Chimerix 2Q21 Corporate Presentation





#### **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, Chimerix's ability to develop and commercialize its drug candidates including ONC201, DSTAT and TEMBXA®; the sufficiency of the data from the current clinical trial of ONC201 to support accelerated regulatory approval; Chimerix's ability to submit and/or obtain regulatory approvals for its clinical candidates; the timing and receipt of a potential procurement contract for TEMBEXA in smallpox; and the anticipated benefits of Chimerix's acquisition of Oncoceutics. Among the factors and risks that could cause actual results to differ materially from those indicated in the forward-looking statements are risks that Chimerix's clinical candidates may not obtain regulatory approval from the FDA or such approval may be delayed or conditioned; risks that development activities related to clinical candidates may not be completed on time or at all; risks that ongoing or future trials may not be successful or replicate previous trial results, or may not be predictive of real-world results or of results in subsequent 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 that Chimerix will not obtain a procurement contract for TEMBEXA in smallpox in a timely manner or at all; risks that the anticipated benefits of the acquisition of Oncoceutics may not be realized and additional risks set forth in the Company's filings with the Securities and Exchange Commission. These forwardlooking 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.

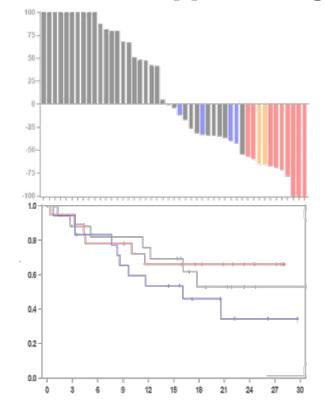
## **Potential TEMBEXA® stockpiling to fund oncology development**

Source of non-dilutive capital directed toward innovative oncology development

TEMBEXA approved June 4,2021 for the treatment of smallpox

Potential \$80-\$100m annual nondilutive capital with potential sales to governments for national preparedness for treatment of smallpox

# Focus on oncology areas of high unmet need supported by strong clinical data



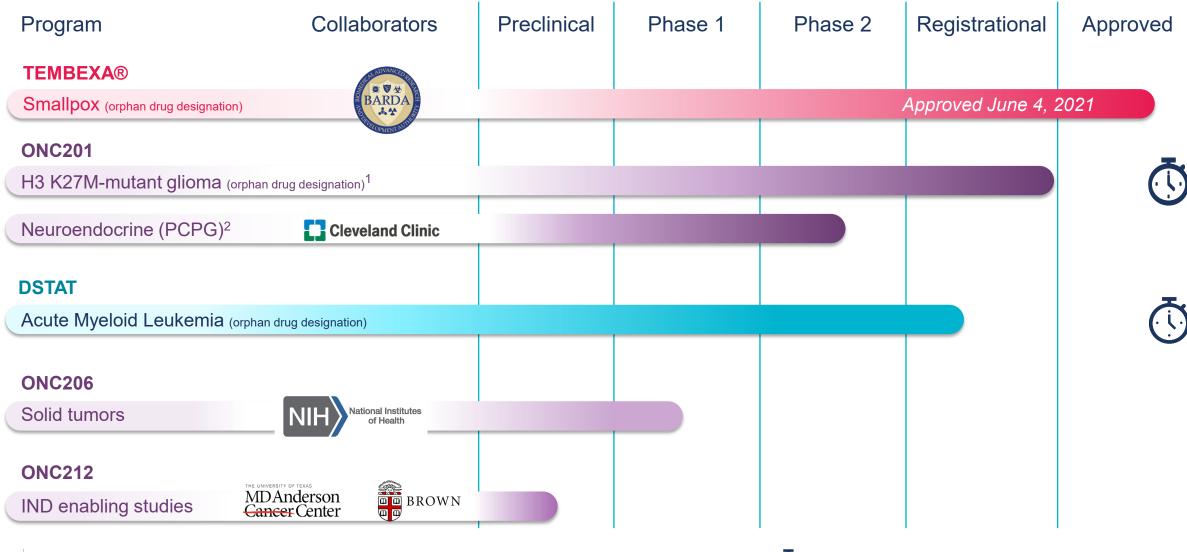
#### ONC201/ONC206/ONC212

- Glioma registration opportunity
- New indication & pipeline expansion



Phase 3 front-line AML trial

# **Deep pipeline across all development stages**





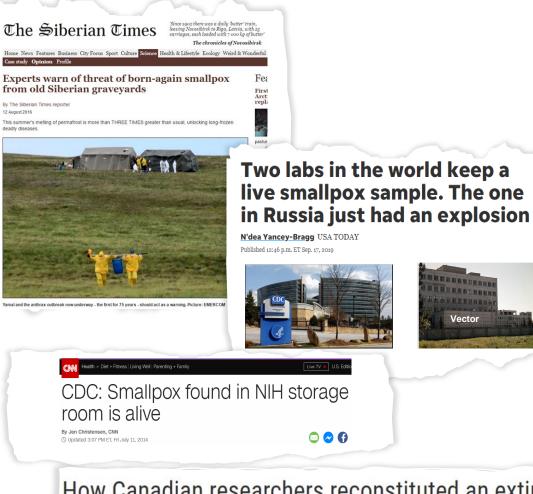
# TEMBEXA® Approved for Treatment of Smallpox as a Medical Countermeasure





