CORPORATE PRESENTATION

January 2022

Forward-Looking Statements

Except for the historical information contained herein, this presentation contains forward-looking statements made pursuant to the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Investors are cautioned that such statements, include, without limitation, those regarding: (i) that for IMerge Phase 3, Geron Corporation ("Geron" or "the Company") expects top-line results to be available in early January 2023, regulatory filings in the United States ("U.S.") in the first half of 2023 and the European Union ("EU") in the second half of 2023, and a potential launch in lower risk MDS in the U.S. in the first half of 2024 and in the EU in the second half of 2024; (ii) for IMpactMF, that Geron expects to conduct an interim analysis in 2024 and a final analysis in 2025; (iii) for the next generation telomerase inhibitor program Geron plans to make a program update in 2022 when and if Geron identifies a lead compound and IND timing is known; (iv) that Geron expects its financial resources, with the projected funding under a current debt facility, to fund operations, including the new imetelstat indications and telomerase inhibition program, through the end of the first quarter of 2023; (v) that Geron plans to engage over 180 sites for IMpactMF; (vi) that IMerge Phase 3 and IMpactMF have registrational intent; (vii) that imetelstat has the potential to demonstrate disease-modifying activity in patients and to target the malignant stem and progenitor cells of the underlying disease; (viii) that the Company expects imetelstat to be a highly differentiated product in the lower risk MDS commercial marketplace; (ix) that the Company projects that the addressable patients in 2030 for imetelstat in LR MDS are approximately 33,000 and for Int-2/HR MF are approximately 18,000; (x) that the Company believes imetelstat has potential large market opportunities with potential peak 2030 revenue from the United States and the five largest countries of the European Union ("EU5") of approximately $3 billion, with $1.2 billion from MDS sales and $1.8 billion from MF sales; (xi) that there are unmet needs in LR MDS and MF potentially addressed with imetelstat treatment; (xii) that the telomerase inhibition of imetelstat gives it the potential for expanding into new indications; (xiii) that the Company expects the first clinical site for IMproveMF to open in the first half of 2022; (xiv) that the Company expects IMpress to begin in the first half of 2022; (xv) that the Company expects TELOMERE to begin in the first half of 2022; (xvi) that the Company expects preliminary results from the preclinical program in lymphoid malignancies to be available at the end of 2022; (xvii) statements regarding potential exclusivity terms and scopes provided by patent and patent term extensions, orphan drug, data and marketing and pediatric coverages; (xviii) that the Company expects to report that, as of December 31, 2021, it had cash, cash equivalents, restricted cash and marketable securities of approximately $210.0 million and a principal outstanding balance of $50.0 million in long-term debt; (xix) Geron's vision to transform the treatment of hematologic malignancies and become a leader in the field ;and (xx) other statements that are not historical facts, constitute forward-looking statements. These forward-looking statements involve risks and uncertainties that can cause actual results to differ materially from those in such forward-looking statements. These risks and uncertainties, include, without limitation, risks and uncertainties related to: (a) whether the current or evolving effects of the COVID-19 pandemic and resulting global economic and financial disruptions will materially and adversely impact Geron's business and business prospects, its financial condition and the future of imetelstat; (b) whether Geron overcomes all of the potential delays and other adverse impacts caused by the current or evolving effects of the COVID-19 pandemic, and overcomes all the enrollment, clinical, safety, efficacy, technical, scientific, intellectual property, manufacturing and regulatory challenges in order to have the financial resources for, and to meet the expected timelines and planned milestones in (i) to (iii) and (xiii) to (xvi) above; (c) whether regulatory authorities permit the further development of imetelstat on a timely basis, or at all, without any clinical holds; (d) whether imetelstat is demonstrated to be safe and efficacious in IMerge Phase 3 and IMpactMF to enable regulatory approval; (e) whether any future efficacy or safety results may cause the benefit-risk profile of imetelstat to become unacceptable; (f) whether imetelstat actually demonstrates disease-modifying activity in patients and the ability to target the malignant stem and progenitor cells of the underlying disease; (g) that Geron may seek to raise substantial capital in order to complete the development and commercialization of imetelstat to meet all of the expected timelines and planned milestones in (i) to (iii) and (xiii) to (xvi) above; (h) whether regulatory authorities require an additional clinical trial for approval even if IMerge Phase 3 or IMpactMF meet their respective primary endpoints; (i) whether there are failures or delays in manufacturing or supplying sufficient quantities of imetelstat or other clinical trial materials in a timely manner; (j) whether imetelstat is able to obtain and maintain the exclusivity terms and scopes provided by patent and patent term extensions, orphan drug, data and marketing and pediatric coverages and have freedom to operate; (k) whether the follow-up period of 12 months for the IMerge Phase 3 primary analysis results in not obtaining adequate data to demonstrate safety and efficacy, including transfusion independence, in the primary analysis; (l) whether Geron can accurately project the timing of complete enrollment in its clinical trials, whether due to the current or evolving effects of the COVID-19 pandemic or otherwise; (m) whether Geron is able to enroll its clinical trials at a pace that would enable the financial resources for, and to meet the expected timelines and planned milestones in (i) to (iii) and (xiii) to (xvi) above; (n) that Geron may be unable to successfully commercialize imetelstat to achieve the peak revenues in (x) above due to competitive products, or otherwise; (o) the completion of financial closing procedures, final audit adjustments and other developments that may arise that would cause the Company's expectations in (xviii) above to differ, perhaps materially, from the financial results that will be reflected in the Company's audited financial statements for the year ended December 31, 2021; and (p) if the FDA does not grant priority review to the IMerge data, then the launch date in lower risk MDS may be later than the first half of 2024. Additional information on the above risks and uncertainties and additional risks, uncertainties and factors that could cause actual results to differ materially from those in the forward-looking statements are contained in Geron's filings and periodic reports filed with the Securities and Exchange Commission under the heading "Risk Factors" and elsewhere in such filings and reports, including Geron's quarterly report on Form 10-Q for the quarter ended September 30, 2021 and future filings and reports by Geron. Undue reliance should not be placed on forward-looking statements, which speak only as of the date they are made, and the facts and assumptions underlying the forward-looking statements may change. Except as required by law, Geron disclaims any obligation to update these forward-looking statements to reflect future information, events or circumstances.

Geron's Vision

Transform the Treatment of Hematologic Malignancies and Become a Leader in the Field

Top-line results from IMerge Phase 3 lower risk MDS trial expected in early January 2023; potential U.S. launch as early as 2024 with a highly differentiated profile

Demonstrate an overall survival benefit in ongoing IMpactMF Phase 3 refractory MF trial; interim analysis expected in 2024

Strategically invest in new hematologic indications and treatment combinations for imetelstat

Commercialize imetelstat in lower risk MDS and refractory MF with annual peak revenue potential of ~$3 billion expected in 2030 in the US and EU5

MDS, myelodysplastic syndromes; MF, myelofibrosis; EU5, key five European Union markets

References on slide 26

Imetelstat and Telomerase Inhibitor Pipeline

Strategically Investing in New Indications and Treatment Combinations

Indications	Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Expected Milestones
LR MDS *Single agent*					IMerge	Top-Line Results: Early Jan 2023
Refractory MF *Single agent*					IMpactMF	Interim Analysis: 2024 Final Analysis: 2025
Frontline MF *Combination therapy*			IMproveMF			First Patient In: 1H 2022
R/R AML & HR MDS *Single agent*				IMpress		First Patient In: 1H 2022
R/R AML *Combination therapy*			TELOMERE			First Patient In: 1H 2022
Lymphoid Malignancies						Initial Data: Year End 2022
Next Generation TI Program						Program Update: 2022

Ongoing; Company Sponsored Planned; Company Sponsored Planned; Investigator Sponsored

MDS, myelodysplastic syndromes; MF, myelofibrosis; R/R AML, relapsed/refractory acute myeloid leukemia; HR MDS, higher risk MDS; TI, telomerase inhibitor

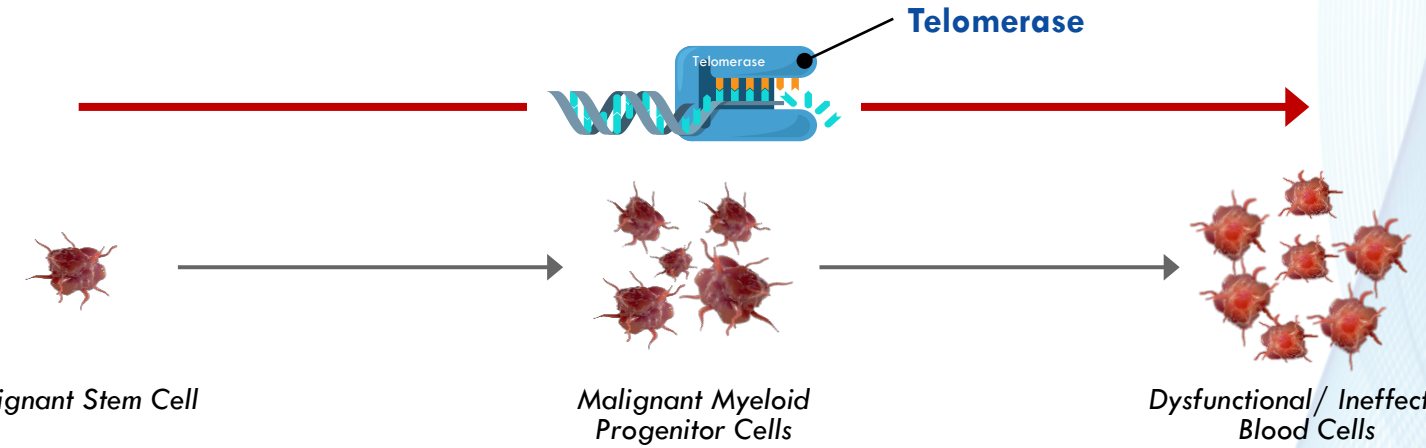
See Appendix 2 for additional information on IMproveMF, IMpress, TELOMERE, lymphoid malignancies and next generation TI program

