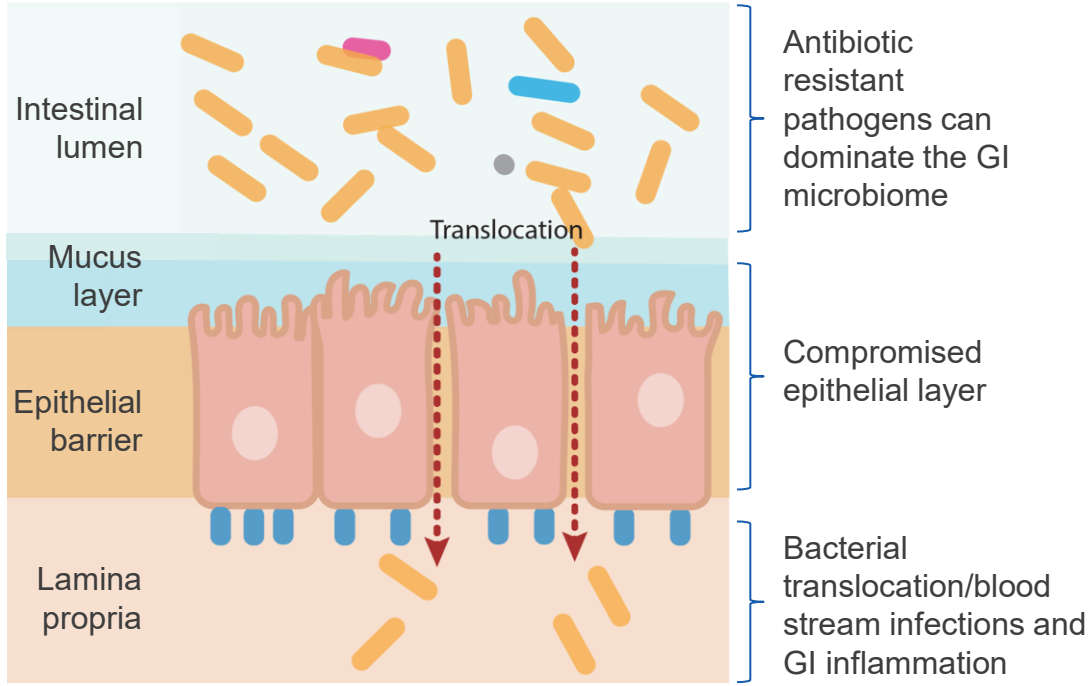
Microbiome Therapeutics are a Potential Novel Approach to Address Infections, Antimicrobial Resistance, & Associated Complications

Disrupted gastrointestinal microbiome has disease-relevant consequences



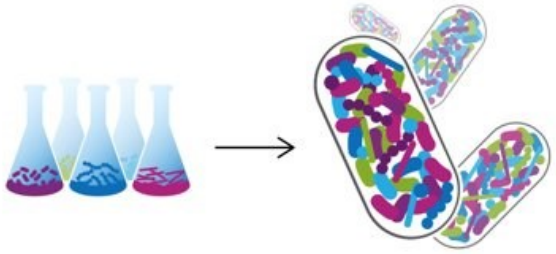
Seres microbiome therapeutics MbTx Platform enables:

- Identification of microbial species and functional targets linked to **disease-specific outcomes**
- Identification of bacterial strains that **engraft successfully** and that **modulate disease functional pathways**
- **Preclinical and SER-109 ECOSPOR III exploratory results** demonstrate microbiome therapeutics may decolonize pathogens with the potential for **clinical outcomes**

* Feuerstadt P NEJM 2022; 386:220-9; *post hoc* analysis of VOWST Phase 3 study data; presented at IDWEEK 2021 conference

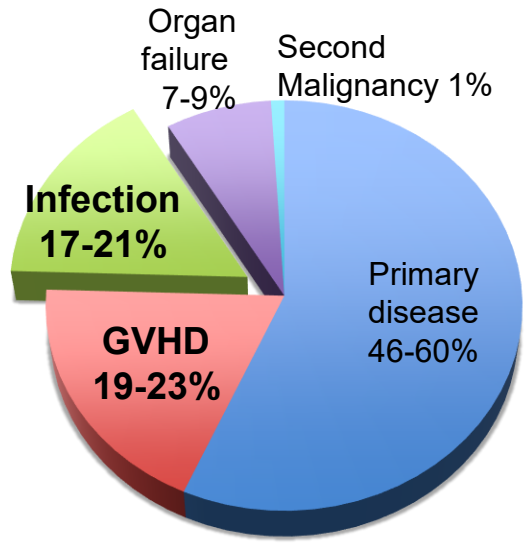
SER-155 Designed to Modulate Targets that Address Leading Causes of Mortality Following Allogeneic HSCT (allo-HSCT)

