



**CHIMERIX**

ACCELERATING INNOVATION

# Forward-Looking Statements

*These slides contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that are subject to risks and uncertainties that could cause actual results to differ materially from those projected. Forward-looking statements include those relating to, among other things, the potential benefits to be derived from the License and Development Agreement with SymBio Pharmaceuticals or Cantex Pharmaceuticals, including any statements related to dociparstat; Chimerix's ability to develop disease modifying and potentially curative treatments for diseases, including AML and smallpox. Among the factors and risks that could cause actual results to differ materially from those indicated in the forward-looking statements are risks that the benefits of the agreements with Cantex or SymBio may never be realized; risks that dociparstat or brincidofovir may not obtain regulatory approval from the FDA or such approval may be delayed or conditioned; risks that development activities related to dociparstat or brincidofovir may not be completed on time or at all; Chimerix's reliance on a sole source third-party manufacturers for drug supply; risks that ongoing or future clinical trials may not be successful or replicate previous clinical trial results, or may not be predictive of real-world results or of results in subsequent clinical trials; risks and uncertainties relating to competitive products and technological changes that may limit demand for our drugs; risks that our drugs may be precluded from commercialization by the proprietary rights of third parties; risks related to procurement of brincidofovir for the treatment of smallpox and additional risks set forth in the Company's filings with the Securities and Exchange Commission. These forward-looking statements represent the Company's judgment as of the date of this release. The Company disclaims, however, any intent or obligation to update these forward-looking statements.*



# Strong balance sheet supports 2 late-stage programs

## Dociparstat (DSTAT) Phase 3 in front-line AML

- Compelling randomized Phase 2 event-free & overall survival data
- Potential for acceleration of hematologic recovery vs standard of care
- Addresses \$1Bn+ market opportunity in 1L AML
- Milestones: end of Phase 2 late 2019, Phase 3 initiation mid 2020

## Brincidofovir (BCV) for smallpox

- Significantly reduced mortality in both required animal models
- Completing final PK dose bridging experiments
- Milestones: pre-NDA meeting early 2020 and NDA filing mid 2020

## Strong balance sheet

- \$158 million in cash as of June 30, 2019
- ~\$110 million expected year-end cash
- Potential non-dilutive capital from smallpox procurement contract



# Proven management team



Mike Sherman  
CEO

Garrett Nichols  
CMO

Mike Andriole  
CFO & CBO

Randall Lanier  
CSO

Roy Ware  
Chief Manufacturing

Michael Alrutz  
General Counsel

Heather Knight  
VP, Regulatory





# **DOCIPARSTAT SODIUM (DSTAT, CX-01): FRONT-LINE ACUTE MYELOID LEUKEMIA**



# DSTAT in-license transaction summary

- Exclusive WW license to DSTAT from Cantex Pharmaceuticals, Inc for all uses
  - Includes assignment of long-term exclusive mfg agreement with Scientific Protein Laboratories
- Full rights to develop and commercialize DSTAT in all markets
  - Chimerix will incur 100% of the development and commercial costs
- Financial Terms
  - \$30 million upfront
  - No additional payments owed Cantex until first approval
  - Milestones for first approval in US, EU and Japan totaling \$105 million<sup>(a)</sup>
  - Milestones for subsequent approvals in US, EU and Japan totaling \$97.5 million<sup>(a)</sup>
  - Sales milestones for achievement of certain revenue amounts totaling \$385 million<sup>(a)</sup>
  - Tiered royalties on net sales starting at 10% and ending in high-teens
  - Equity: 10,000,000 shares of Chimerix common stock



# DSTAT: A compelling opportunity in front line AML

*Improvement of durable benefit of front-line intensive therapy is a major unmet need*

## AML high unmet need

- Few improvements in 7+3 standard front-line therapy over the last 40 years
- 2/3 patients eligible and fit for 7+3<sup>1</sup>
- Low response rates: ~ 50% among intermediate/unfavorable risk population
- High mortality with high relapse rate
  - 5yr survival < 30%<sup>2</sup>, median overall survival < 1yr in high risk
  - Relapse common, particularly in older patients
- Challenging to combine 7+3 with other agents due to hematologic and GI toxicities
- Recent approvals in AML are in second line & for specific genetic mutations; few in de novo

## DSTAT well positioned

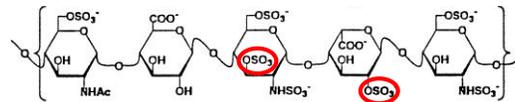
- Attractive profile – Ph2 data suggests DSTAT amplifies 7+3 efficacy without additive toxicity
- Rationale for combination with standard chemotherapy and targeted agents
- Fast track designation and orphan drug designation in the U.S. for AML
- Has multi-modal mechanism, potentially needed for resistance redundancies
- Randomized Phase 2 trial of DSTAT outperformed standard 7 + 3 chemotherapy on event free survival, relapse free survival, overall survival and platelet count recovery time



# DSTAT targets multiple proteins that mobilize AML from bone marrow and accelerate platelet recovery

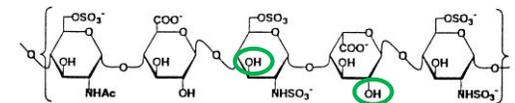
DSTAT is chemically and biologically distinct from heparin

Unfractionated Heparin (UFH)

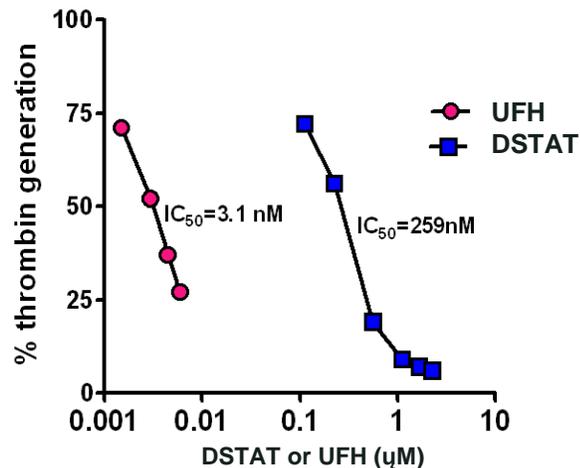


Remove 2-O and 3-O sulfates

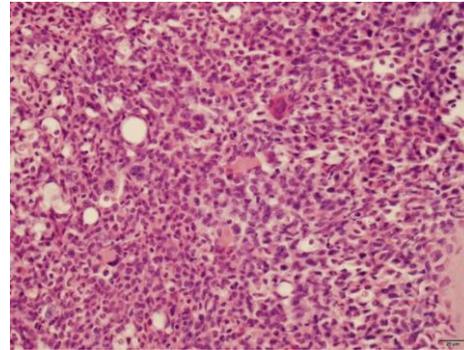
DSTAT: O-desulfated heparin



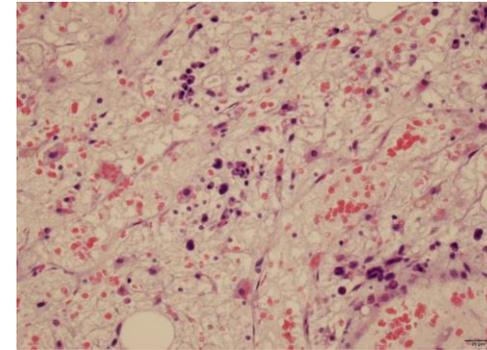
DSTAT has 80-fold less anticoagulant activity