IMETELSTAT: A TELOMERASE INHIBITOR WITH DISEASE-MODIFYING POTENTIAL

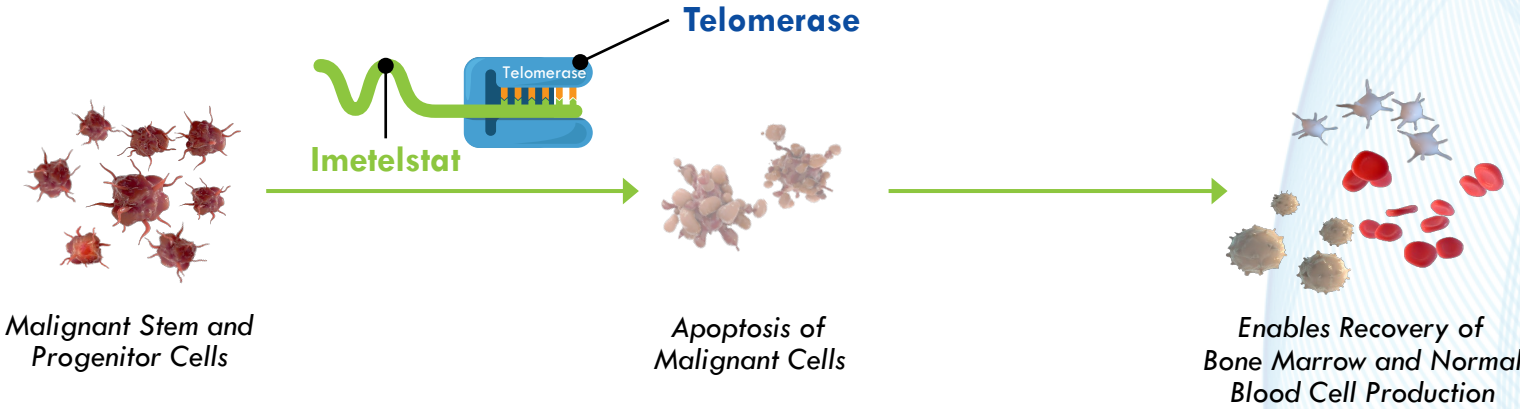
Telomerase – A Critical Target in Hematologic Malignancies

Inhibition of Telomerase by Imetelstat Results in Potential Disease Modification

Telomerase Continually Upregulated in Malignant Cells Enabling Their Uncontrolled Proliferation



Imetelstat Inhibits Telomerase Leading to Selective Killing of Malignant Cells



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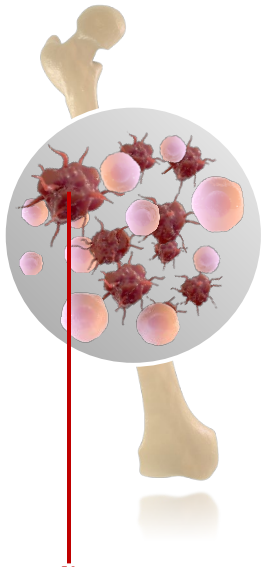
IMETELSTAT IN LOWER RISK MDS

Lower Risk Myelodysplastic Syndromes (LR MDS)

Durable TI, Ability to Treat Both RS+ve and RS-ve Patients and Disease Modification Needed

Disease Characteristics



Malignant stem and progenitor cells in bone marrow result in ineffective blood production (anemia) and disease progression

Chronic Transfusion-Dependent Anemia

Patient Subgroups Include:

Ring Sideroblast Positive (RS+ve)

Ring Sideroblast Negative (RS-ve)

High Transfusion Burden (4-6 units/8wks)

Very High Transfusion Burden (>6 units/8wks)

Current Unmet Needs

- Higher rate of transfusion independence (TI)
- Durable transfusion independence
- Ability to treat both RS+ve and RS-ve patients
- Disease-modifying therapy

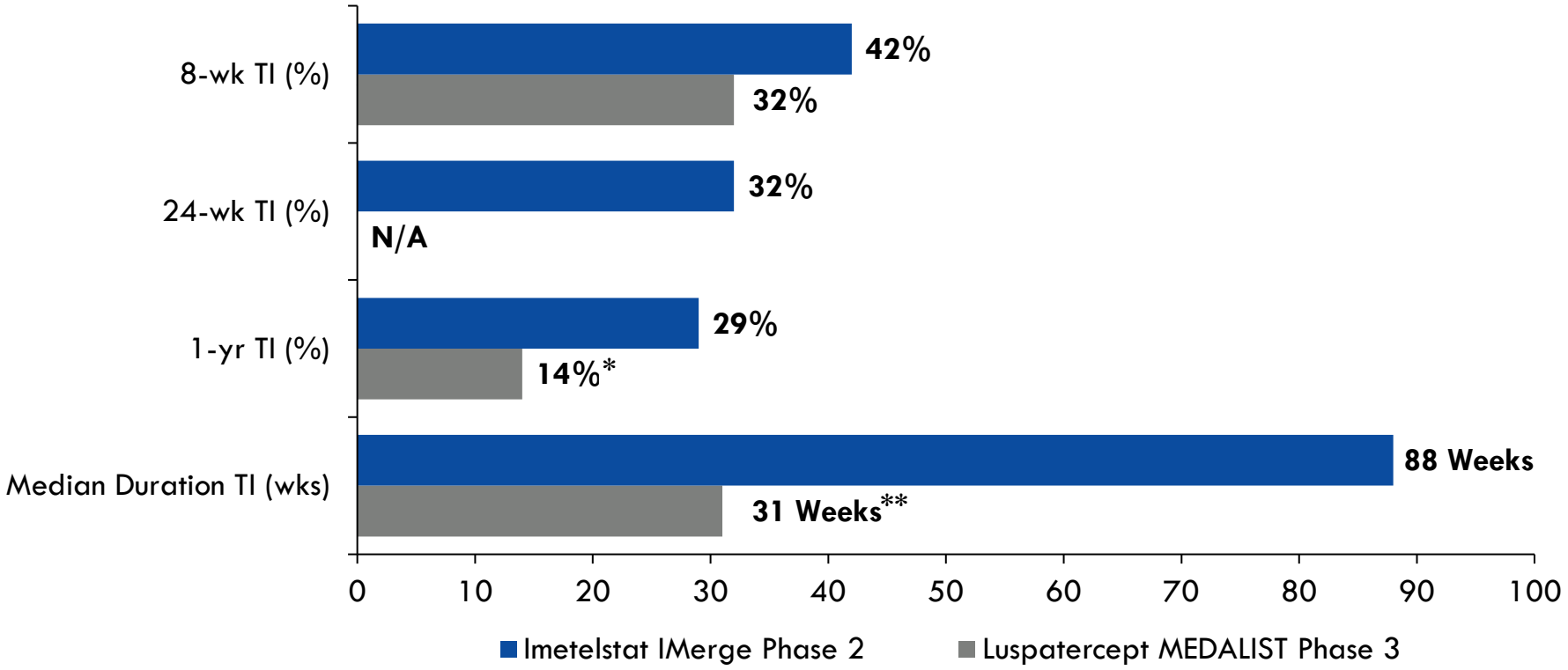
Current Treatment Paradigm

- Initial treatment with erythropoiesis stimulating agents (ESAs) mostly fail after 2+ years
- Patients relapsed/refractory (R/R) to ESAs become RBC transfusion dependent
- Treatment options for R/R ESA patients include:
  - Reblozyl (luspatercept) labeled for use in RS+ve patients only; 8-wk TI rate: 32%; worldwide sales ~$400M through Q3 '21
  - Hypomethylating agents (HMAs); 8-wk TI rate: 17%
  - Lenalidomide approved only for deletion (5q) patients

References on slide 26

Depth and Durability of Transfusion Independence in IMerge Phase 2

Imetelstat (IMerge Phase 2, RS+ve and RS-ve) and Luspatercept (MEDALIST Phase 3, RS+ve)
Patients with Baseline Transfusion Burden ≥4 units/8wks



*Reported as 14% for MEDALIST patient population with baseline transfusion burden ≥2 units/8wks; MEDALIST data not available for patients with baseline transfusion burden ≥4 units/8wks

**Reported as median duration of TI for the 58/153 (38%) of luspatercept-treated patients in MEDALIST with baseline transfusion burden ≥2U/8wk who achieved a TI ≥8 weeks during study weeks 1-24

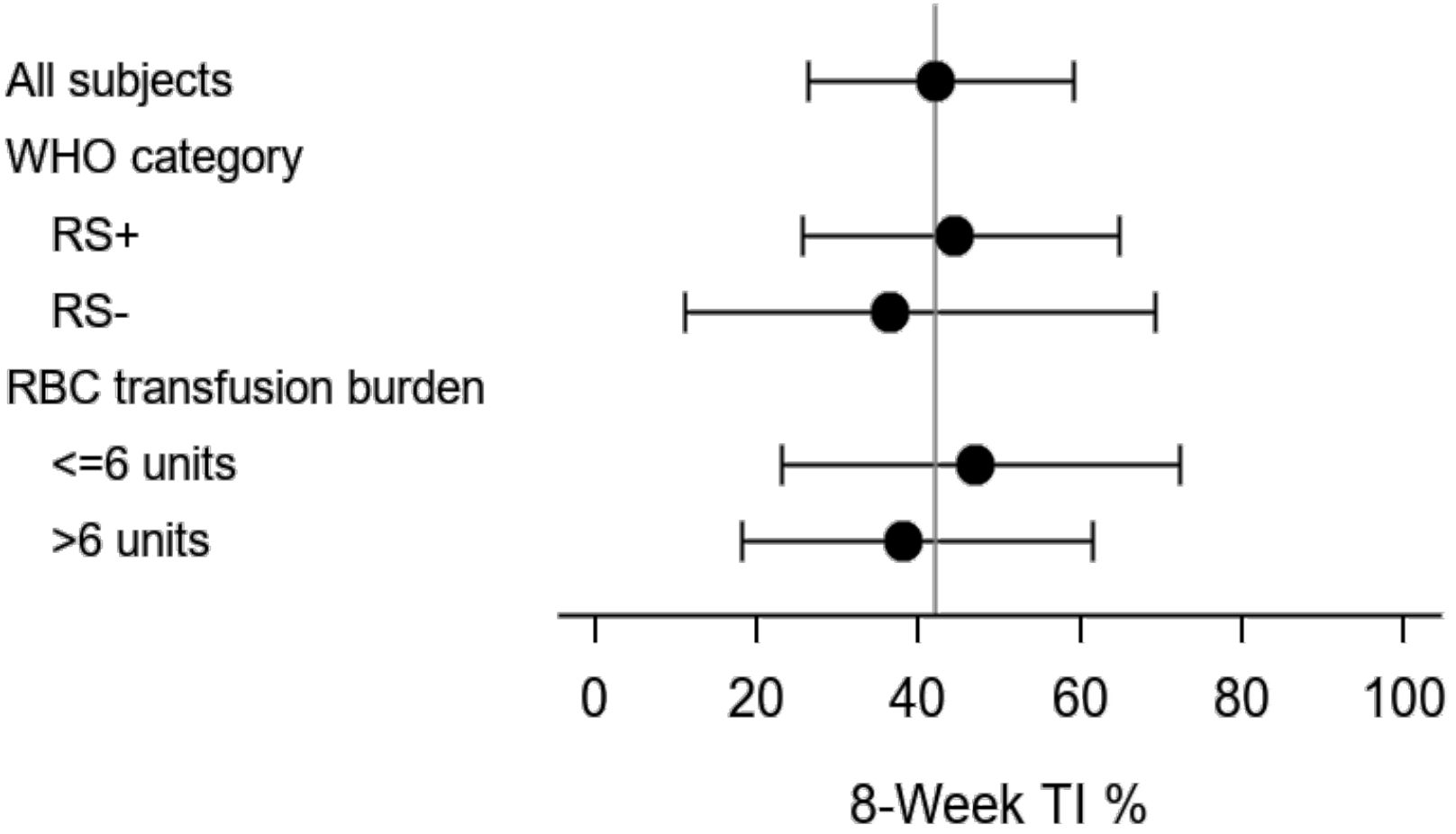
Comparative MEDALIST Phase 3 data provided for informational purposes only and should not be relied upon as demonstrative or indicative of imetelstat's potential in LR MDS. There are several limitations when comparing results from an open-label Phase 2 trial to a blinded, placebo-controlled Phase 3 trial with a significantly greater patient population; in addition, luspatercept is an approved treatment with a relatively benign safety profile. MEDALIST sponsor – Celgene/Acceleron