# The value of preparedness has never been more evident

- Highly infectious virus with ~30% mortality<sup>1</sup>
- Population is unvaccinated since early '70s
- Considered a Class A security threat by PHEMCE<sup>2</sup>, CDC and NIAID
- Weaponized virus could be engineered to increase transmission and resistance
- BARDA mandate to stockpile countermeasures with alternative mechanism of action
- SIGA Technologies awarded >\$1B in contracts for development and stockpile of TPOXX
- TEMBEXA® approved June 4,2021 for the treatment of smallpox



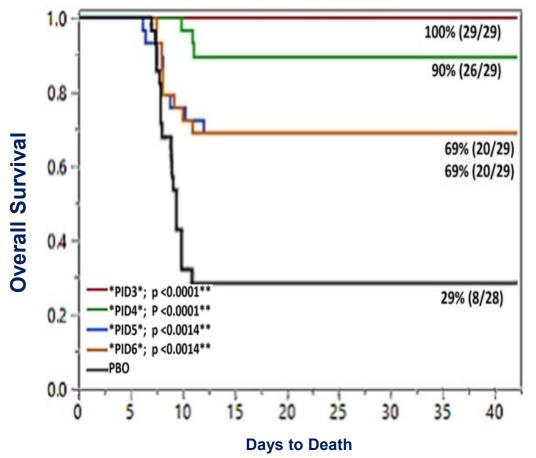
# How Canadian researchers reconstituted an extinct poxvirus for \$100,000 using mail-order DNA

By Kai Kupferschmidt | Jul. 6, 2017 , 5:00 PM

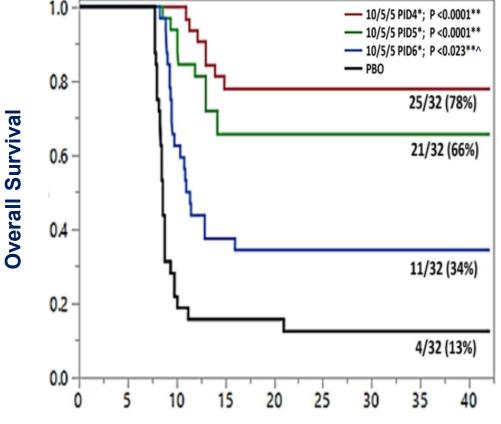
Posted in: Health, Science and Policy, Scientific Community doi:10.1126/science.aan7069

### **TEMBEXA®** significantly reduced mortality in required models

Survival improved even with administration of TEMBEXA well beyond midpoint of disease progression



#### **Rabbit Model**



#### **Mouse Model**

Days to Death

\* PID = Post Inoculation Day
 \*\* Versus Placebo (PBO); Boschloo one-sided
 ^ Day 6 was not determined to be statistically significant in mouse

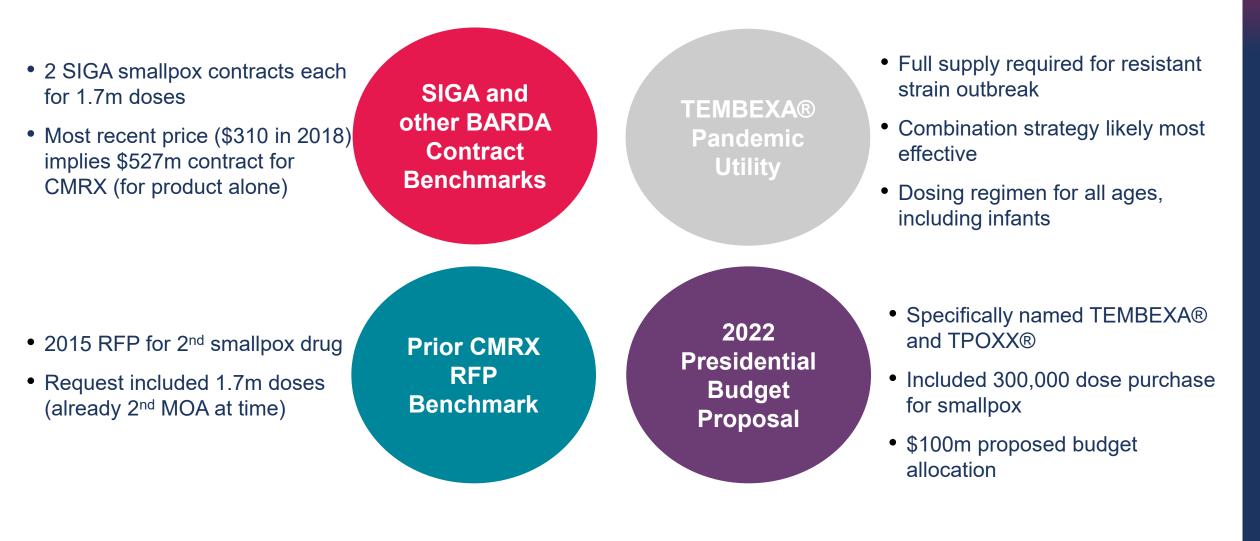
## **TEMBEXA®** positioned as an attractive addition to SNS