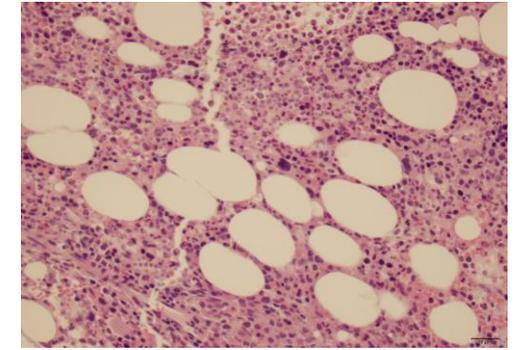
Day 0: AML patient: bone marrow packed with leukemia cells



Day 14 after DSTAT and "7+3" chemo; leukemia cells eliminated in marrow



Day 28 post therapy: no evidence of leukemia and marrow appears normal



Proteins of Interest	Mechanism(s) promoting AML survival or platelet recovery <sup>3</sup>	Effect of DSTAT inhibition
CXCL12/CXCR4	CXCL12 recruits and binds CXCR4+ cells in marrow	Mobilization of AML out of protective marrow niche
Selectins (P/L/E)	Recruit and bind AML cells in bone marrow	Mobilization of AML out of protective marrow niche
HMGB1	Inhibits cell death; enhances chemoresistance	Increased sensitivity of AML to chemotherapies
NFkB	Regulation of adhesion molecules	Reduced expression of E-selectin, VCAM-1, ICAM-1; AML mobilization from marrow
Platelet factor 4	Delays platelet recovery through inhibition of megakaryocytopoiesis	Accelerated platelet recovery

# DSTAT Phase 2 study informs likely Phase 3 population

- Key Phase 2 inclusion criteria:
  - Newly diagnosed AML in patients > 60 years of age (observed median age 67 years old)
  - Favorable, immediate and unfavorable prognostics, both de novo and secondary AML allowed
  - ECOG 0 – 2 (good performance status)
- Patients randomized to one of three arms (1:1:1, n=75<sup>(a)</sup>)
  - DSTAT low dose<sup>(b)</sup>: 4mg/kg bolus followed by 0.125mg/kg/hr infusion plus standard 7+3 chemo, n=25
  - DSTAT high dose: 4mg/kg bolus followed by 0.25mg/kg/hr infusion plus standard 7+3 chemo, n=24
  - Standard induction chemo (cytarabine 100mg/m<sup>2</sup> infusion for 7 days, idarubicin for 3 days), n=26
- Likely Phase 3 ITT patient population targets 39 of 50 patients from high dose and control arms
  - Patients with known favorable cytogenetics may have lower unmet need and will likely be excluded (n=5)
  - Patients with secondary AML (sAML) will likely use Vyxeos for induction therapy and will likely be excluded (n=6)

(a) 4<sup>th</sup> arm in this study (4mg/kg bolus followed by 0.325mg/kg/hr infusion plus 7+3) discontinued after two patients were enrolled (1 had hemorrhage deemed possibly related to DSTAT)

(b) Low dose was deemed sub-therapeutic and the following data presented is limited to the high dose arm and the control arm

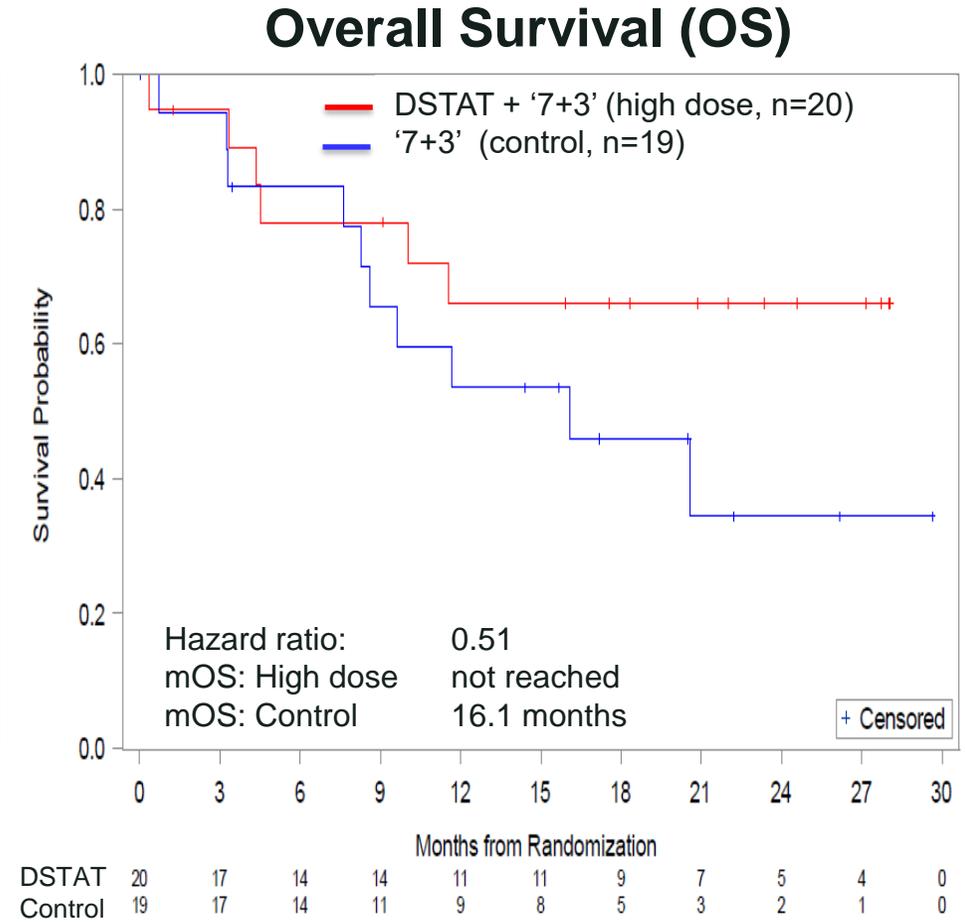
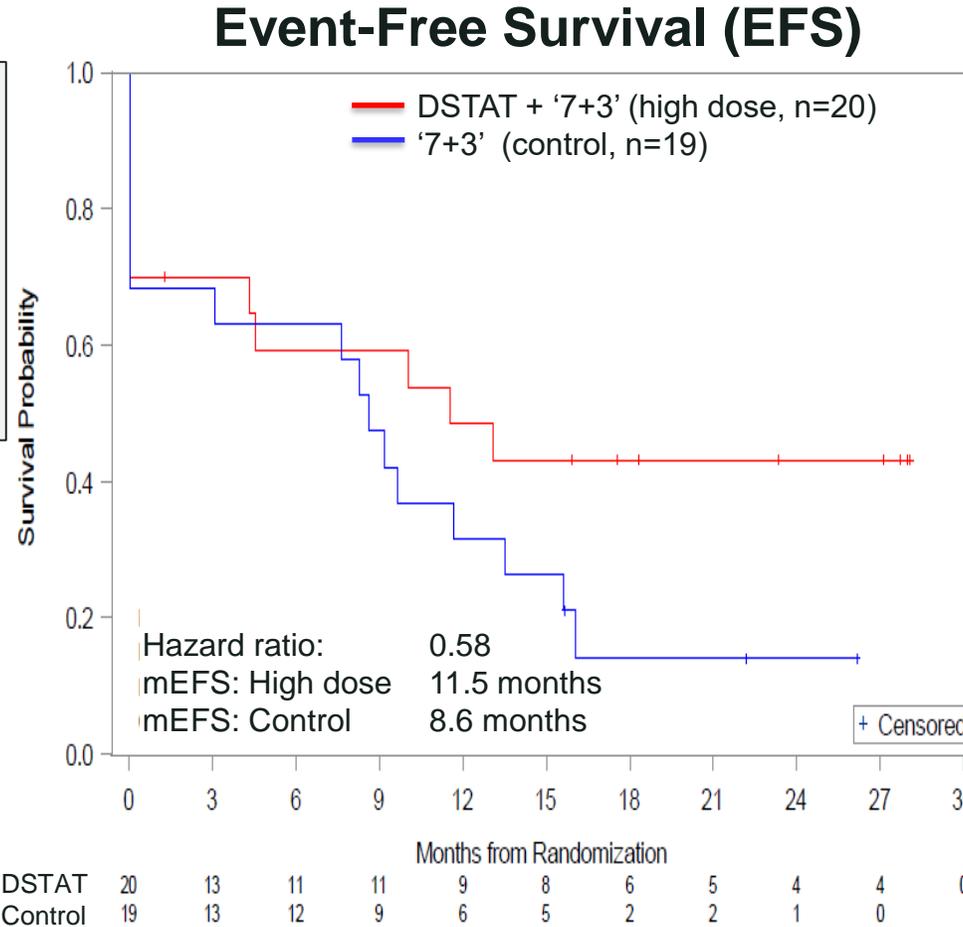