References on slide 26

Efficacy Results in IMerge Phase 2 Across Patient Subgroups

ClinicalTrials.gov (NCT02598661)

Similar 8-Wk TI Rates Across RS+ve and RS-ve Patients and High/Very High Transfusion Burden Patients



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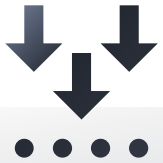
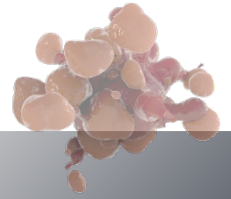
Strong Evidence of Imetelstat Disease-Modifying Activity in IMerge Phase 2

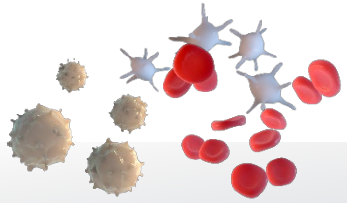
ClinicalTrials.gov (NCT02598661)

Depletion of Mutated Malignant Cells Correlates with Clinical Benefits

	Telomerase Activity Inhibited in Imetelstat-Treated Patients	**Killing of Malignant Cells**	**Recovery of Bone Marrow and Normal Blood Cell Production**	**Clinical Benefits**
MDS	Reduction in telomerase activity correlated with clinical benefits confirms MOA	Depletion of mutated and cytogenetically abnormal malignant cells correlated with greater 8-wk TI and longer duration of TI	Long duration of transfusion independence (TI); ≥3g/dL rise in hemoglobin in 75% of responders	• **42% 8-wk TI** • **29% 1-year TI** • **88 wks (~1.8 yrs) median duration of TI**







See Appendix 1 for additional data

References on slide 26

Imetelstat Safety Profile in IMerge Phase 2

Cytopenias Manageable and Reversible with Limited Clinical Consequences

TEAE	All Grades N=38 (n, %)	Grade 3/4 N=38 (n, %)
Hematologic AEs (≥20% in either arm)		
Thrombocytopenia	25 (66)	23 (61)
Neutropenia	22 (58)	21 (55)
Anemia	11(29)	8 (21)
Non-hematologic AEs (≥15% in either arm)		
Back Pain	9 (24)	2 (5)
ALT Increased	7 (18)	2 (5)[a]
AST Increased	6 (16)	3 (8)[a]
Bronchitis	6 (16)	3 (8)
Headache	6 (16)	1 (3)
Asthenia	6 (16)	1 (3)
Other AEs[b]	6 (16)	0

Hematologic adverse events were treatment emergent, per reported adverse events (not laboratory values). Frequency of reported Grade 3/4 hematologic adverse events was consistent with cytopenias reported through laboratory values. For nonhematologic adverse events, the number and frequency of patients per reported adverse events are shown.

[a] No Grade 4 LFT elevations; all Grade 3 LFT elevations were reversible; [b] nasopharyngitis, diarrhea, constipation, and edema peripheral

References on slide 26

Most common adverse events (AEs) are on target Grade 3/4 thrombocytopenia and neutropenia:

- **Median time to onset:** 4 weeks (~1 cycle)
- **Median duration:** <2 weeks
- **Reversible:** >85% within 4 weeks
- **Manageable with dose hold and modifications**
- **Limited clinical consequences:**
  - 5% Grade 3/4 febrile neutropenia
  - 8% Grade 3/4 bleeding

IMerge
ClinicalTrials.gov (NCT02598661)

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IMerge Phase 3 Trial Focuses on Durability of Transfusion Independence

Top-Line Results (TLR) Expected in Early January 2023

IMerge
ClinicalTrials.gov (NCT02598661)

- Broad patient enrollment
  - RS-ve and RS+ve
  - ESA ineligible
  - Luspatercept-experienced
- Designed to confirm Phase 2 results including broad, durable transfusion independence by using the same:
  - Patient population
  - Dose and schedule of administration
  - Primary and secondary endpoints
- Designed with >85% power to detect statistically significant difference in 8-wk TI rate between placebo and imetelstat (one-sided alpha=0.025)
  - For example: an 8-wk TI rate of 7.5% in the placebo arm vs. 30% in the imetelstat arm

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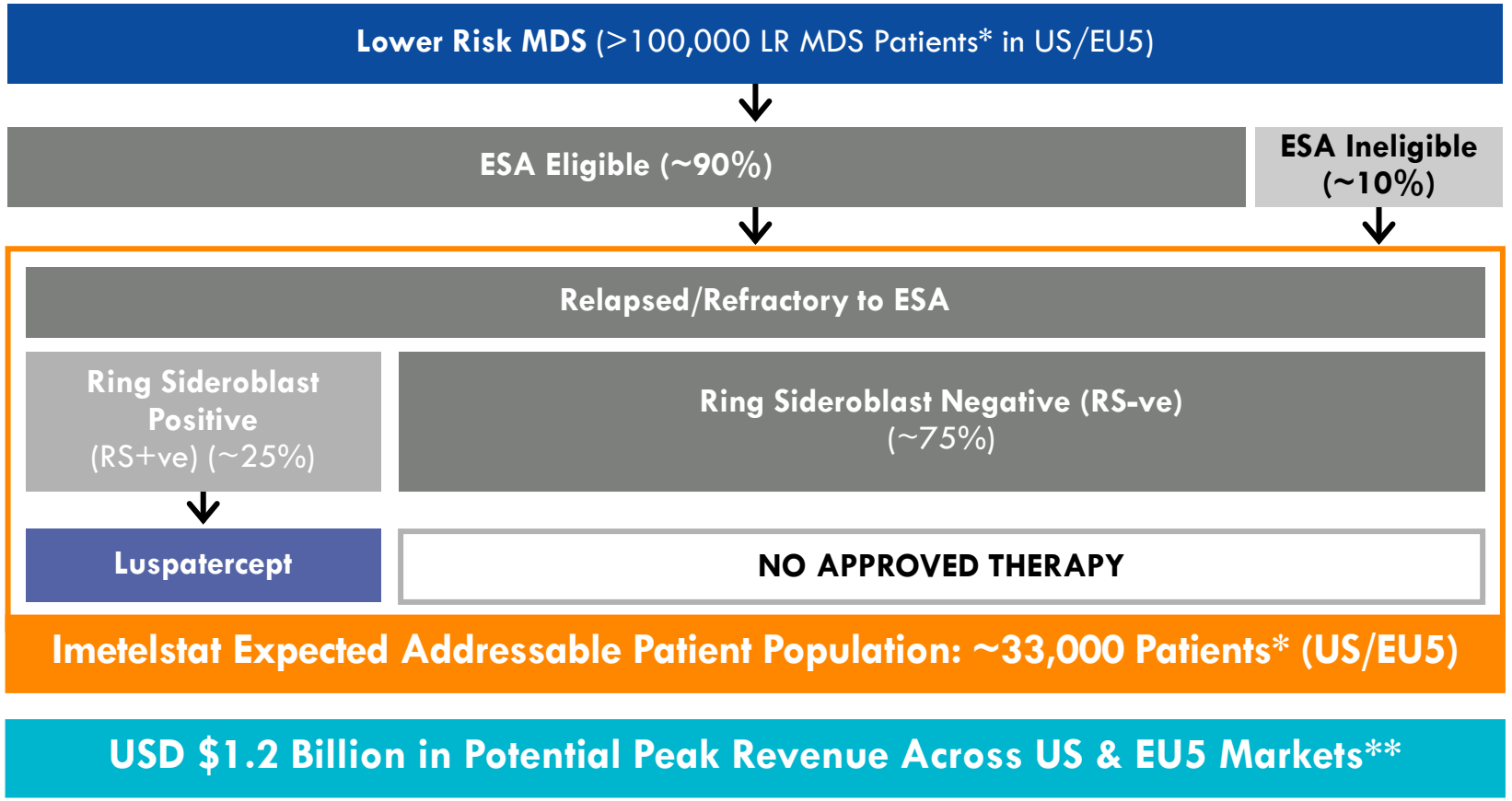
Expected Broad Imetelstat Opportunity in LR MDS

Patients Relapsed/Refractory to ESAs Expected to be Addressable by Imetelstat



ESA, erythropoiesis stimulating agent; Reblozyl – tradename for Celgene/Merck's drug luspatercept

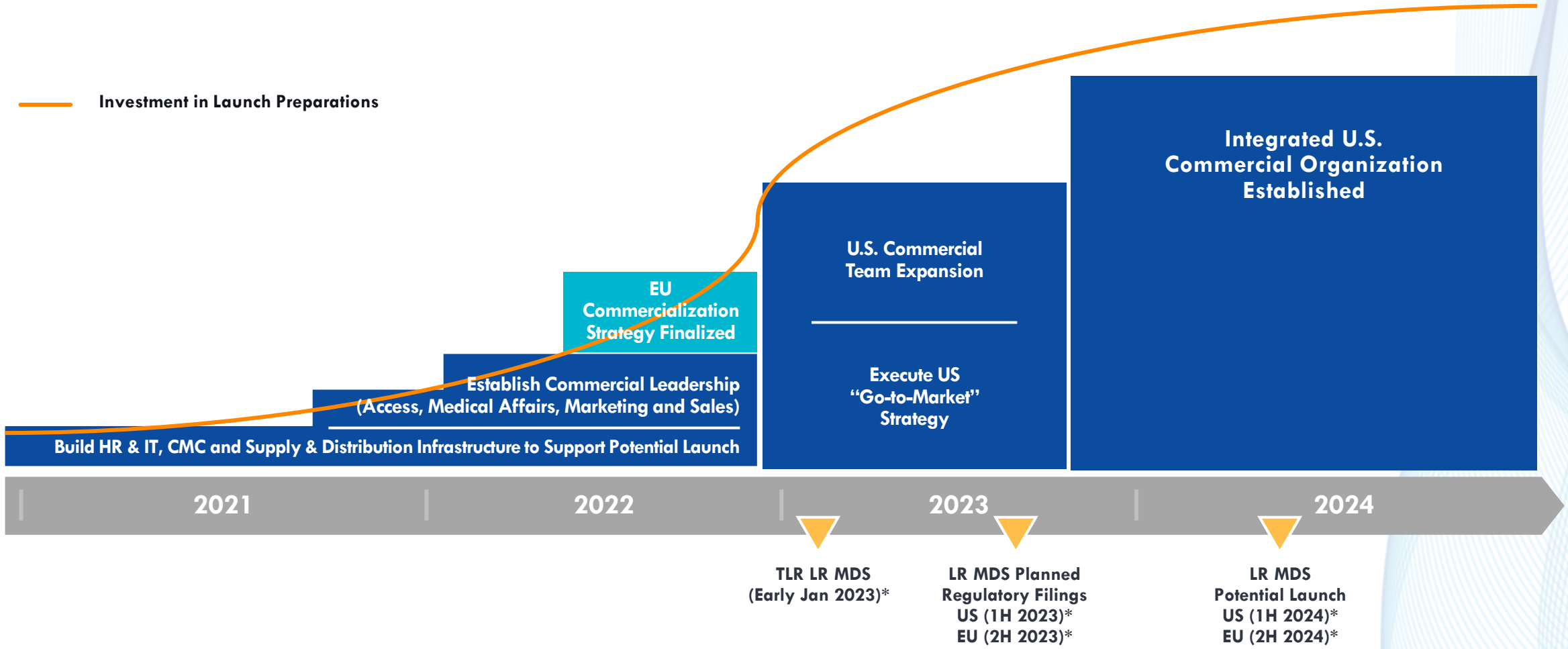
* Company projections in 2030

** Company projections in 2030: based on treated prevalence estimates for imetelstat eligible patient populations in LR MDS; DRG syndicated data, Payor research (US/EU5) and Geron analysis using assumptions for a) expected target product profile at launch, b) obtaining regulatory approvals and favorable reimbursement in US and key European markets, c) duration of treatment and d) potential market penetration