- Approved by the FDA in tablet and oral suspension ۲ formulations for the treatment of smallpox disease in adult and pediatric patients, including neonates/infants
- TEMBEXA impairs viral replication with a different mechanism of action than TPOXX®, important hurdle to an engineered bioterror attack
- Short-course therapy, oral tablet and suspension (two • tablets once weekly for 2 doses oral suspension once weekly for 2 doses)
- Complementary with existing countermeasures and vaccines
- TEMBEXA has a higher barrier to resistance compared to TPOXX
- TEMBEXA and TPOXX work well in combination in • animal studies
- Initial quantities available for delivery to the SNS in 2H2021

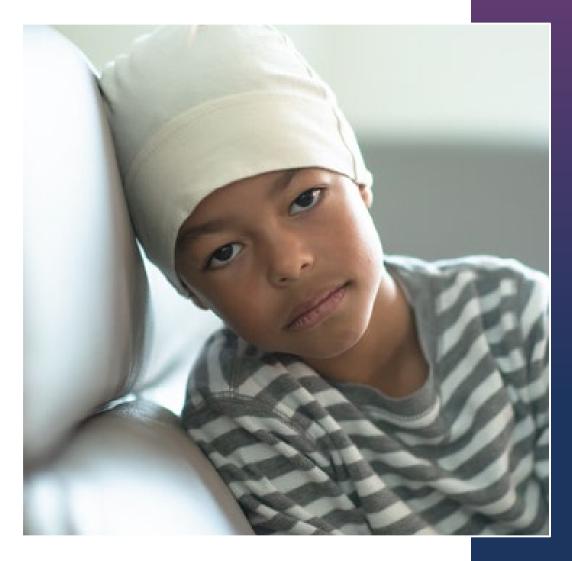
10 mg/mL oral suspension | 100 mg tablets



## **Rationale for significant revenue opportunity**



Acquisition of Oncoceutics Adds Targeted Oncology Pipeline with Near-term Registration Potential





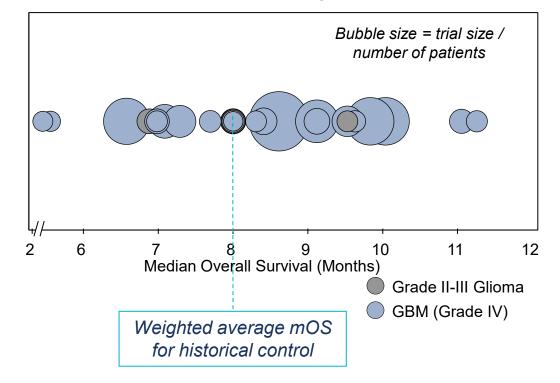
## **ONC201** provides attractive near-term opportunity

- Unprecedented single agent activity in recurrent H3 K27M-mutant glioma
- Pivotal 50 subject registrational data anticipated in 4Q2021, comprised of 50 subjects pooled across multiple-sponsored clinical studies and expanded access
- Attractive commercial market potential
  - >\$500M global peak sales opportunity in first indication
  - Extraordinary awareness of ONC201 among KOLs
  - Mutation already identified through standard diagnostics
- Compelling single agent response in second indication
- Attractive safety to date, easy administration
- IP portfolio into mid to late 2030s
- Path ahead leverages organizational strengths

## **Recurrent H3 K27M+ recurrent glioma, a devastating disease** where single agent responses are rare and lack durability

- Most frequent histone mutation in glioma
  - Frequent (>50%) in younger patients with midline brain tumors
  - Classified as grade IV by WHO, regardless of diffuse glioma histology
  - Mutation routinely identified via immunohistochemistry (IHC) or next generation sequencing (NGS), e.g. Foundation One
- FDA acknowledge available therapy is palliative
  - Often not possible to resect
  - Recurrence inevitable after first-line radiation
  - Invariably lethal; ~8 months median overall survival
  - Chemotherapy ineffective; objective responses by RANO-HGG<sup>1</sup> rarely observed