# Likely Ph 3 ITT population shows promising effect on EFS & OS

## Clinically relevant separation in EFS/OS curves

### Response Summary

	% CR/CR <sub>i</sub> <sup>(a-c)</sup>
High Dose Arm	70% (14/20)
Control Arm	68% (13/19)
(historical control ~50%)	



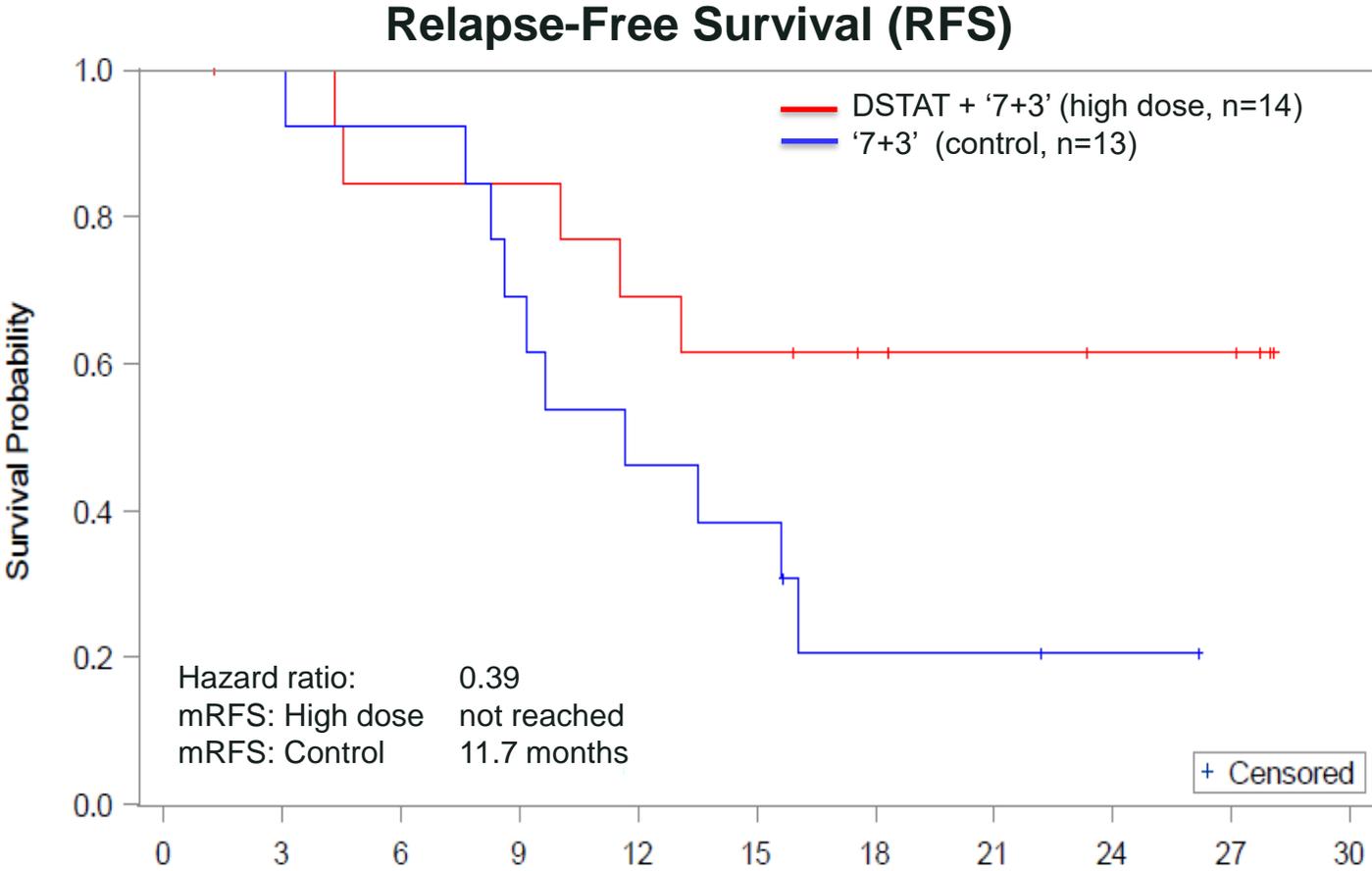
- (a) Complete Response (CR) or Complete Response without complete hematologic recovery (CR<sub>i</sub>)
- (b) Confirmed with post day 14 (D14) bone marrow (BM) biopsy and less than 5% blasts. If no post D14 was performed, the D14 BM biopsy was used to determine response
- (c) Responses and Kaplan-Meier curves do not include sub therapeutic low dose arm



# Likely Ph 3 ITT population shows durability of CR/CRi

*Relapse-free survival median not reached on high dose arm*

- Relapse-Free Survival = survival without relapse following induction success (CR/CRi)