References on slide 26

Preparations to Become a Commercially Capable Company

Comprehensive, Milestone-Driven, Stage-Gated Plan



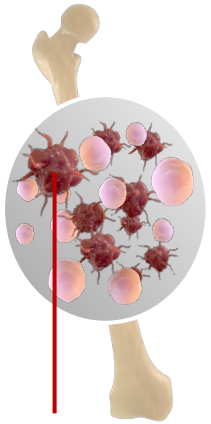
* Expected timing
TLR, top-line results

IMETELSTAT IN REFRACTORY MF

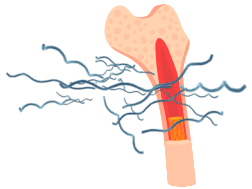
Intermediate-2/High-Risk (Int-2/HR) JAKi Refractory Myelofibrosis

A Disease with Limited Treatment Options and Poor Survival

Disease Characteristics

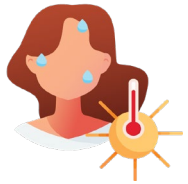


Malignant stem and progenitor cells in bone marrow continue to proliferate despite JAKi treatment, resulting in disease progression



Bone Marrow Fibrosis

Symptoms (fever, weight loss, night sweats)



Splenomegaly

Current Unmet Needs

- Treatment option for patients who are refractory to JAK inhibitor (JAKi) therapy
- Disease-modifying therapy
- Improvement in overall survival (OS)

Current Treatment Paradigm

- Only approved therapies in the US are JAKis – ruxolitinib and fedratinib
- Most patients eventually become refractory to JAKis with 75% discontinuation rate in 5 yrs
- Dismal survival (median OS ~14 – 16 months) after discontinuation from ruxolitinib due to suboptimal response or loss of therapeutic effect

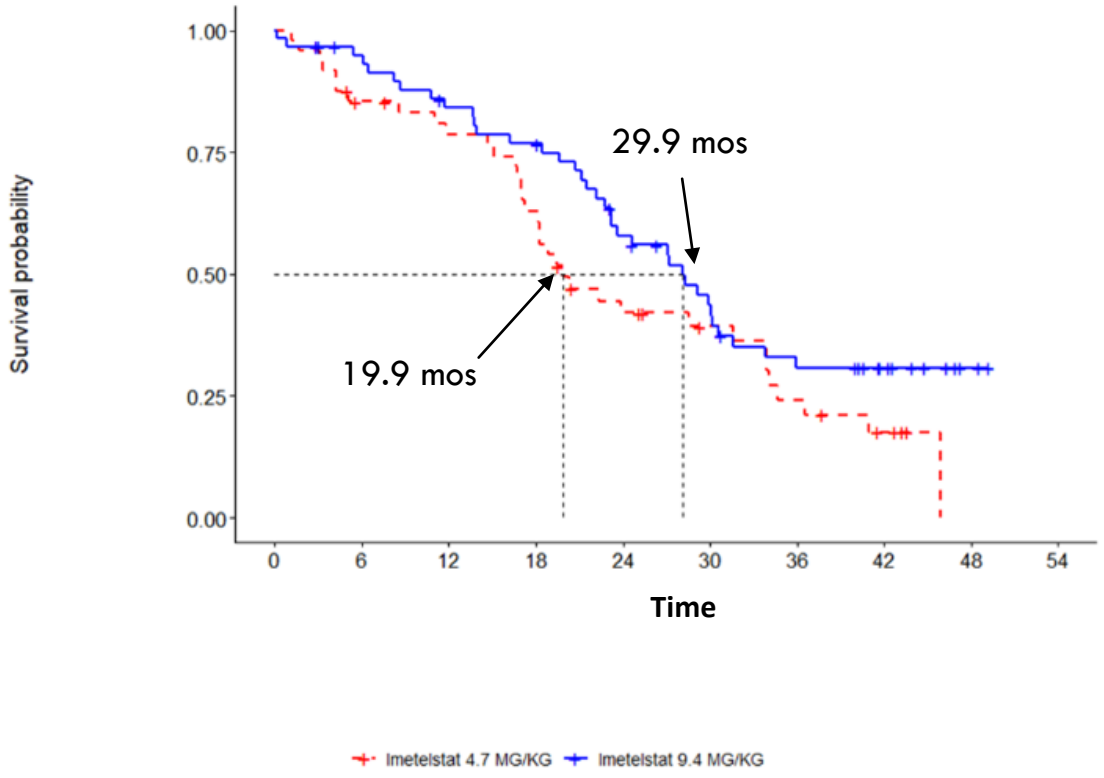
References on slide 26

OS Improvement in JAKi Relapsed/Refractory MF Patients

Median Overall Survival (OS) in IMbark Phase 2 Compares Favorably to Historical Controls

ClincialTrials.gov (NCT02426086)

Imetelstat 4.7 mg/kg vs 9.4 mg/kg



Improvement in overall survival in 9.4 mg/kg arm

- 29.9 mos median OS in 9.4 mg/kg arm compares favorably to historical controls of 14 – 16 mos for JAKi refractory patients
- 9.4 mg/kg administered every 3 weeks is being used in IMpactMF Phase 3 trial

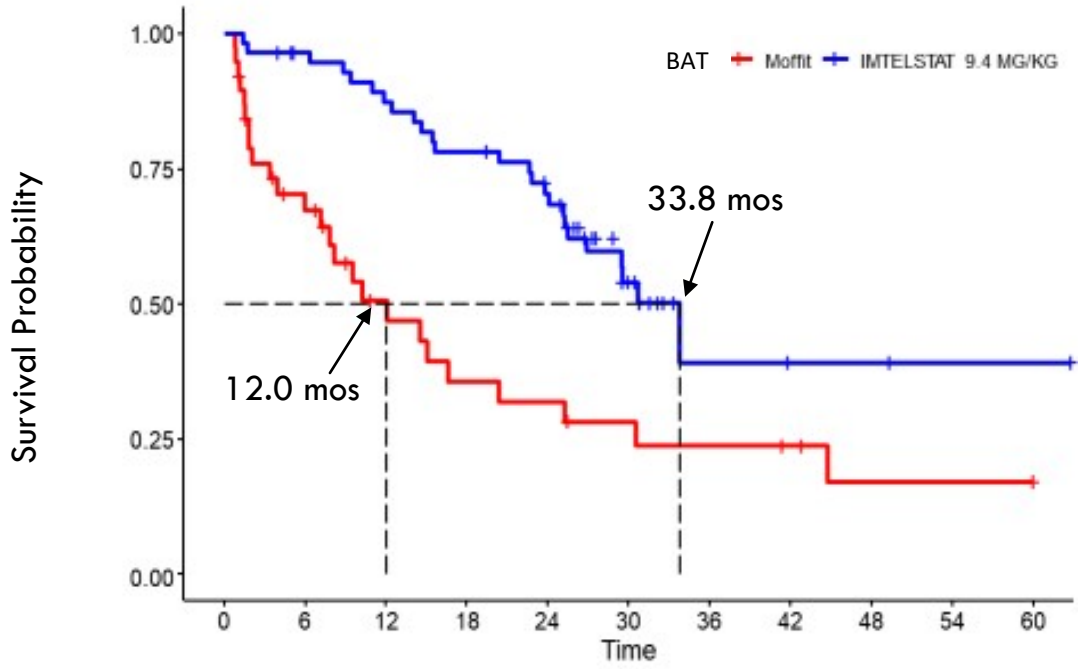
References on slide 26

OS Improvement in Real-World Data Study of Refractory MF Patients

ClincialTrials.gov (NCT02426086)

Median OS More Than Double Compared to BAT Treatment in Real-World Data (RWD)

RWD BAT vs. Imetelstat 9.4 mg/kg



Acknowledging the limitations of such comparative analyses between RWD and clinical trial data, we believe the favorable OS of imetelstat treatment suggested by these comparative analyses in this very poor prognosis patient population warrants further evaluation.

Study designed to evaluate imetelstat benefit vs. BAT treatment in JAKi refractory MF patients

- IMbark Phase 2 data compared to RWD from a closely-matched cohort of patients at the Moffitt Cancer Center who had discontinued ruxolitinib and were subsequently treated with best available therapy (BAT)

Improvement in overall survival (OS) and lower risk of death for imetelstat vs. BAT in RWD study

- Imetelstat: 33.8 mos median OS
- BAT RWD: 12.0 mos median OS
- 65% lower risk of death with imetelstat compared to BAT from RWD

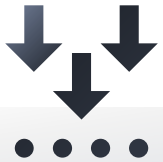
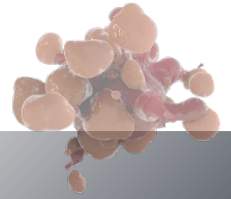
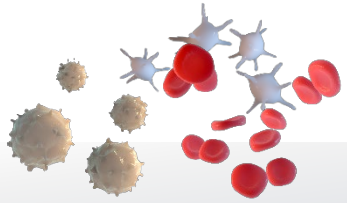
Data support IMpactMF Phase 3 trial design

References on slide 26

Strong Evidence of Imetelstat Disease-Modifying Activity in IMbark Phase 2

ClincialTrials.gov (NCT02426086)

Clinical Benefits Correlated with Decreased Telomerase Activity and Depletion of Malignant Cells

	Telomerase Activity Inhibited in Imetelstat-Treated Patients	**Killing of Malignant Cells**	**Recovery of Bone Marrow and Normal Blood Cell Production**	**Clinical Benefits**
				
Myelofibrosis	Reduction in telomerase activity correlated with clinical benefits	Depletion of cells with key driver mutations and abnormal cytogenetics correlated with improved OS	Improvements in bone marrow fibrosis correlated to improved OS	• **Improved overall survival (OS)** • **Improved symptoms**

See Appendix 1 for additional data

References on slide 26

Imetelstat Safety Profile in IMbark Phase 2

Cytopenias Manageable and Reversible with Limited Clinical Consequences

IMbark

ClincialTrials.gov (NCT02426086)

n (%)	9.4 mg/kg (n=59)	
	All Grades	Grade ≥ 3
Hematologic (≥10% in either arm)*		
Thrombocytopenia	29 (49)	24 (41)
Anemia	26 (44)	23 (39)
Neutropenia	21 (36)	19 (32)
Non-hematologic (≥20% in either arm)		
Nausea	20 (34)	2 (3)
Diarrhea	18 (31)	0
Fatigue	16 (27)	4 (7)
Dyspnea	14 (24)	3 (5)
Abdominal Pain	14 (24)	3 (5)
Asthenia	14 (24)	6 (10)
Pyrexia	13 (22)	3 (5)
Edema peripheral	11 (19)	0

* Treatment emergent, per reported AEs (not laboratory values). Frequency of reported Grade 3/4 hematologic AEs were consistent with cytopenias reported through lab values.