# Median overall survival weighted average: ~8 months in recurrent glioma<sup>2</sup> post TMZ



1 Response Assessment in Neuro-Oncology-High Grade Glioma

2 Data collected from 17 literature sources since 2010 with trial arms size >30 pts each reporting data on 1937 pts with recurrent, unstratified disease. 13 trials were in post-TMZ patients and four trials with 282 pts did not explicitly declare prior TMZ, rather "radiotherapy + chemo"

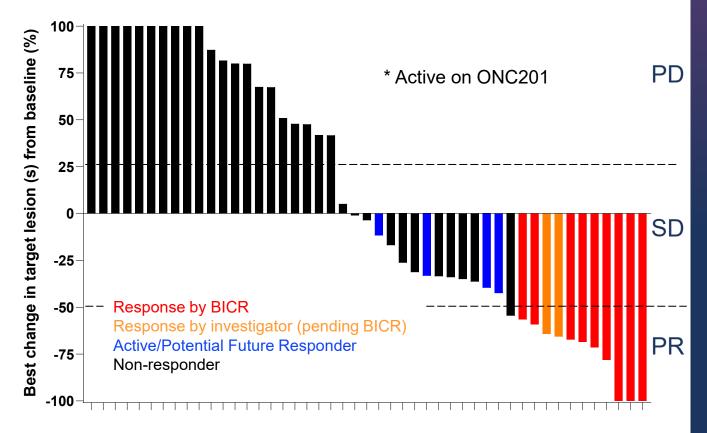
## H3 K27M-mutant glioma: market dynamics and opportunity

- U.S. annual incidence of ~2,000
- Market research
  - Nearly all mid-line glioma patients tested for H3 K27M-mutation; rate to increase with targeted therapy
  - ~20% ORR and/or clinically relevant durability deemed clinically meaningful
  - ONC201 use expected in >80% of H3 K27M-mutant glioma patients based on current profile
  - Interest in combination with radiation if possible, in the front-line setting
- Competitive landscape: chemotherapy and bevacizumab ineffective; targeted agents, vaccines and CAR-T therapies are in early development with limited efficacy analysis available
- Low barriers to adoption
  - No effective treatment options available
  - K27M already on commercial and site-specific NGS panels, oral dosing (QW), good safety profile
  - High unaided awareness of ONC201 among neuro-oncologists
  - Longer-term, potential combinable with other glioma therapies

# Compelling ONC201 responses in recurrent H3 K27M mutant disease drives strong KOL engagement

- 30% ORR by BICR in first 30 patients
- Maturing data from the next 20 patients so far demonstrated:
  - 2 additional responders by investigator assessment
  - 4 additional patients remain on therapy >6 months
- ORR from full cohort supported by
  - Clinically relevant durability
  - Clinically relevant disease control in nonresponders
  - Other clinical benefits (e.g., reduction in steroid use, improved performance status)
  - Complete responses
  - Objective responses in CNS tumors exclusive to H3 K27M mutations

Assessed using RANO-HGG; T1 Contrast Enhancement



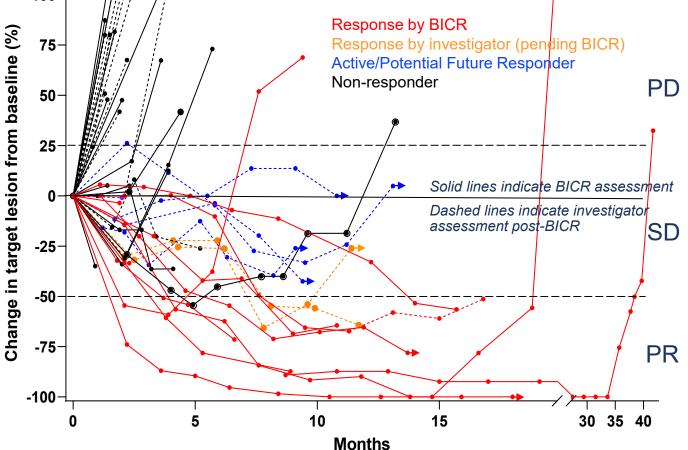
Data cutoff for ONC006 study is November 17,2020, others is December 4, 2020

# Meaningful durability of response

#### Interim Response Summary\*

- Subject to change with maturing data
- 11 responses so far by RANO HGG
  - 9 responses by BICR
  - 2 investigator assessed
  - 4 patients could still achieve response
- Meaningful duration of response
  - mPFS among responders: > 15 months

\* All responses planned to be reconfirmed by a three-party adjudicated blinded independent central review in 2021 100-