SER-155 is a 16 strain cultivated bacterial consortium optimized using MbTx Platform



- Consortium of **unique, human commensal bacterial strains**
- **Cultivated** and encapsulated for **oral delivery**
- **Strain selection** based on broad pre-clinical screening for defined functions and insights from microbiome clinical data
- Preclinical data show SER-155 leads to multi-log reductions of *Enterococcus* (including VRE) and *Enterobacteriaceae* (including CRE) linked to GvHD in allo-HSCT patients*

SER-155 specifically designed to reduce infections and GvHD in allo-HSCT recipients



Causes of allo-HSCT mortality at 1 year**

- Allo-HSCT recipients are **medically vulnerable**; 50% 3 year mortality

* Seres data shared in Jan 2022 Infection Protection Investor Event; VRE = vancomycin-resistant *Enterococci*; CRE = carbapenem-resistant *Enterobacterales*; VRE and CRE both included in US CDC Antibiotic Resistance Threats
** CIBMTR 2020

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SER-155 Phase 1b: Two-Cohort Study to Evaluate SER-155 in Allogeneic HSCT Patients

15 patients — ***Cohort 1* – open-label**

- Evaluate safety, tolerability of SER-155 dosed before and after allogeneic HSCT
- Evaluate the engraftment (PK) of SER-155 strains in the GI microbiome
- Assess the impact of SER-155 engraftment on gastrointestinal microbiome domination

Day 100 data available

~60 patients — ***Cohort 2* - randomized, double-blind, placebo-controlled**

- Continue to evaluate safety, tolerability, PK/PD
- Explore clinical outcomes of infection & GvHD and candidate biomarkers associated with clinical impact and mechanism

Enrolling

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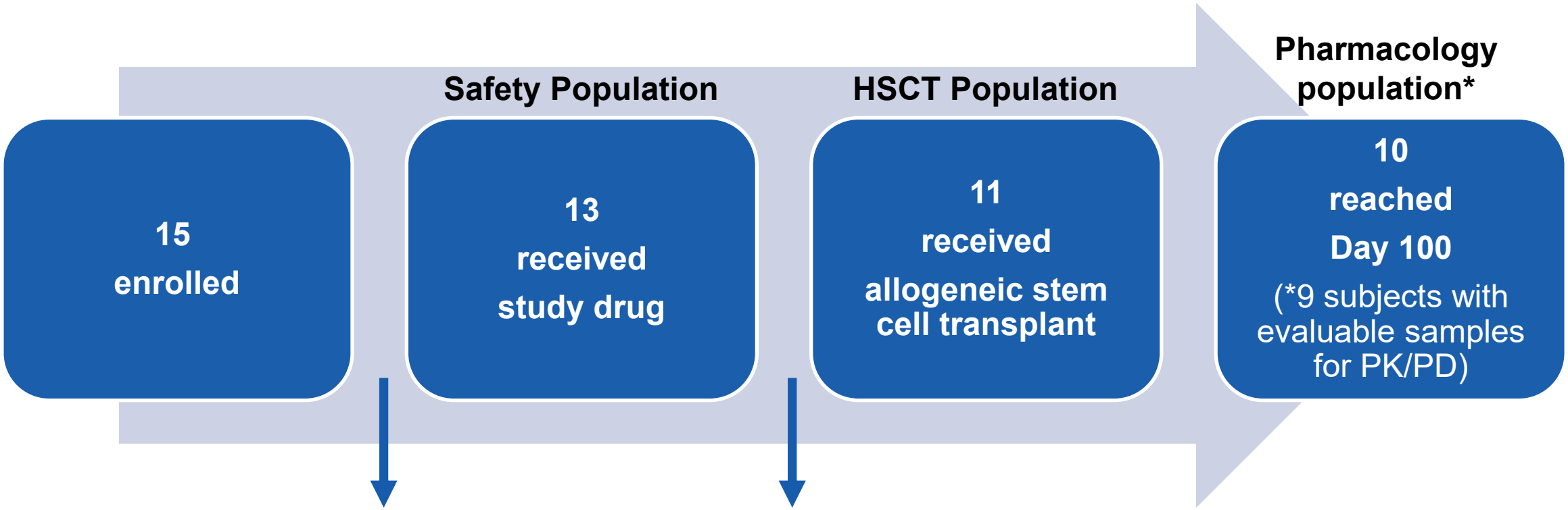
SER-155 Cohort 1 Enrollment Summary: Majority of Subjects Retained Post Transplant