Thrombocytopenia and neutropenia characterization:

- **Median time to onset:** 9 weeks (~3 cycles)
- **Median duration:** ≤2 weeks
- **Reversible:** >70% within 4 weeks
- **Manageable with dose hold and modifications**
- **Limited clinical consequences:**
  - 2% Grade 3 febrile neutropenia
  - 5% Grade 3/4 hemorrhagic events
  - 10% Grade 3/4 infections

References on slide 26

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IMpactMF – Global Phase 3 Trial in Refractory MF

IMpactMF

ClincialTrials.gov
(NCT0457615)

Actively Enrolling Patients Now

- First and only Phase 3 trial in MF with OS as primary endpoint
- BAT treatment options in IMpactMF include BAT options similar to those used in the RWD study
- Designed with >85% power to detect a 40% reduction in the risk of death in the imetelstat treatment arm compared to the BAT arm (hazard ratio=0.60; one-sided alpha=0.025)
  - For example: median OS of 14 mos for the BAT arm vs. 23 mos for the imetelstat arm
- Interim Analysis expected in 2024 when ~35% of the patients planned to be enrolled have died; alpha spend ~0.01
- Final Analysis expected in 2025 when more than 50% of the patients planned to be enrolled have died

References on slide 26

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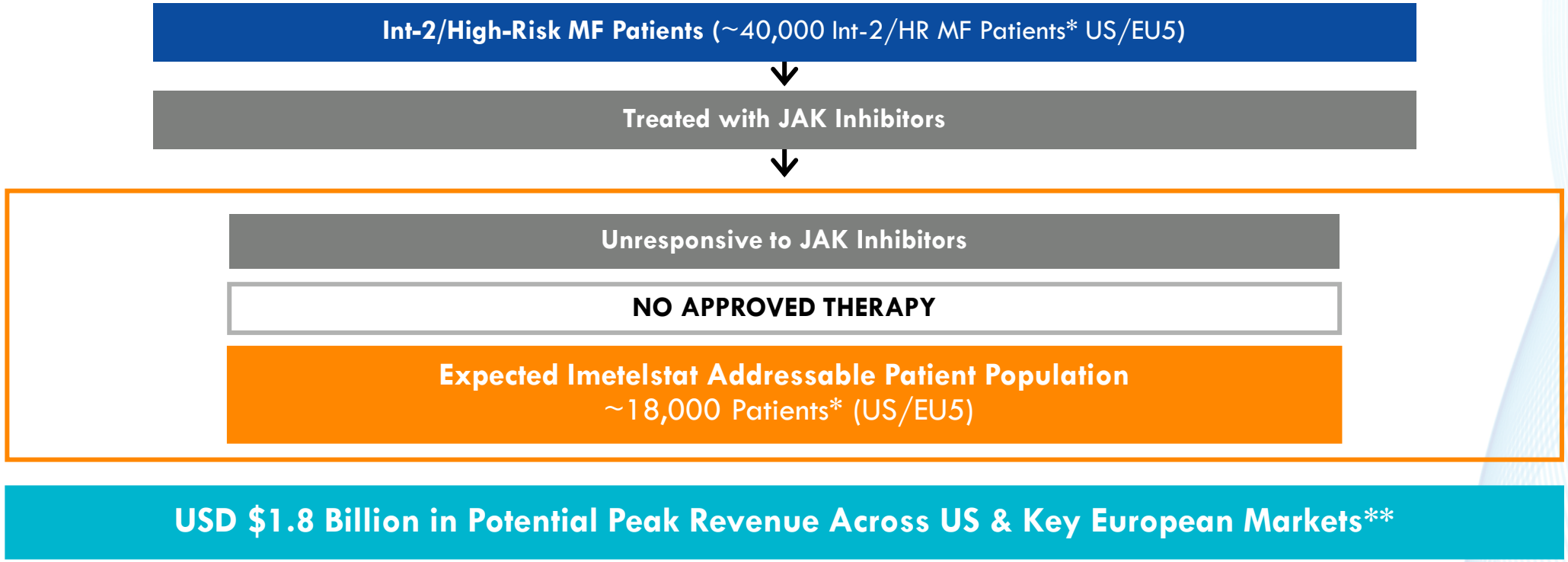
Expected MF Market Evolution and Imetelstat Opportunity

JAKi-Treated Patients Expected to Become Refractory to JAKis and Addressable by Imetelstat

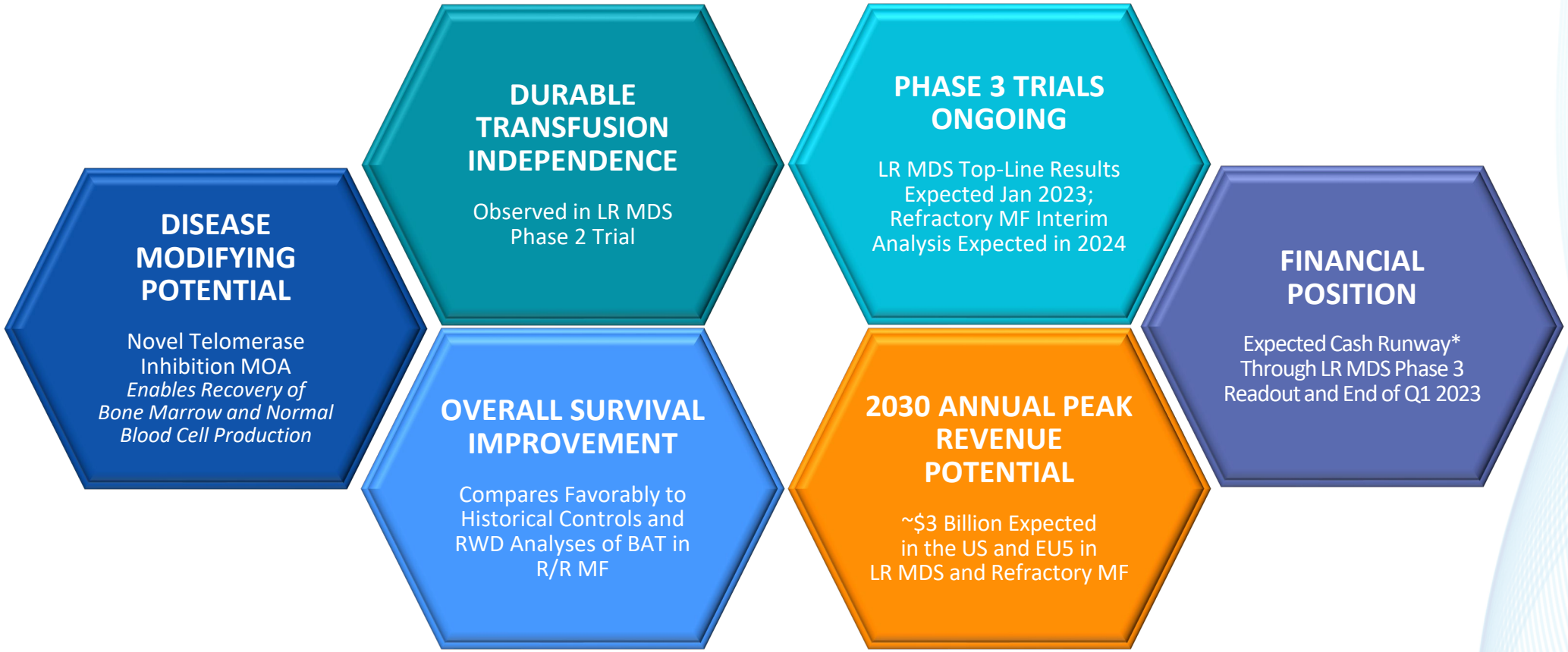


* Company projections in 2030

**Company projections in 2030 in Int-2/HR MF based on treated prevalence estimates for imetelstat eligible patient populations in Int-2/HR MF (2030); DRG syndicated data, US/G5 payor research and Geron analysis using assumptions for a) expected target product profile at launch, b) obtaining regulatory approvals and favorable reimbursement in US and key European markets, c) duration of treatment and d) potential market penetration; Company estimate does not include Int-1 & platelets <50K pts.

References on slide 26

Geron Take-Aways



* Geron expects to report cash, cash equivalents, restricted cash and marketable securities of approximately $210.0 million and a principal outstanding balance of $50.0 million in long-term debt as 12/31/21

References on slide 26

MOA, mechanism of action; LR MDS, lower risk MDS; RWD, real-world data; BAT, best available therapy; R/R MF, relapsed/refractory myelofibrosis; MF, myelofibrosis; EU5, key five European Union markets

In the U.S.: expected orphan drug protection seven years from approval; composition of matter patent coverage expires Dec 2025 with potential patent term extension until 2030; extended patent term coverage of an additional six months for LR MDS as allowed under pediatric extension; and methods of use patent coverage until 2033 for MDS and MF

In Europe: expected data/marketing exclusivity 10 years from date of approval for first indication; composition of matter patent coverage expires Sep 2024; expected orphan drug exclusivity 10 years from date of approval of each indication and extended orphan drug exclusivity up to two years for LR MDS as allowed under pediatric extension; and methods of use patent coverage until 2033 for MDS and MF