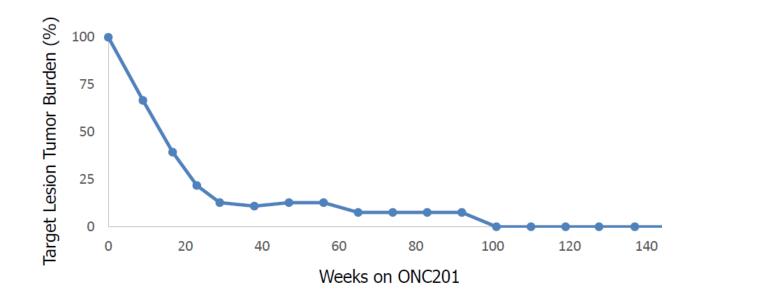


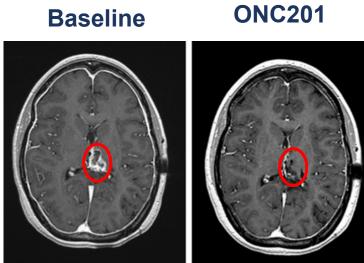
Assessed using RANO-HGG; T1 Contrast Enhancement

Data cutoff for ONC006 is November 17,2020, data cutoff for other studies is December 4, 2020

## **ONC201** patient: near complete tumor regression

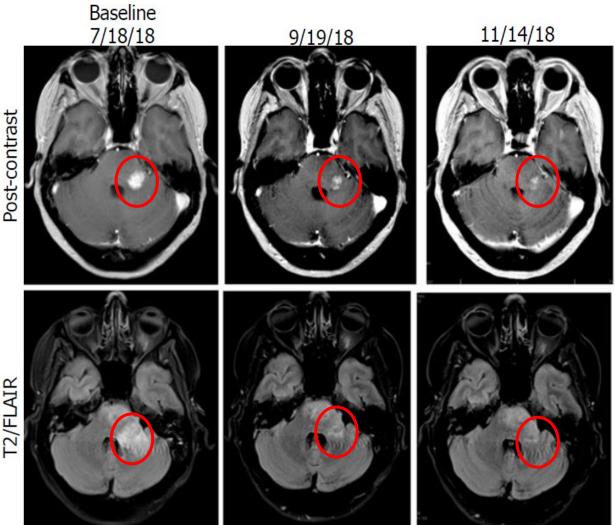
- 22-year-old with recurrent H3 K27M mutant glioma
- Started single agent ONC201 treatment after recurrence of tumor in March 2016
- Experienced deep and durable complete regression in the primary lesion





### ONC201 partial responses have driven clinical benefit in recurrent H3 K27M-mutant glioma

- 55-year-old received single agent ONC201 at recurrence following radiation therapy (RT) and temozolomide (TMZ)
- Objective partial response was associated with normalization of neurological deficits by NANO<sup>1</sup> within two cycles
  - Improved gait
  - Improved facial strength
  - Improved language
- Radiographic response and neurologic response >7 months



## **ONC201 demonstrated attractive safety profile, oral administration**

Treatment-emergent and related AEs<sup>1</sup> occurring in >5% of ONC201-treated recurrent H3 K27M-mutant glioma patients (all 52 subjects enrolled in study ONC013)

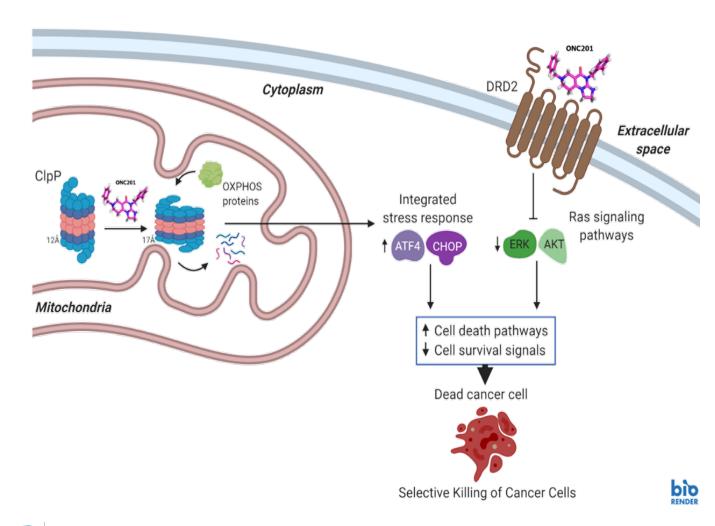
Study ONC 013: Adverse Reactions (N=52)	All Grades n(%)	Grade 3-4 n(%)
General disorders and administration site conditions	11 (21.2)	3 ( 5.8)
Fatigue	10 (19.2)	3 ( 5.8)
Investigations	10 (19.2)	1 ( 1.9)
Lymphocyte count decreased	5 ( 9.6)	-
Nervous system disorders	8 (15.4)	-
Headache	3 ( 5.8)	-
Gastrointestinal disorders	7 (13.5)	-
Nausea	7 (13.5)	-
Vomiting	3 ( 5.8)	-
Metabolism and nutrition disorders	6 (11.5)	-
Decreased appetite	4 (7.7)	-
Skin and subcutaneous tissue disorders	4 (7.7)	3 ( 5.8)
Rash maculo-papular	4 (7.7)	3 ( 5.8)