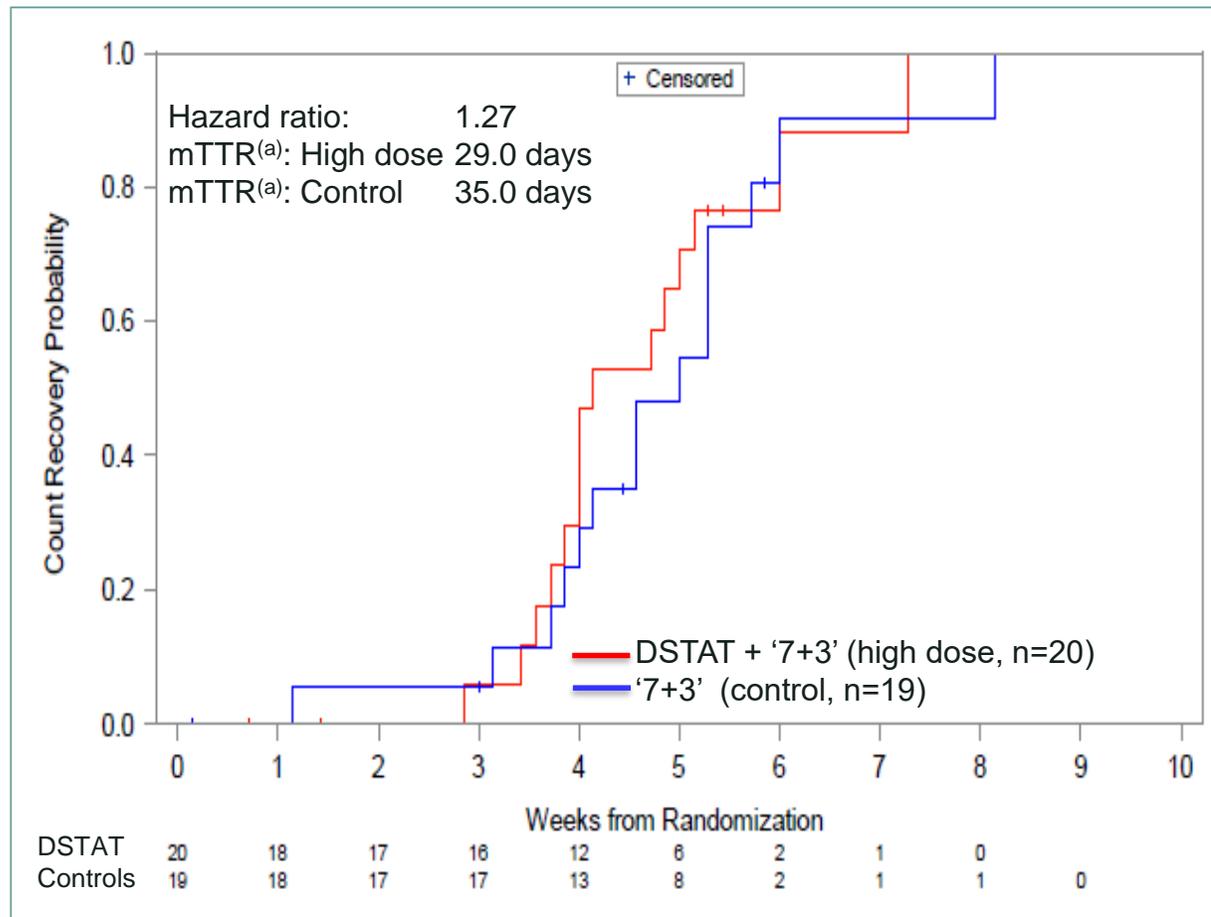
	0	3	6	9	12	15	18	21	24	27	30
DSTAT	14	13	11	11	9	8	6	5	4	4	0
Control	13	13	12	9	6	5	2	2	1	0	



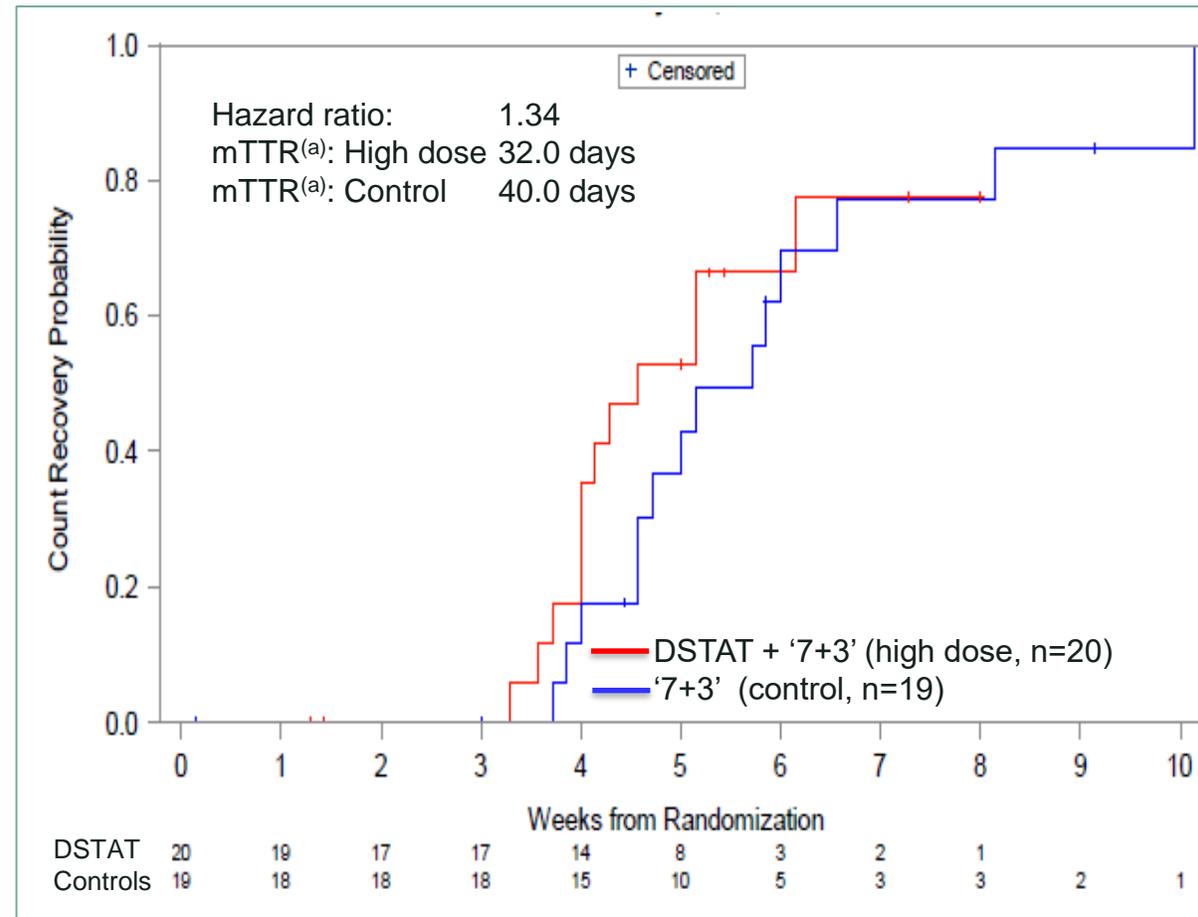
# DSTAT does not delay, and may accelerate, hematologic recovery