SER-155 Was Generally Well-Tolerated in Cohort 1 (Day 100 Data)

TEAEs observed as expected in this patient population

- All subjects experienced at least 1 TEAE
- 1 TEAE resulted in study discontinuation (unrelated to SER-155 administration)
- GI disorders were most common, with diarrhea being the most common AE

No SAEs were considered related to SER-155

- No SUSARs observed
- Majority of SAEs and AESIs occurred during vulnerable time for patients (from HSCT to neutrophil recovery, start of SER-155 Course 2)

Data Safety Monitoring Board approved advancement to Cohort 2

- Data Safety Monitoring Board met at predefined points, including at Day 100 data cut for Cohort 1, to review all safety events
- No deaths prior to Day 100; 3 after Day 100, none considered related to drug

TEAE: treatment-emergent adverse event; SAE: serious adverse event; AESI: adverse event of special interest; SUSAR: suspected unexpected serious adverse reaction

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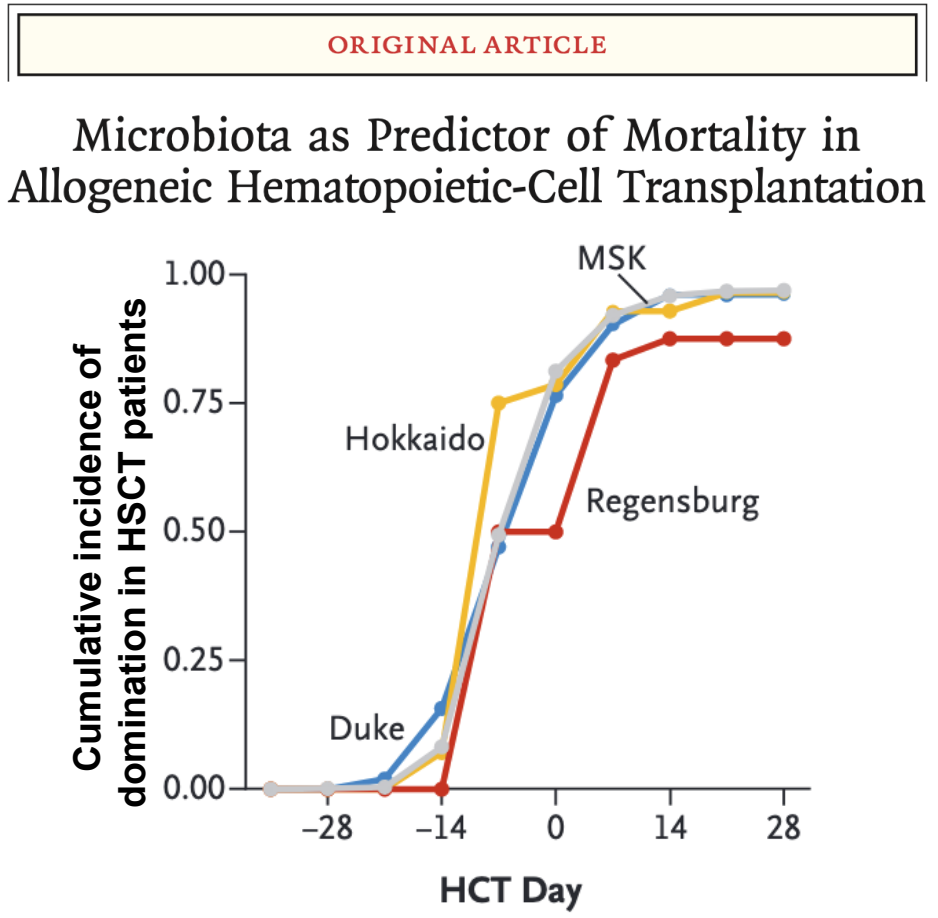
GI Microbiome Pathogen Domination as a Driver of Infection & GvHD in Allo-HSCT has been Reported in Peer-Reviewed Literature

Seres ongoing 7-year partnership with Memorial Sloan Kettering Cancer Center (MSKCC) to elucidate role of microbiome in HSCT:

Gastrointestinal (GI) microbiome domination, a state in which a **single type of bacteria is unusually abundant**, is a common occurrence in HSCT patients.