- Integrated safety database for NDA will consist of >350 glioma patients
- Dose-limiting toxicities have not been observed with weekly dosing in any indication
- Study allows single weekly dosing until progression
- Safety results and oral dosing potentially enable:
  - Fixed dosing in adults
  - High rate of compliance
  - Evaluation in multiple therapeutic settings
  - Evaluation of combination therapies

1. A treatment-emergent AE (TEAE) is defined as a newly occurring or worsening AE after the first dose of study treatment and through 30 days after the last dose of study treatment. TEAEs that are definitely related, probably related, possibly related or missing relationship to the study drug are considered as study drug related treatment-emergent adverse events. Adverse events were coded using the MedDRA Dictionary, Version 22.0. Date Cutoff: 31AUG2020

# **ONC201 targets DRD2 and ClpP**

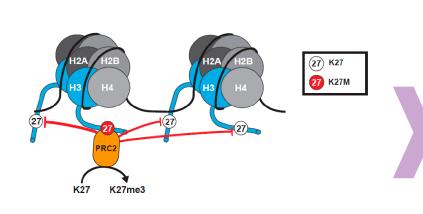
ONC201 upregulates integrated stress response, inactivates Akt/ERK, selectively inducing tumor cell death



- ONC201 can selectively induce apoptosis in cancer cells by altering activity of two proteins
- DRD2 antagonism
  - DRD2 is a G protein-coupled neuroreceptor that regulates Ras signaling
  - ONC201 antagonizes DRD2, inhibiting Ras signaling pathways
- ClpP agonism
  - ClpP normally degrades misfolded proteins in mitochondria
  - ONC201 modifies ClpP conformation, promoting excess degradation of specific mitochondrial proteins important for cancer cell viability

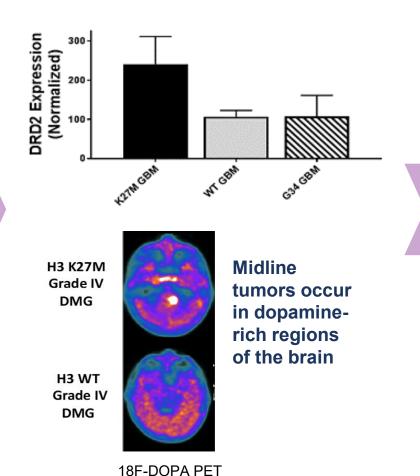
## H3 K27M-mutant gliomas exhibit enhanced sensitivity to ONC201

Lysine to methionine ("K-to-M") histone H3 mutation reduces H3 K27 methylation



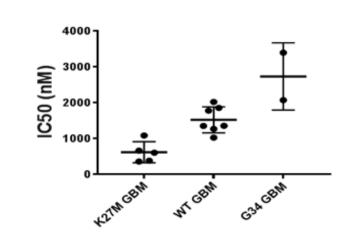
K27M-mutants bind PRC2 which normally methylates H3 K27 via EZH1/2; binding/tethering PRC2 prevents methylation of even nonmutant H3 K27

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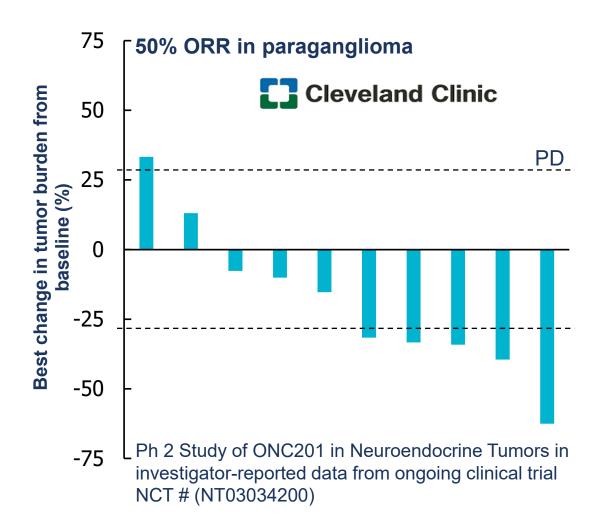
#### H3 K27M elevates DRD2 expression