THANK YOU

If you have any questions,
please contact us:
investor@geron.com

References

Slide #	Reference	Slide #	Reference	Slide #	Reference
3	Company estimates	17	Newberry et al, Blood 2017; Kuykendall et al, Annals of Hematol 2018; Schieber et al, Blood Cancer Journal 2019; Spiegel et al, Blood Advances 2017; BMS Q3 2021 financial results; Company market research	28	Steensma et al, JCO 2020
6	Hiyama et al, J Immunol 1995; Hiyama et al, Br J Cancer 2007; Bruedigam et al, Cell Stem Cell 2014; Mosoyan et al, Leukemia 2017; Wang et al, Blood Adv 2018; Company data	18	Mascarenhas et al, JCO 2021	29	Mascarenhas et al, JCO 2021
8	Greenberg et al, Blood 2012; Park et al, JCO 2017; Cogle et al, Curr Hematol Malig Rep 2015; Greenberg et al, Blood 1997; Tobiasson et al, Blood Cancer Journal 2014; Fenaux et al NEJM 2020 Supplement Appendix; Santini et al, JCO 2016; Acceleron Q3 2021 conference call; Company market research	19	Kuykendall et al, Annals of Hematol 2021	30	Mascarenhas et al, ASH 2020
9	Platzbecker et al, ASH 2020; Steensma et al JCO 2020; Fenaux et al, ASH 2019; Fenaux et al, NEJM 2020 Supplement Appendix	20	Mascarenhas et al, JCO 2021; Mascarenhas et al, ASH 2018 and 2020; Kiladjian et al, ASH 2020	31	Mascarenhas et al, ASH 2020
10	Steensma et al, JCO 2020; Platzbecker et al, ASH 2020	21	Mascarenhas et al, JCO 2021; Mascarenhas et al, ASH 2018 and 2020; Mascarenhas et al, EHA 2021	33	Hu et al, ASH 2019
11	Steensma et al, JCO 2020; Platzbecker et al, ASH 2020	22	IMpactMF clinical trial protocol	34	Bruedigam et al, Cell Stem Cell 2014; Bruedigam et al, ASH 2017
12	Steensma et al, JCO 2020; Platzbecker et al, ASH 2020	23	Kuykendall et al, Annals of Hematol 2018; Newberry et al, Blood 2017; Schieber et al, Blood Cancer Journal 2019; Decision Resources; Company market research; Company estimates	35	Rusbuldt et all, AACR 2016; Rusbuldt et all, AACR 2017; Company data
13	IMerge clinical trial protocol	24	Steensma et al, JCO 2020; Mascarenhas et al, JCO 2021; Kuykendall et al, Annals of Hematol 2021; Company market research; Company estimates	36	Chevret et al, Blood 2014; Arekawa et al, Cancer Med 2021
14	Incidence and Outcomes for Lower Risk MDS, ASH 2012; Greenberg et al, Blood 2012; Malcovati et al, Blood 2013; Platzbecker et al, Blood 2019; NCCN Guidelines v2, 2021; MDS Landscape and Forecast, DRG Clarivate, Nov 2020; Company market research; Company estimates				

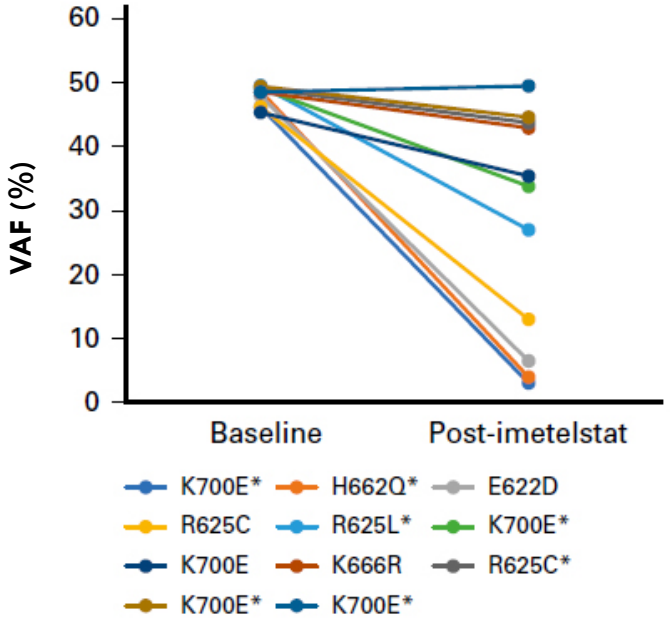
APPENDIX 1
EVIDENCE OF DISEASE MODIFICATION POTENTIAL

Strong Evidence of Disease Modification Potential

Imetelstat Results in Reduction of Malignant Clones in IMerge Phase 2

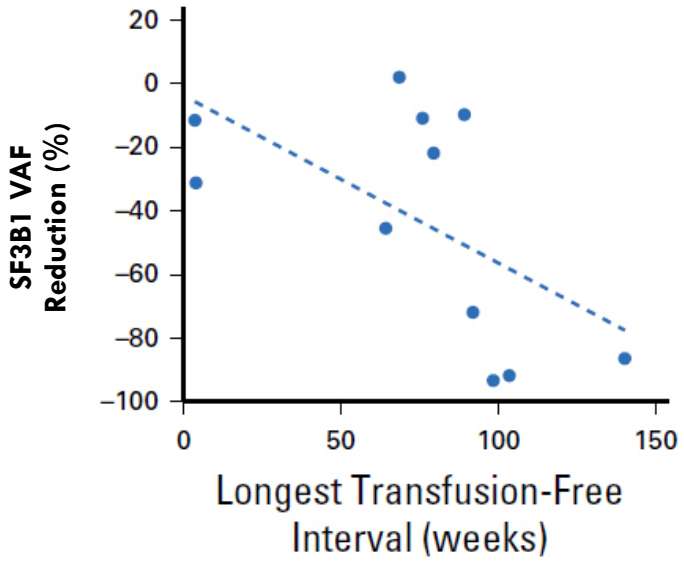
IMerge
ClinicalTrials.gov (NCT02598661)

A Change in VAF of SF3B1 Mutations



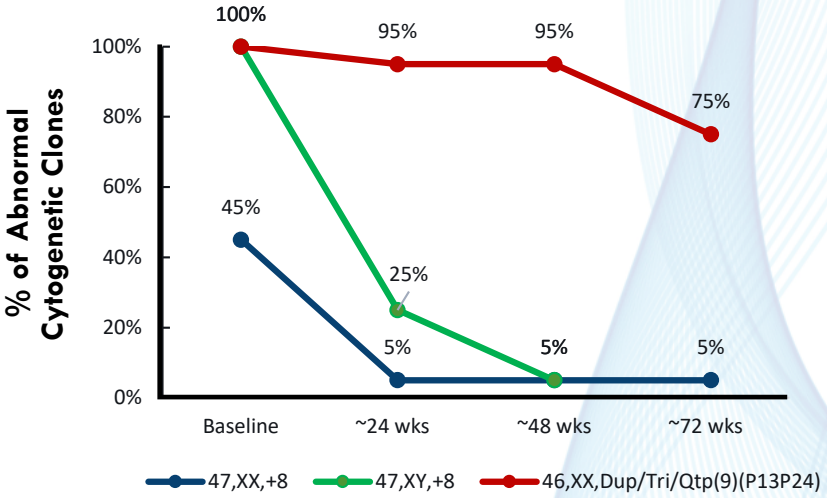
Reduction of SF3B1 mutation burden in LR MDS patients treated with imetelstat

B Percent SF3B1 VAF Reduction vs. Longest TI Duration



Greater SF3B1 variant allele frequency reduction (VAF) correlates with longer duration of TI

C Imetelstat Reduces Abnormal Cytogenetic Clones



Patients with abnormal cytogenetics at baseline have reduction of their clones and long (>1year) TI; 2 of 3 patients achieved partial cytogenetic response

References on slide 26

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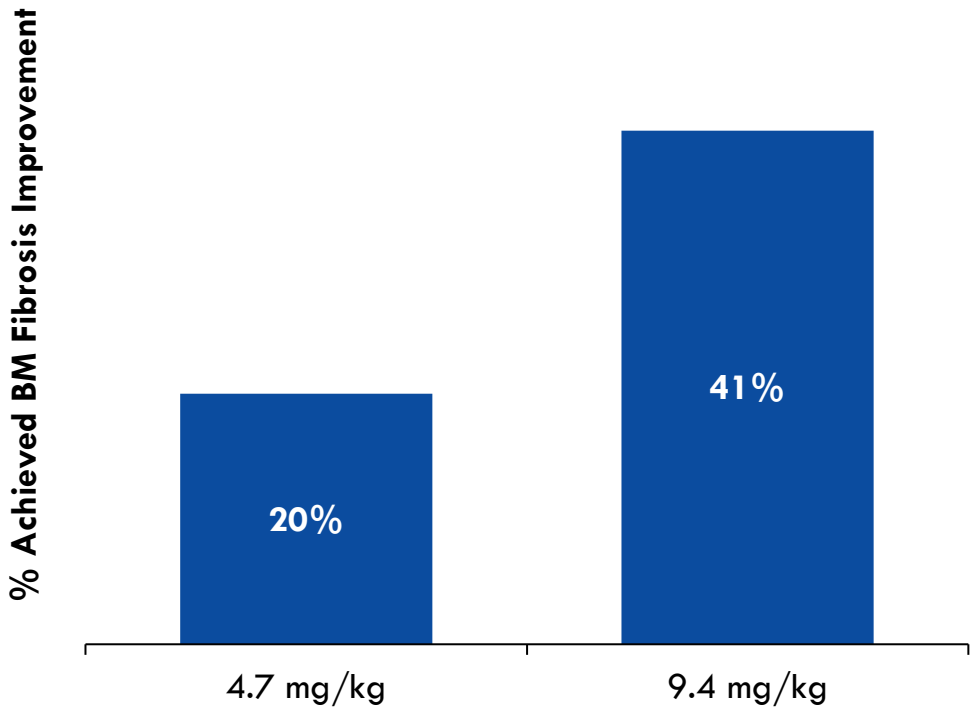
Strong Evidence of Disease Modification Potential:

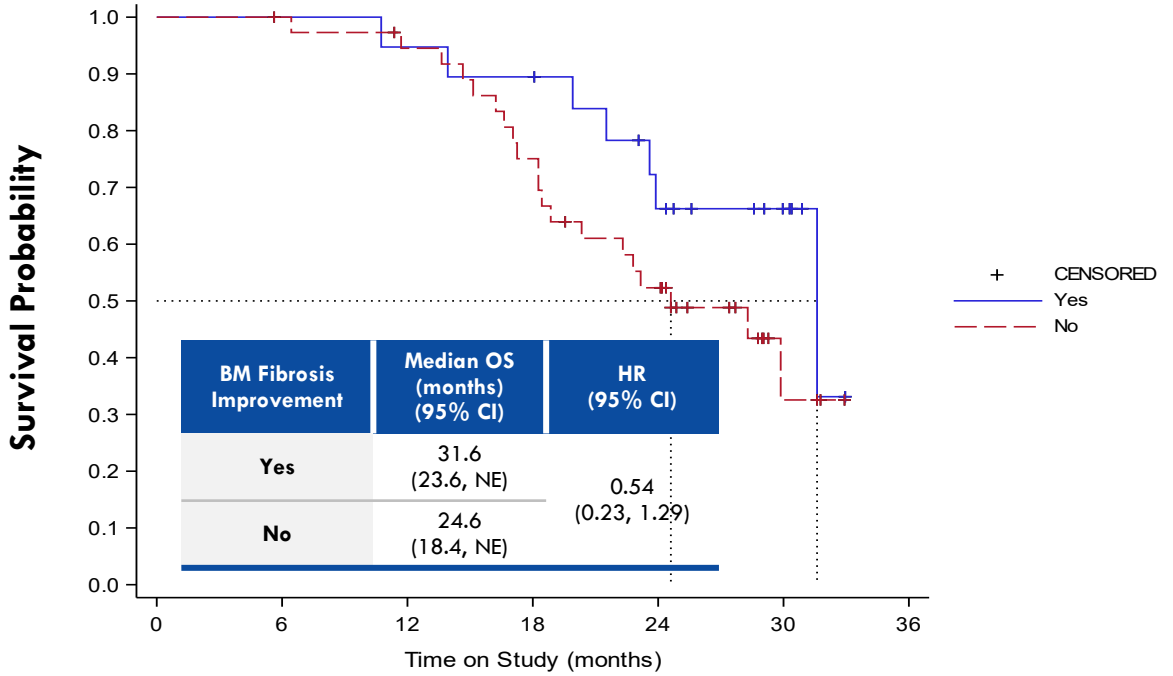
Improved Bone Marrow Fibrosis Correlated to Improved Survival in IMbark Phase 2