*Median days to neutrophil and platelet recovery reduced by 17% and 20%, respectively*

**Likely Ph 3 ITT**  
**Neutrophil recovery > 500 cells/uL**



**Likely Ph 3 ITT**  
**Platelet recovery > 100,000 cells/uL**



# DSTAT potentially amplifies efficacy without significant toxicity

## *Generally well tolerated in newly diagnosed AML patients*

- DSTAT was generally well tolerated in newly diagnosed AML patients treated with backbone 7+3 standard chemotherapy
- Most common serious adverse event in DSTAT arms was febrile neutropenia
  - 3 on high DSTAT arm, 1 on control arm; no difference in infection SOC SAEs (3 each)
- Gastrointestinal SAEs comparable between arms
  - 4 on high DSTAT arm (colitis, ileus/gastric ulcer, small bowel obstruction, vomiting – none deemed related to DSTAT), 1 on control (lower GI hemorrhage)
- Asymptomatic, transient elevation of hepatic transaminases observed in both arms
  - Well-described and non-adverse effect of cytarabine and heparin therapy<sup>(4)</sup>
- aPTT remained in the normal range for most patients in DSTAT and control arms
  - Comparable incidence of Gr<sub>≥3</sub> hemorrhagic events (1 on high DSTAT arm, 2 control)

# Full ITT population outperforms standard 7+3 chemotherapy

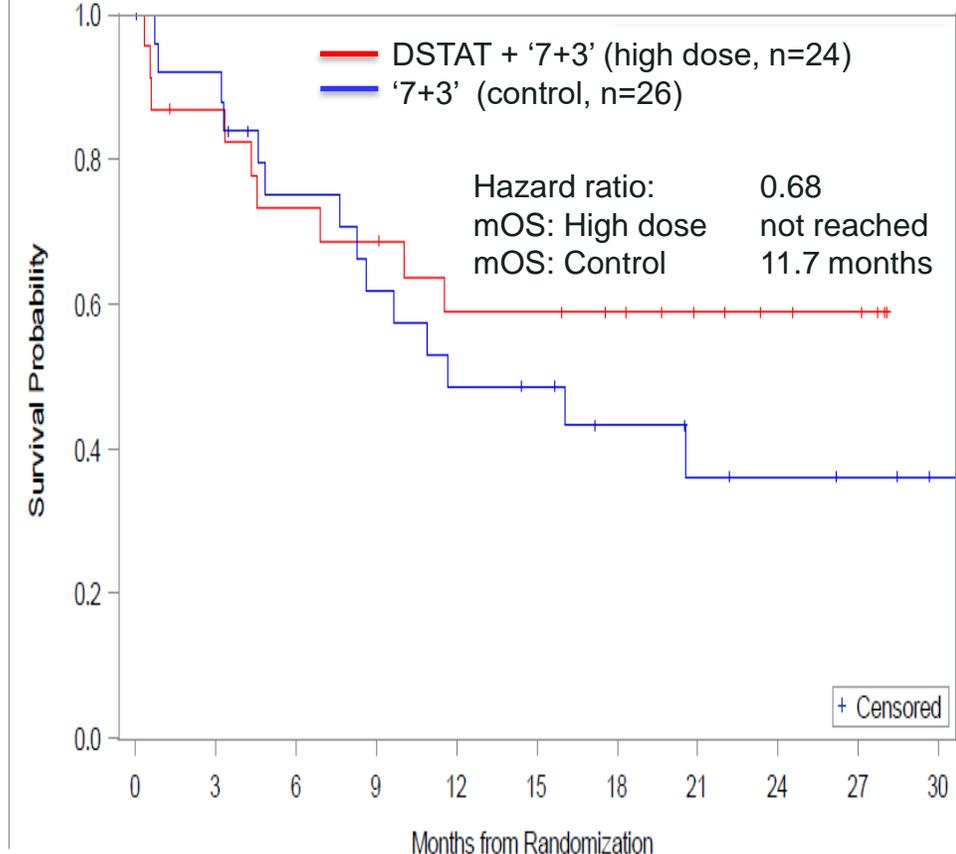
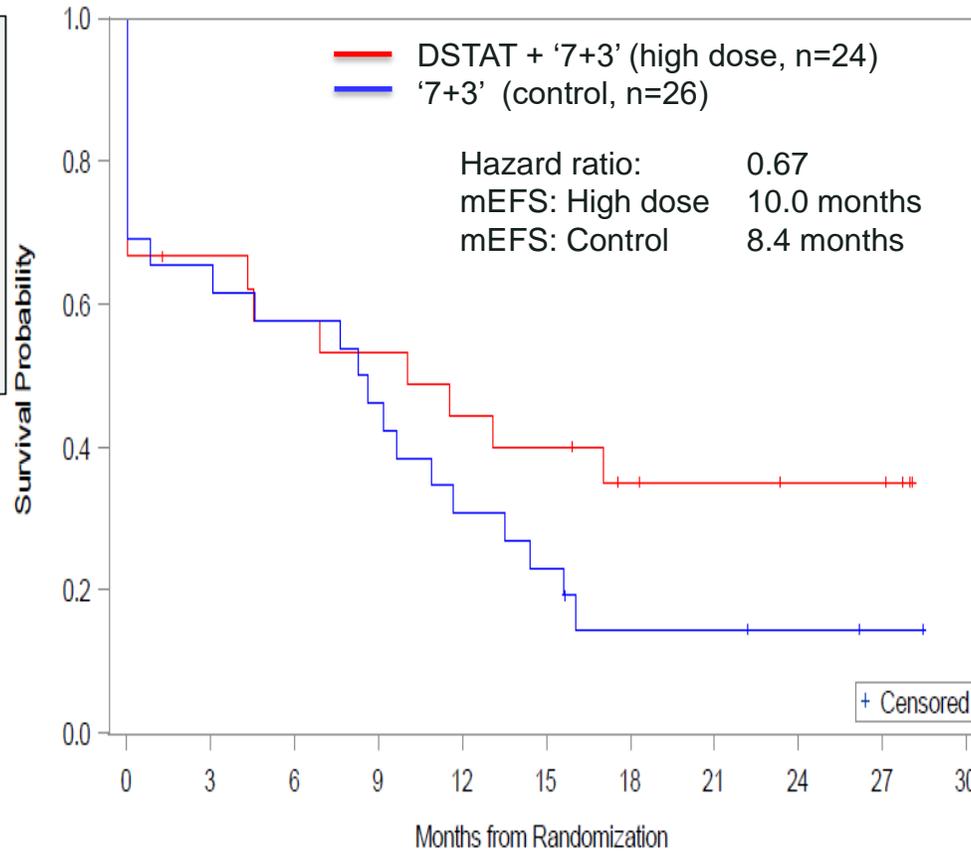
Similar CR/CRi rate, benefit in EFS and OS in full ITT Ph 2 population