High sensitivity to ONC201



Lowe et al., Cancers, 2019; Chi et al., Society of Neuro-Oncology, 2017; Kawakibi et al, Society of Neuro-Oncology, 2019; Koschmann et al., Pediatric Society of Neuro-Oncology 2019; Prabhu et al, Clinical Cancer Research, 2018; Ishizawa et al, Cancer Cell, 2019; Prabhu et al., Society of Neuro-Oncology, 2019, Piccardo et al., Eur J. Nucl Med Mol Imaging, 2019

## **ONC201 interim efficacy results in dopamine-secreting tumors outside the brain**



- Single agent responses in Ph 2 neuroendocrine trial of ONC201 observed in subset (paraganglioma)
- Paraganglioma are adrenal-related tumors with elevated DRD2 expression
- Five patients have been treated > 1 year
- Less short-term and potential long term toxicities than other paraganglioma therapies
- Objective responses in patients with tumor genetic driver alterations in metabolic enzymes (SDHA, SDHB, SDHD) and diverse prior therapy

## **ONC201 FDA designations**



Orphan Drug Designation (ODD) (treatment of glioblastoma and treatment of malignant glioma)



Fast Track Designation (FTD) for adult recurrent H3 K27M-mutant high-grade glioma



Rare Pediatric Disease Designation for treatment of H3 K27M mutant glioma

- Potential to receive rare pediatric voucher<sup>1</sup>

## **Promising pipeline in development**

#### **ONC206**:

- Differentiated DRD2 antagonist + ClpP agonist
- Phase 1 for recurrent CNS tumors





#### ONC212:

- GPR132 agonist + ClpP agonist
- IND-enabling studies



Making Cancer History®



# Dociparstat Sodium (DSTAT) for Firstline Treatment in AML





## More than 21,000 new cases of AML annually in the U.S.

- Rapidly progressive disease with low survival rates
- Existing therapies are seldom cures
  - 1-year survival for older patients

5 out of 10

- 5-year survival for older patients

**1** out of 10

- Relapse can occur if not all AML blasts and stem cells are eradicated
- AML is heterogenous and has multiple mechanisms of resistance to treatment

## **Compelling pilot study results in treatment-naïve AML patients**

Strong Complete Response, Overall Survival and improved hematologic recovery

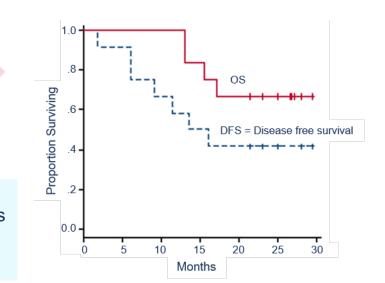
- **11 of 11 (100%)** patients with treatment-naïve primary AML achieved a CR with single induction cycle of 7+3 chemotherapy plus DSTAT; none reported serious adverse events related to DSTAT
- 12th patient enrolled with granulocytic sarcoma secondary to chronic myelomonocytic leukemia achieved a CR with second induction cycle without DSTAT
- All 5 baseline FLT3+ patients achieved CR with single induction cycle

Survival Rates

Count Recovery

Complete Response

- Median survival not yet reached after 29.4 months
- Median disease-free survival of 14.8 months
- 4 patients remained in remission

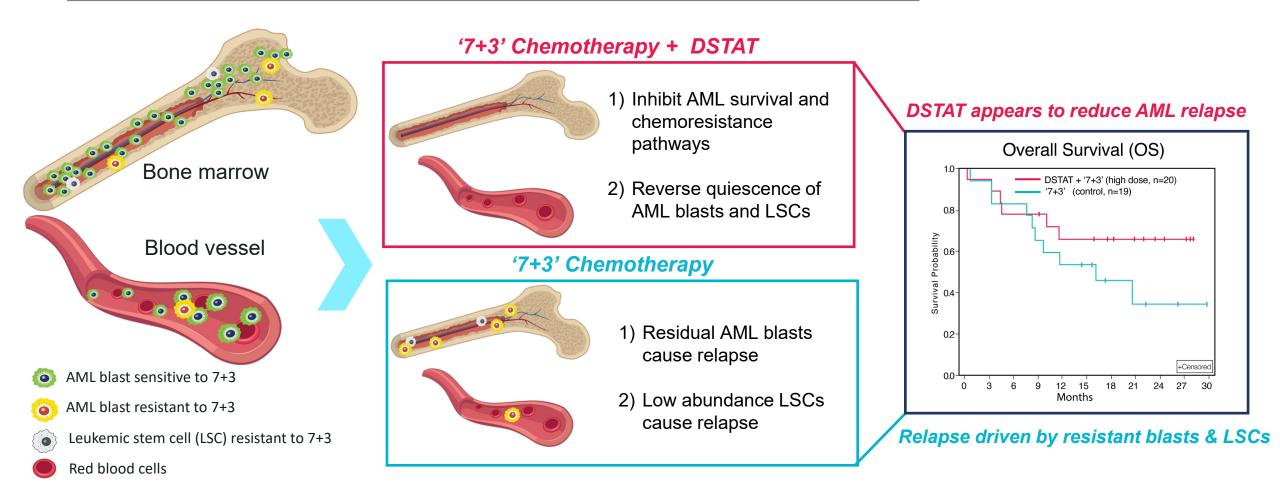


- Median time to recovery of an untransfused platelet count of a least 50 x 10<sup>9</sup>/L of 23.5 days
- Median time to ANC recovery of at least 0.5 x 10<sup>9</sup>/L of 22 days