Cumulative incidence of GI microbiome **domination was observed in majority of subjects by Day 30** after HSCT*

- Similar rates were observed at 3 other centers
- Domination with ESKAPE pathogens was common



* Peled et al, NEJM 2020; Seres-supported study

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GI Microbiome Pathogen Domination is Associated with Worse Clinical Outcomes in Allo-HSCT Recipients

Domination **increases bloodstream infection risk** with the dominating bacteria*

Table 3. Association of Intestinal Domination With Bacteremia[a]

	VRE Bacteremia		Gram-negative Bacteremia	
Dominating Taxon[b]	HR (95% CI)	*P*	HR (95% CI)	*P*
Enterococcus	9.35 (2.43–45.44)	.001	1.35 (.25–5.08)	.690
Streptococcus	0.21 (.00–1.75)	.184	0.82 (.09–3.65)	.823
Proteobacteria	0.75 (.01–6.14)	.837	5.46 (1.03–19.91)	.047

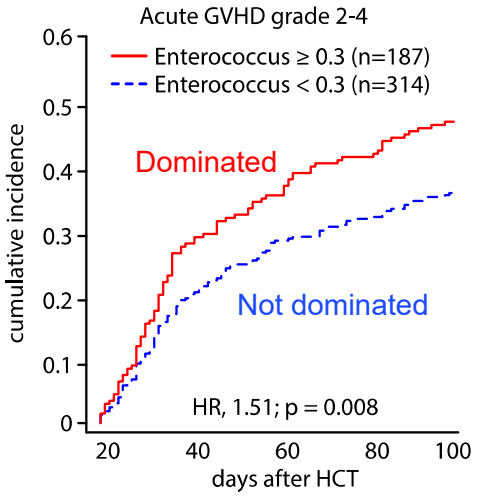
Abbreviations: CI, confidence interval; HR, hazard ratio; VRE, Vancomycin-resistant *Enterococcus*.

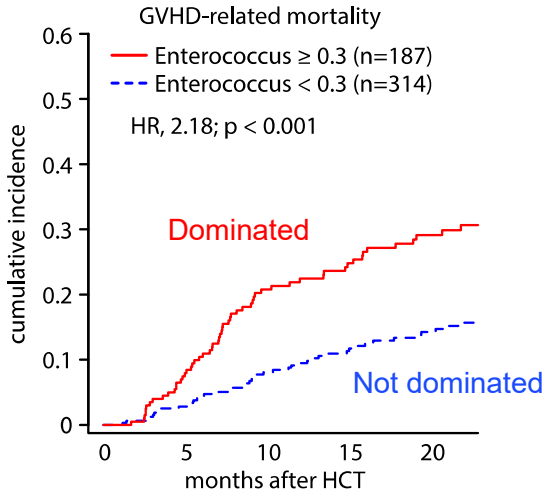
[a] Bacteremia for each organism was defined as at least one positive blood culture within the study period.

[b] Intestinal domination was analyzed as a time-varying predictor.

Taur *et al.*, *Clin Inf Dis* 2012

Enterococcus domination is a **risk factor for acute GvHD and mortality****





* Taur *et al*, Clin Inf Dis 2012; extended in Tamburini *et al* Nat Med, 2018
** Stein-Thoringer *et al* Science 2019; also supported by Jenq *et al* Bio BMT 2015

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ESKAPE Pathogen Domination was Rare and Transient in Cohort 1

ESKAPE pathogen domination* in SER-155 administered subjects observed at rates substantially lower than reference cohort