## Event Free Survival

## Overall Survival

### Response Summary

	% CR/CR <sub>i</sub> <sup>(a-c)</sup>
High Dose Arm	67% (16/24)
Control Arm	69% (18/26)
(historical control ~50%)	

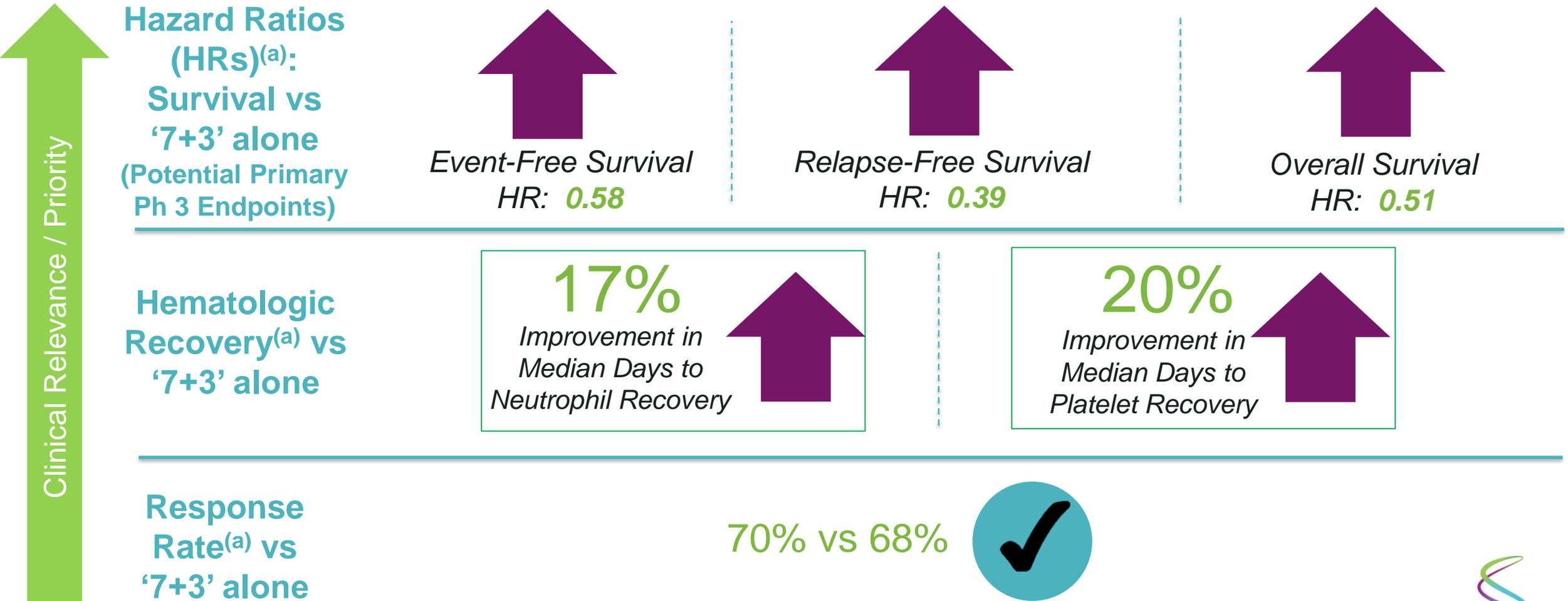


	24	15	13	12	10	9	6	5	4	4	0
DSTAT	24	15	13	12	10	9	6	5	4	4	0
Controls	26	17	15	12	8	6	3	3	2	1	0

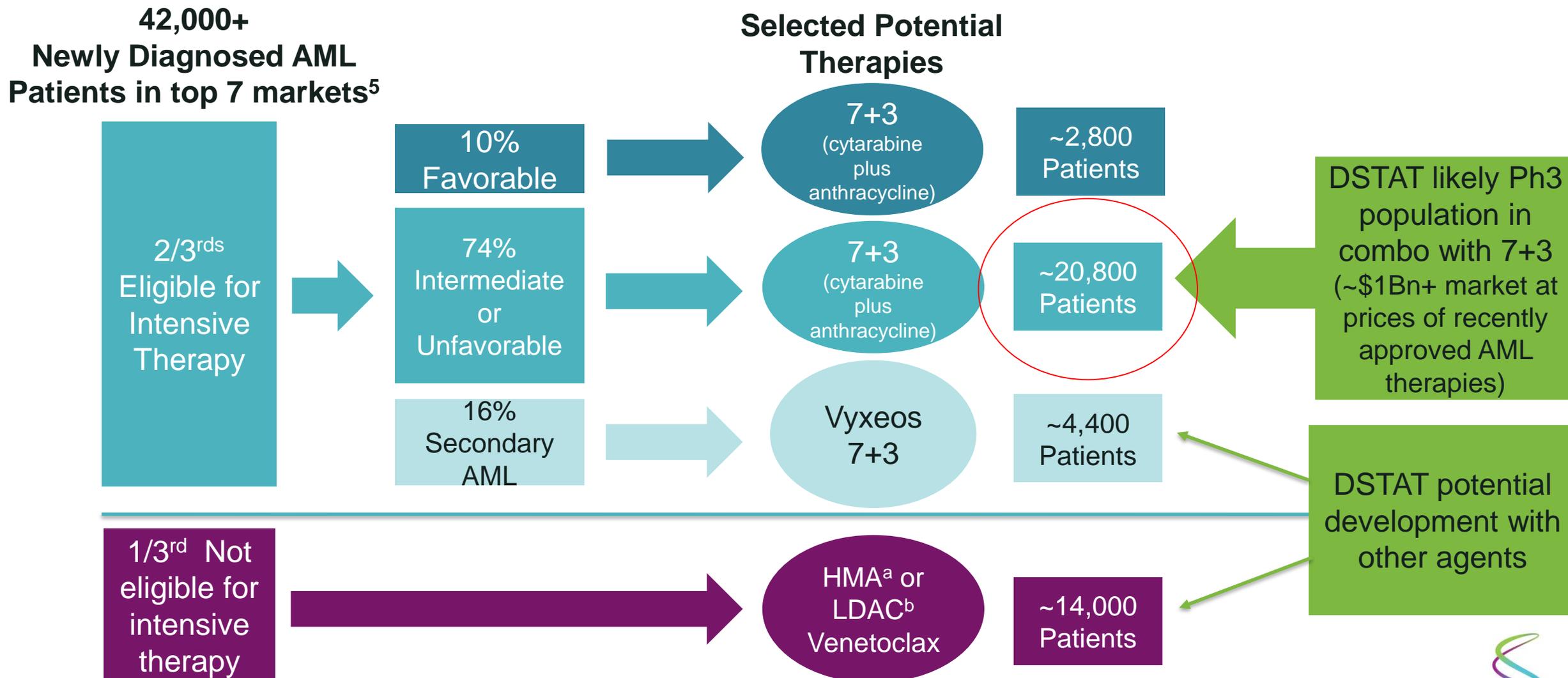
	24	19	16	15	12	12	10	7	5	4	0
DSTAT	24	19	16	15	12	12	10	7	5	4	0
Controls	26	23	17	14	11	10	7	5	4	3	1