ClinicalTrials.gov (NCT02426086)

Significant Dose-Dependent Fibrosis Improvement with Imetelstat Treatment



Longer Median OS and Higher Survival Rate in Patients with Improved Fibrosis



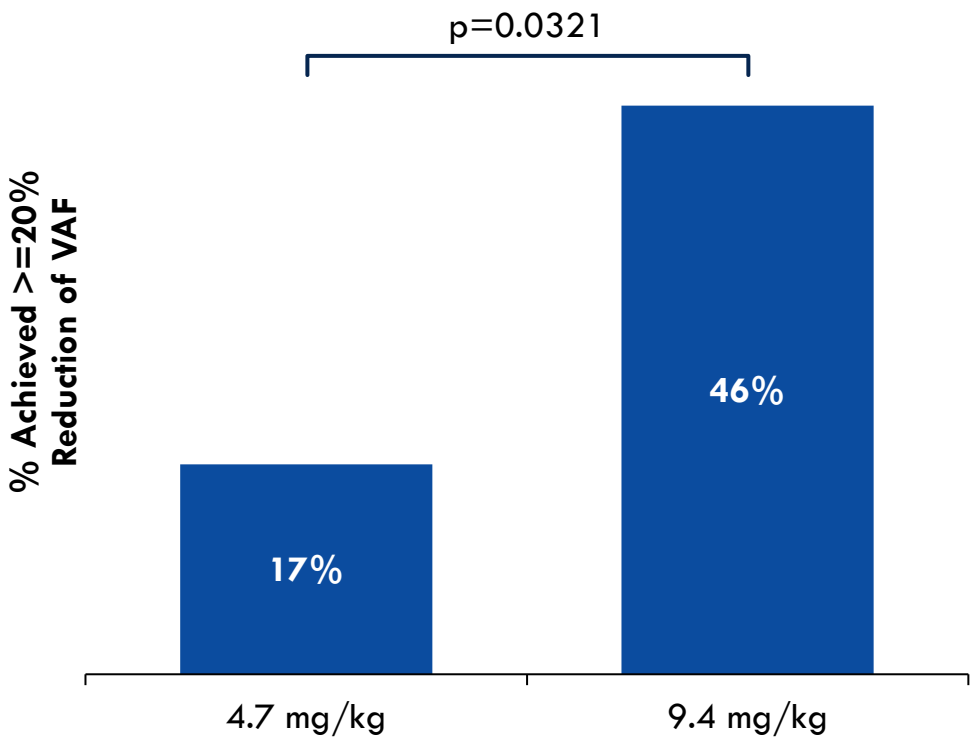
References on slide 26

Strong Evidence of Disease Modification Potential

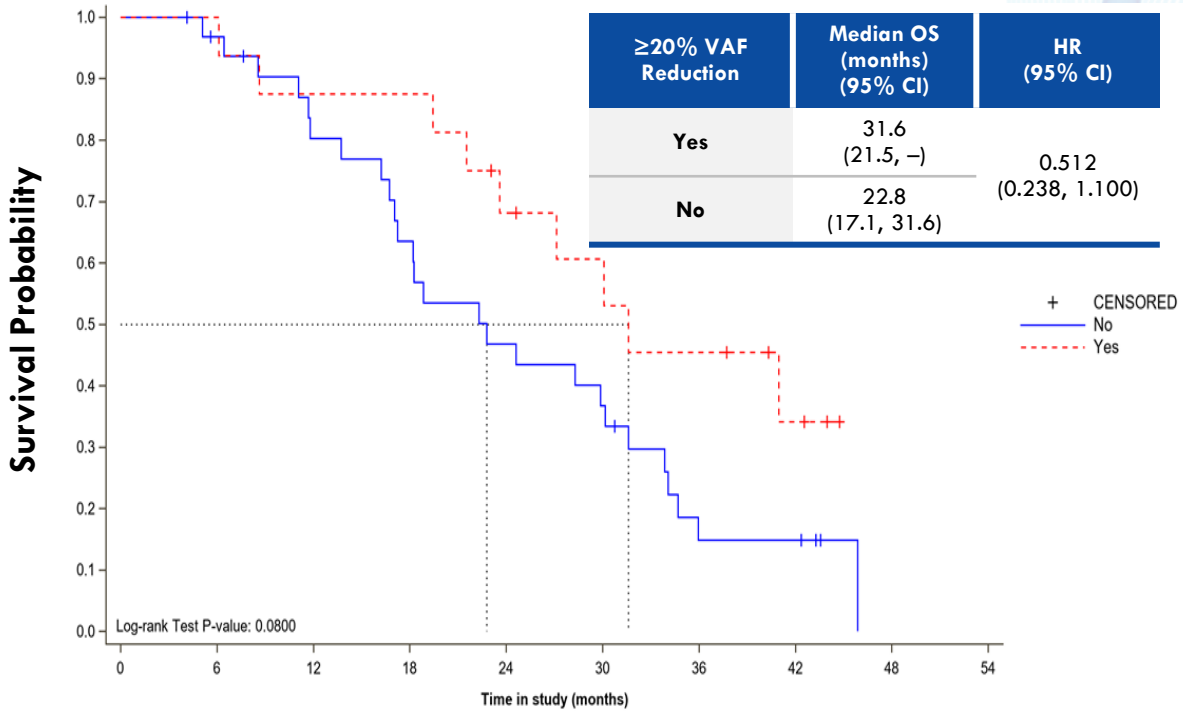
Reduction in Key MF Driver Mutations Correlated to Improved Survival in IMbark Phase 2

ClincialTrials.gov (NCT02426086)

Significant Dose-Dependent ≥20% VAF Reduction with Imetelstat Treatment



Longer Median OS and Higher Survival Rate in Patients Who Achieved ≥ 20% VAF Reduction



≥20% VAF Reduction	Median OS (months) (95% CI)	HR (95% CI)
Yes	31.6 (21.5, –)	0.512 (0.238, 1.100)
No	22.8 (17.1, 31.6)	

VAF, variant allele frequency

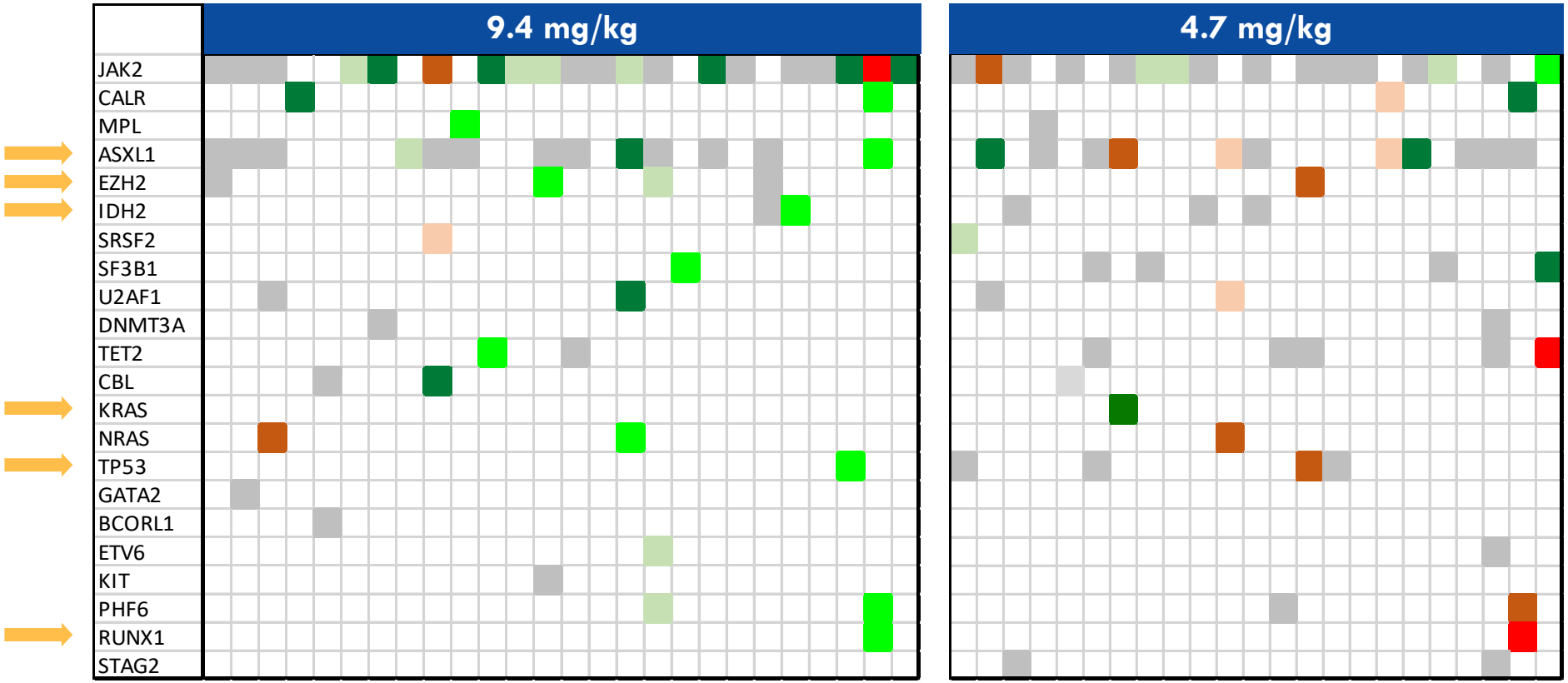
References on slide 26

Strong Evidence of Disease Modification Potential

Malignant Clones Reduced in Imetelstat-Treated Patients in IMbark Phase 2

ClincialTrials.gov (NCT02426086)

Dose-Dependent Complete Elimination of Mutation Burden from Multiple Driver- and Non-Driver Genes