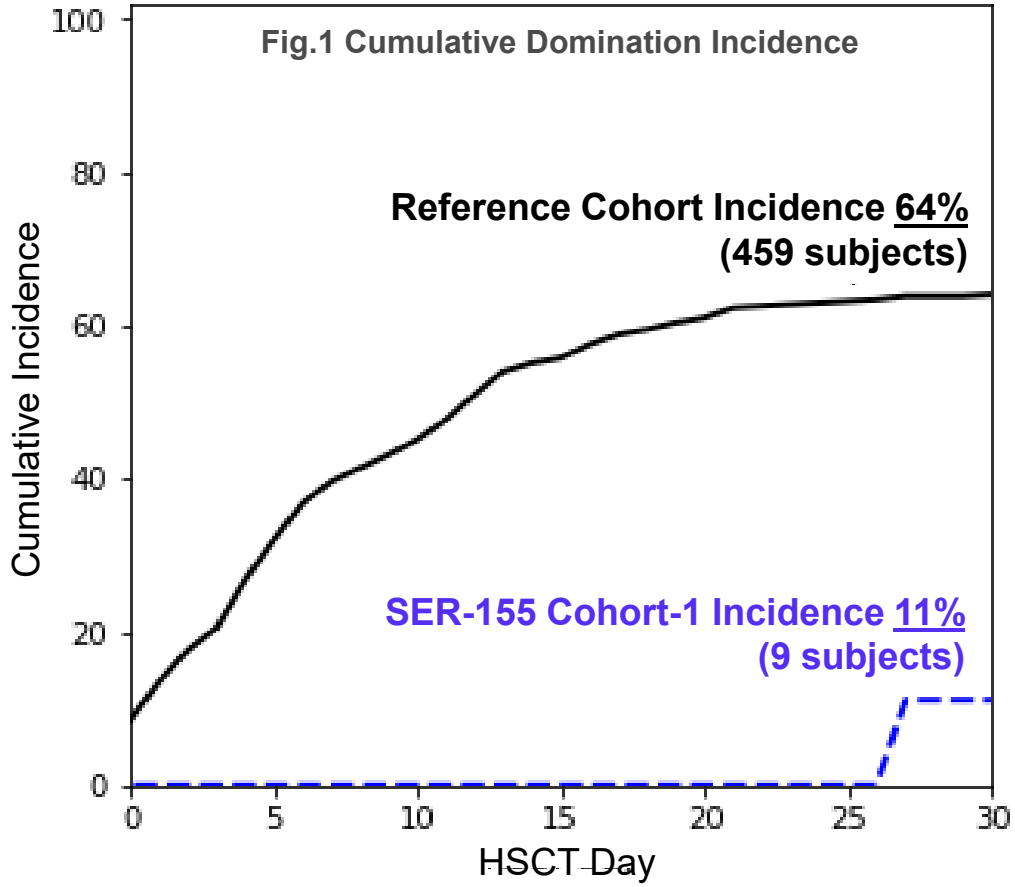
SER-155 Cohort 1

- From HSCT Day 0-30, 11% of patients (1 subject, **Fig.1** blue line)
- From HSCT day 0-100, 22% of patients (2 subjects, not shown)
- All instances of pathogen domination were transient

Reference Patient Cohort (MSKCC; Peled et al. 2020)

- Day 0 through 30, 64% of patients (Fig.1 black line)

Pathogen domination has been shown to be associated with risk of blood stream infections (Taur, CID 2012) and GvHD (Jenq Bio BMT 2015; Stein-Thoeringer Science 2019)



* i.e., the families: *Enterococcaceae, Enterobacteriaceae, Streptococcaceae & Staphylococcaceae*

SER-155 Bacterial Strains Engrafted in Cohort 1 Patients

Engraftment magnitude and kinetics were consistent with our expectations

Engraftment is the colonization of the GI tract by metabolically active drug product strains; assessed throughout the study period via proprietary genomic technologies.

Most of the strains engrafted in a majority of the individuals evaluated.

These engraftment data, as well as those that will come from Cohort 2, will be used to inform Phase 2 trial design.

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SER-155 Phase 1b Cohort 2: What We Expect to Learn

SER-155 safety, strain engraftment (PK) and pathogen abundance (PD) in the **context of placebo comparator arm**

Further elucidate **mechanism of action of SER-155**

Explore impact of **SER-155 on clinical outcomes**, including the incidence of enteric infections, BSI, BSI with enteric bacteria, and GvHD, with contemporaneous placebo rates

Broaden dosing experience in allo-HSCT patients to confirm optimal dosing strategy

Cohort 2 topline data expected in mid-2024

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SER-155 Could Become Core Part of Allogeneic HSCT Treatment Regimen

Unique potential clinical and economic value for allogeneic HSCT patients

Substantial impact for patients: almost 30,000 transplants / year across US and Europe

Favorable safety profile appropriate for use across HSCT population

Double benefit of reducing infections and GvHD, 2 of 3 leading causes of mortality at 1 year

Avoids costs of post-transplant complications: $181K average additional costs for US patients with complications

Sources: CIBMTR 2020; Passweg et al Bone Marrow Transplantation 57 (2022) 742-752; Perales et al Biol Blood Marrow Transplant 23 (2017) 1788–1794; Broder, et al. "The Cost of Hematopoietic Stem-Cell Transplantation in the United States" Am Health and Drug Benefits 10 (2017) 366–374; https://data.cms.gov/provider-summary-by-type-of-service/medicare-inpatient-hospitals/medicare-inpatient-hospitals-by-geography-and-service/data/2019; Seres physician interviews