- (a) Complete Response (CR) or Complete Response without complete hematologic recovery (CRi)
- (b) Confirmed with post day 14 (D14) bone marrow (BM) biopsy and less than 5% blasts. If no post D14 was performed, the D14 BM biopsy was used to determine response
- (c) Responses and Kaplan-Meier curves do not include sub therapeutic low dose arm

# Potential for quicker recovery, more durable response and longer survival underpins strong Phase 3 rationale



# Potential phase 3 design may position DSTAT to become standard of care for up to ~20,800 patients in the top 7 markets



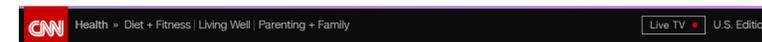


## **BRINCIDOFOVIR (BCV): SMALLPOX**

Animal rule registration path and potential stockpile procurement

# Smallpox – A significant public health risk

- Considered a Class A threat by PHEMCE<sup>a</sup>
- Population is unvaccinated since early '70s
- Highly infectious with >30% mortality
- Potential sources of smallpox
  - Official stocks are at CDC in Atlanta and Vector Labs in Novosibirsk, Russia
  - Potential undeclared stocks
  - 2014 incident - live variola virus stocks found at NIH Bethesda campus
  - “Old” virus from thawing permafrost
- Weaponized virus may have increased transmission and resistance



## CDC: Smallpox found in NIH storage room is alive

By Jen Christensen, CNN  
Updated 3:07 PM ET, Fri July 11, 2014



## The Siberian Times

*Since 1902 there was a daily 'butter' train, leaving Novosibirsk to Riga, Latvia, with 25 carriages, each loaded with 7,000 kg of butter.*  
The chronicles of Novosibirsk

Home News Features Business City Focus Sport Culture Science Health & Lifestyle Ecology Weird & Wonderful  
Case study Opinion Profile

## Experts warn of threat of born-again smallpox from old Siberian graveyards

By The Siberian Times reporter  
12 August 2016

This summer's melting of permafrost is more than THREE TIMES greater than usual, unlocking long-frozen deadly diseases.



Yamal and the anthrax outbreak now underway - the first for 75 years - should act as a warning. Picture: EMERCOM

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# Ongoing collaboration with BARDA

*Mandated to stockpile 2 smallpox countermeasures with differing mechanisms of action*

- BARDA funds most direct & some indirect costs for development of BCV for smallpox
- Animal rule allows approval of drugs for life-threatening conditions where human trials are not feasible or ethical
- BARDA may initiate stockpile procurement prior to FDA approval with Emergency Use Authorization (EUA)
- Government has provided CMRX over \$100 million of support for the development of smallpox countermeasures
- Siga Technologies, Inc. awarded procurement contracts of \$460m in 2011 and \$546m in 2018 for 1<sup>st</sup> stockpiled treatment (TPOXX)



About BARDA: Biomedical Advanced Research and Development Authority (BARDA); part of the HHS Office of the Assistant Secretary for Preparedness and Response, was established to aid in securing The U.S. from chemical, biological, radiological, and nuclear (CBRN) threats, as well as from pandemic influenza (PI) and emerging infectious diseases (EID). BARDA supports the transition of medical countermeasures such as vaccines, drugs, and diagnostics from research through advanced development towards consideration for approval by the FDA and inclusion into the Strategic National Stockpile.



# Potential resistance necessitates two drug stockpile

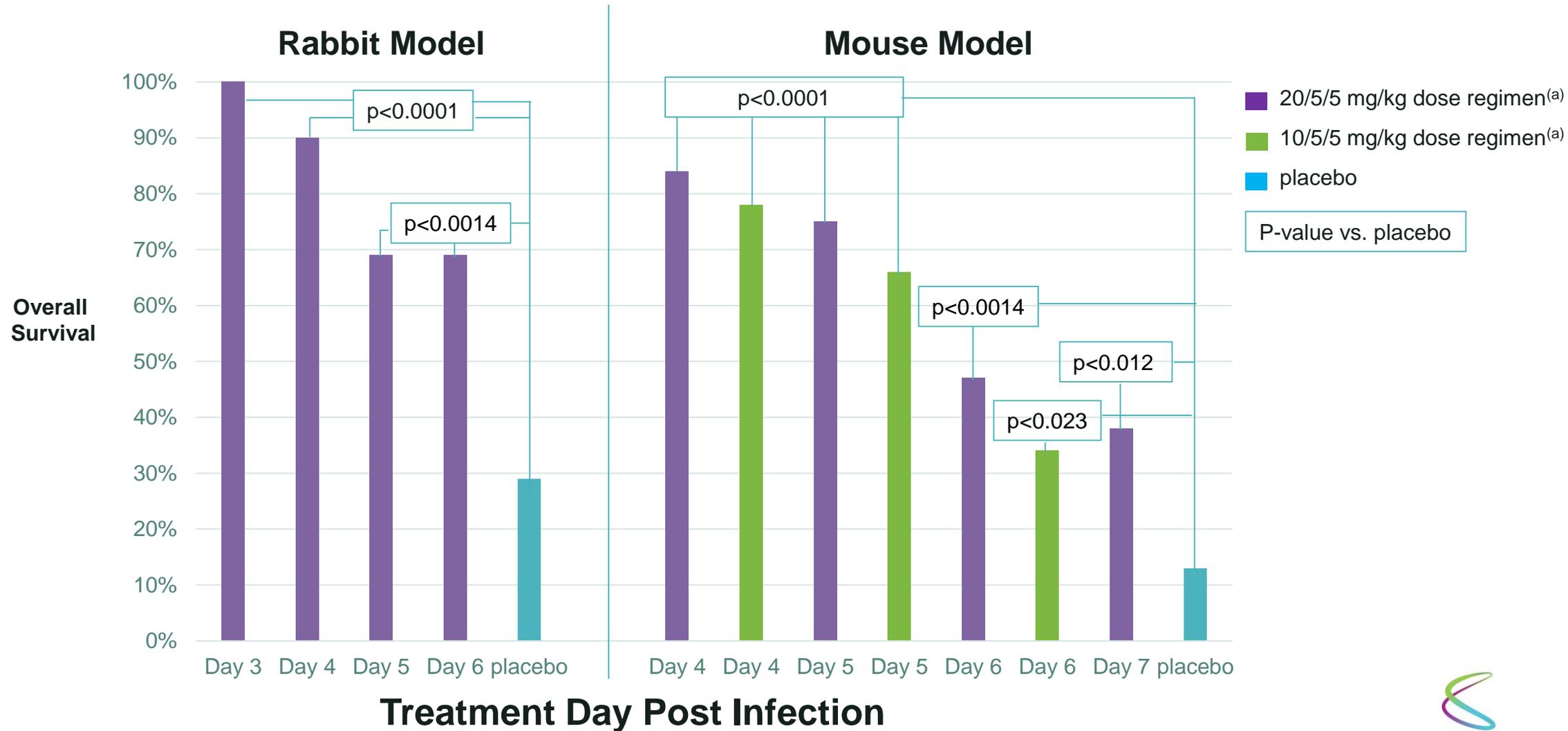
*BCV well positioned as attractive alternative mechanism*