- Mutation status and variant allele frequency (VAF) were evaluated by next-generation sequencing (NGS) using Illumina TruSight Myeloid Sequencing Panel of 54-genes
- Lower limit detection is 5% and 2% for well documented hotspots
- 49 pts had matched pre- and at least a post-imetelstat treatment NGS data

References on slide 26

APPENDIX 2
LIFE CYCLE MANAGEMENT (LCM) PROGRAMS

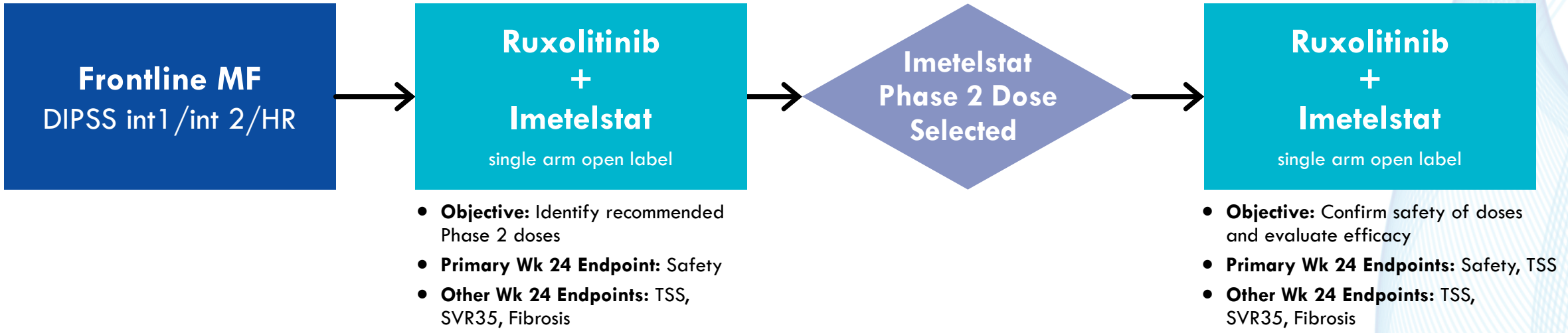
IMproveMF – Planned Phase 1 Geron-Sponsored Study in Frontline MF Combination Treatment of Ruxolitinib Followed by Imetelstat

University of Miami / Mt. Sinai / Moffit Cancer Center

Rationale

- Preclinical data for ruxolitinib followed by imetelstat:
  - Additive inhibitory effect on MF stem cells *in vivo*
  - Synergistically depletes stem cells from MF patients (PDX model)

First Patient Expected: 1H 2022



RP2D, Recommended Phase 2 Dose DIPSS, dynamic international prognostic scoring system; int1, intermediate-1; int2, intermediate-2; HR, high risk; TSS, total symptom score; SVR35, spleen volume reduction ≥ 35%; TI, transfusion independence; IWG-MRT, international working group-myeloproliferative neoplasms treatment

References on slide 26

IMpress – Planned Phase 2 Investigator-Sponsored Study of Single Agent Imetelstat in Post-HMA Relapsed/Refractory AML

EMSCO
European Myelodysplastic Syndromes Cooperative Group

Lead Principal Investigator: Dr. Uwe Platzbecker, University Hospital, Leipzig, Germany

Rationale

- In preclinical models, imetelstat:
  - Prevented expansion of human AML leukemic stem cells (PDX model)
  - Prolonged survival of AML PDX mice

First Patient Expected: 1H 2022

Open-label, Single-arm Multicenter
(n = ~ 45)

R/R/Intolerant HR MDS and AML
Post HMA

→

Imetelstat
7.5mg/kg I.V.

→

- **Objective:** Evaluate efficacy
- **Endpoint:** Overall Response Rate per IWG 2018 criteria (MDS) and the criteria of the European LeukemiaNet (AML)

PDX, patient-derived xenografts; R/R, relapsed or refractory; HR MDS, intermediate-2 or high risk MDS per International Prognostic Scoring System; AML, acute myeloid leukemia; HMA, hypomethylating agent; IWG 2018, international working group 2018 criteria for hematologic response

References on slide 26

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TELOMERE – Planned Phase 1/2 Investigator-Sponsored Study of Imetelstat in Combination with Venetoclax or Azacitidine in Relapsed/Refractory AML

The Tisch Cancer Institute

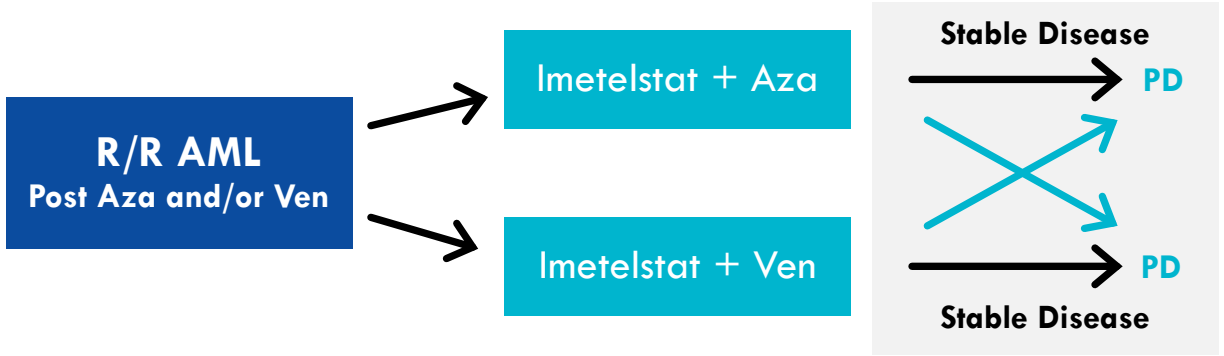
Lead Principal Investigator: Dr. John Mascarenhas, Mt. Sinai Hospital, New York, New York

Rationale

- In preclinical models, imetelstat + venetoclax (Ven):
  - Synergistically induced apoptosis in primary AML blasts ex vivo
  - Enhanced survival with potential cure in AML xenograft model
- In preclinical models, imetelstat + azacitidine (Aza):
  - Synergistically induced apoptosis in AML cell lines

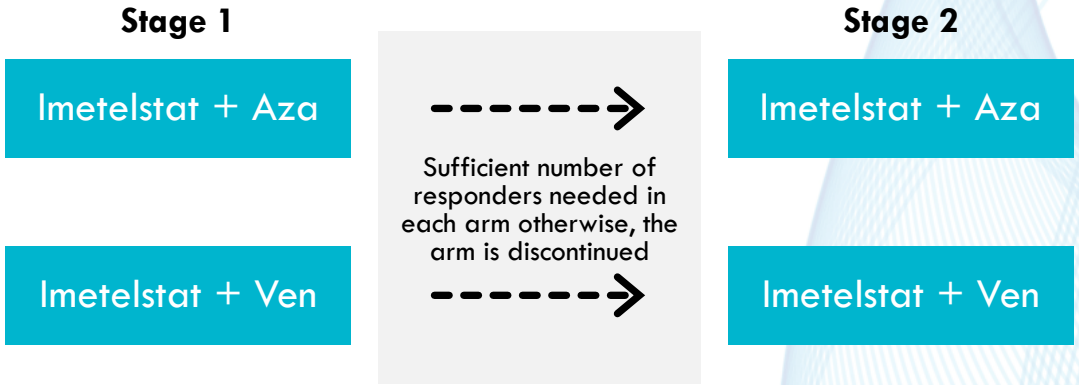
First Patient Expected: 1H 2022

Phase 1 Dose Finding
(n = up to 20)



- **Objective:** Identify recommended Phase 2 dose for each combination
- **Endpoint:** Safety for each combination

Phase 2 SIMON 2 Stage Design
(n = ~ 50)



- **Objective:** Evaluate efficacy for each combination
- **Endpoint:** Overall Response Rate for each combination

R/R, relapsed or refractory; AML, acute myeloid leukemia; PD, progressive disease

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Ongoing and Planned Preclinical Experiments to Define the Role of Imetelstat in Lymphoid Malignancies

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Lead Principal Investigator: Dr. Swaminathan Iyer, MD Anderson Cancer Center, Houston, Texas

Rationale

- T-Cell lymphoma cell lines *in vitro* have shown:
  - Short telomere length (Sezary syndrome; transformed mycosis fungoides)
  - High telomerase activity (cut. anaplastic large-cell lymphoma; mycosis fungoides)
- In Cutaneous T-Cell lymphoma cell lines in vitro:
  - Telomerase overexpression increased T-Cell proliferation
  - RNAi inhibition of telomerase decreased T-Cell proliferation

Initial Data Expected: **YE 2022**

Studies Planned To Be Conducted at MD Anderson Cancer Center

- *In vitro* assays in cell lines and patient-derived materials (blood, etc.) from T and B-cell lymphomas
  - Apoptosis (cell death) assays
  - Colony forming cell (CFCs) assays
  - Cytokine assays
  - TA, TL, hTERT assays
- *In vivo* mouse studies in T and B-cell lymphoma models

TA, telomerase activity, TL, telomere length, hTERT, human telomerase reverse transcriptase

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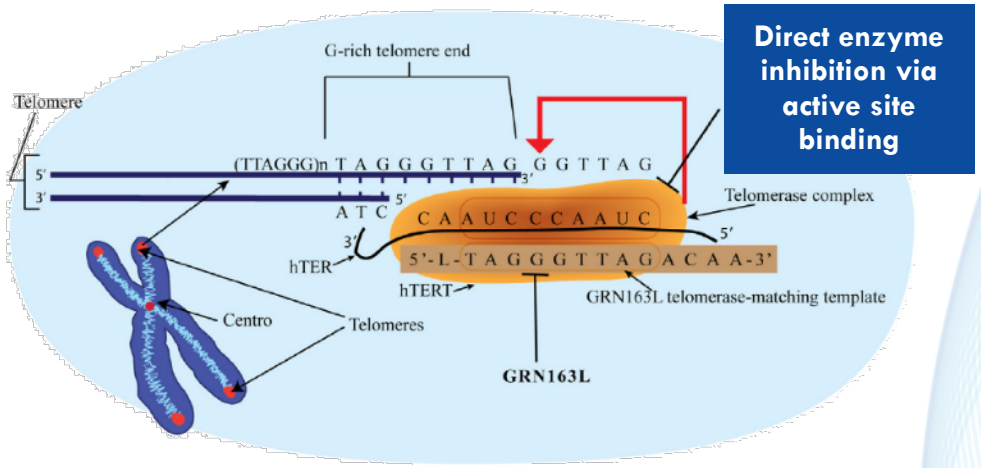
Long-Term Next Generation Telomerase Inhibitor Discovery Program

- **Program Goal:** discover and develop novel small molecules based on chemistry platforms proprietary to Geron that bind to the active site of the telomerase molecule and directly inhibit telomerase activity
- Aspirational profile of a lead compound candidate:
  - Oral delivery
  - High potency & selectivity
  - High potential for combinability
- Development of novel, chemistry platform(s) for lead compound identification underway
- Updates expected when lead compound(s) identified and IND timing known



References on slide 26