- Resistant smallpox viruses easily generated in lab or synthesized de novo
- Resistance to BCV impairs smallpox virulence due to reduced viral fitness
- Combination therapy likely most effective
- BCV has safety database of ~1,500 patients (both healthy and infected)
- BCV available as short course oral tablet regimen and suspension for pediatrics

	BCV
Antiviral Target	Virus replication
In Vitro Resistance	Slower and lower level
Fitness of resistant virus	Low
In Patients	No resistance detected to date



# BCV significantly reduced mortality in 2 animal models of orthopoxvirus infection



<sup>(a)</sup> administered at 48-hour intervals with treatment initiation on post-infection days 3, 4, 5, 6 or 7





**CORPORATE**

# Strategic priorities

Strong balance sheet to achieve milestones, expect 2019 ending cash ~\$110 million

- Quickly advance DSTAT to a pivotal Ph 3 registration study
  - End of Phase 2 meeting with U.S. FDA
  - Phase 3 protocol finalization
- Evaluate new indications to expand and maximize DSTAT opportunities
- Complete execution of work to advance BCV to NDA as a medical countermeasure for smallpox
  - Potential non-dilutive funding to invest in DSTAT and other programs
  - Achieve commercialization without need to build commercial infrastructure

## SymBio BCV out-license deal (30Sept2019)

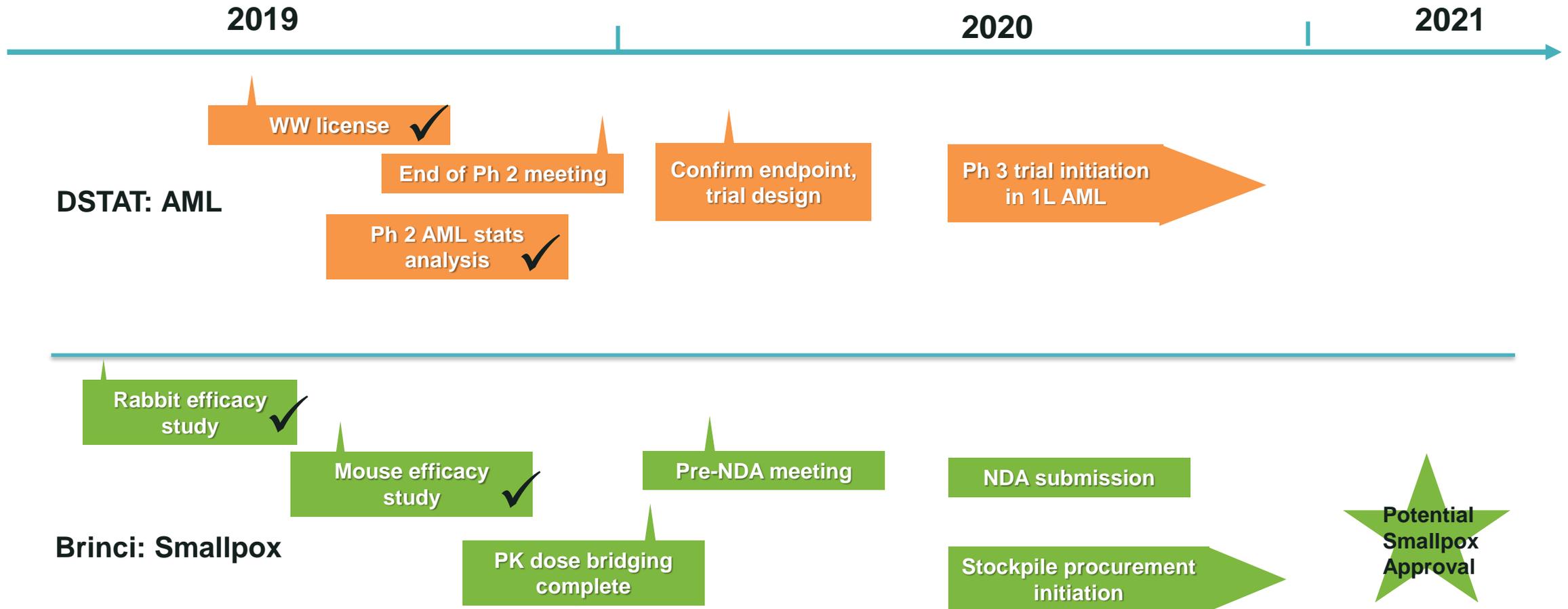
- SymBio acquires rights to develop and commercialize all indications of BCV excluding the prevention and treatment of smallpox
- SymBio will develop and commercialize BCV in all markets and will incur 100% of the future development and commercial costs
- SymBio will pay to Chimerix:
  - \$5 million upfront to Chimerix
  - \$180 million in development, regulatory and approval milestones
  - Double digit royalties on net sales

# June YTD financial statements

Year to Date June 30, 2019 (millions USD)	
Revenue	\$ 3.8
R&D expense	(27.3) ))
G&A expense	(14.0) )))
Operating Expense	41.3 ))
Interest income, unrealized loss, net	2.2
Net loss	\$ (35.3)
Net cash burn used (6 months)	\$ 28.1
Ending Cash	\$ 158.4

- Expected year end cash ~\$110m
- Includes one-time restructuring charge of \$6.5 million in 2Q19
- 2019 exit quarterly burn rate reduced by approximately 25% compared to first two quarters of 2019 and all of 2018, includes incremental development investment into DSTAT

# Numerous potential value-driving catalysts in next 12 months





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# References

- (1) Global Pharma Data, Acute Myeloid Leukemia (AML) - Dynamic Market Forecast to 2026
- (2) SEER 2019 statistics
- (3) Ziarek et al. 2013 J Biol Chem 288 (1):737; Wang et al. 2002 J Clin Invest 110:127; Rashidi and Uy 2015 Curr Hematol Malig Rep 10(2):126; Duckworth et al. 2015 Oncotarget 6(27): 23671; Zheng et al. 2017 Am J Respir Cell Mol Biol 56 (1):90; Rao et al. 2010 Am J Physiol Cell Physiol 299:C97; Liu et al. 2019 Biomedicine and Pharmacotherapy 112:1; Joglekar et al. 2012 Thrombosis and Haemostasis 107:1; Kovacsovics 2018 Blood Advances 2(4):381
- (4) Harrill AH et al. Clin Pharmacol Ther. 2012 Aug; 92(2): 214–220
- (5) CMRX internal estimate of the US, UK, Germany, France, Spain, Italy and Japan