Tibor J. Kovacsovics, Alice Mims, Mohamed E. Salama, et al. Combination of the low anticoagulant heparin CX-01 with chemotherapy for the treatment of acute myeloid leukemia. Blood Advances. 16 October 2017; accepted 21 January 2018. DOI 10.1182

## **DSTAT** may improve duration of response & overall survival

DSTAT targets proteins involved in resistance pathways and LSC/blast quiescence, including HMGB1, PF4, CXCR4 / CXCL12, neutrophil elastase and selectins



### **Randomized Phase 2B AML study in U.S. cancer centers**

	Subjects	<ul> <li>Treatment-naïve AML patients</li> <li>Age 60+</li> <li>N = 75</li> </ul>
Design <sup>1,2</sup>	Treatment Arms	<ul> <li>Cytarabine + idarubicin (control)</li> <li>Cytarabine + idarubicin + low dose DSTAT (4 mg/kg IV bolus followed by 0.125 mg/kg/hr for 7 days)</li> <li>Cytarabine + idarubicin + higher dose DSTAT (4 mg/kg IV bolus followed by 0.25 mg/kg/hr for 7 days)</li> </ul>
	Subset Matching Phase 3 Population	<ul> <li>Targets 39 of 50 patients from high dose and control arms</li> <li>Excludes patients with favorable genetic risk profile who have lower unmet need (n=5)</li> <li>Excludes patients with secondary AML (sAML) who will likely receive Vyxeos for induction (n=6)</li> </ul>

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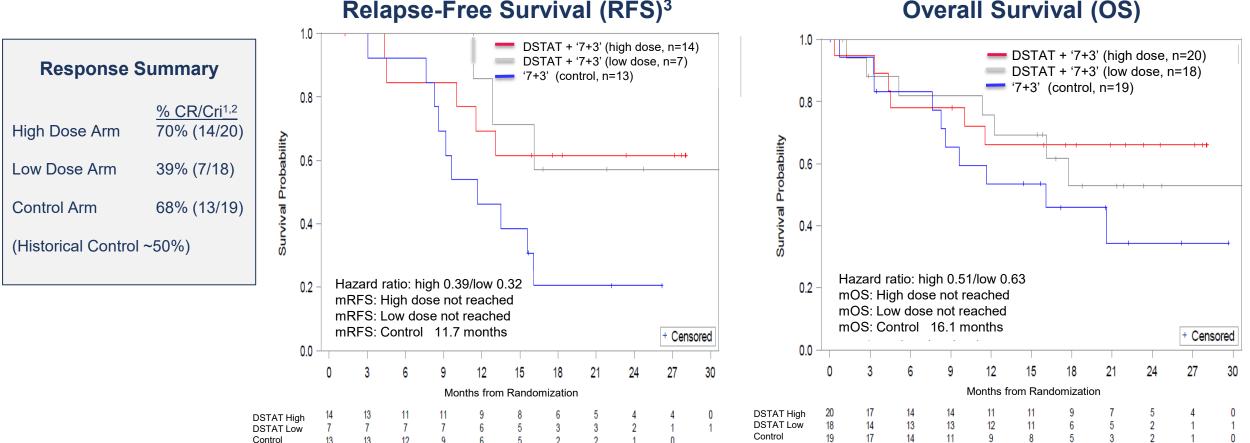
## **DSTAT** potentially amplifies efficacy without significant toxicity

Generally well tolerated in newly diagnosed AML patients

- 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)
- Four gastrointestinal SAEs on DSTAT arm none deemed related to DSTAT (colitis, ileus/gastric ulcer, small bowel obstruction, vomiting – single events and did not increase rate of mucositis)
- One SAE of lower gastrointestinal hemorrhage was reported in the control group
- Asymptomatic, transient elevation of hepatic transaminases observed in both arms
  - Well-described and non-adverse effect of cytarabine therapy
- aPTT remained in the normal range for most patients in DSTAT and control arms
- Comparable incidence of Gr>3 hemorrhagic events (1 on high DSTAT arm, 2 control)

### Phase 3 ITT population shows durability of CR/CRi

Clinically relevant separation in RFS/OS curves



**Relapse-Free Survival (RFS)**<sup>3</sup>

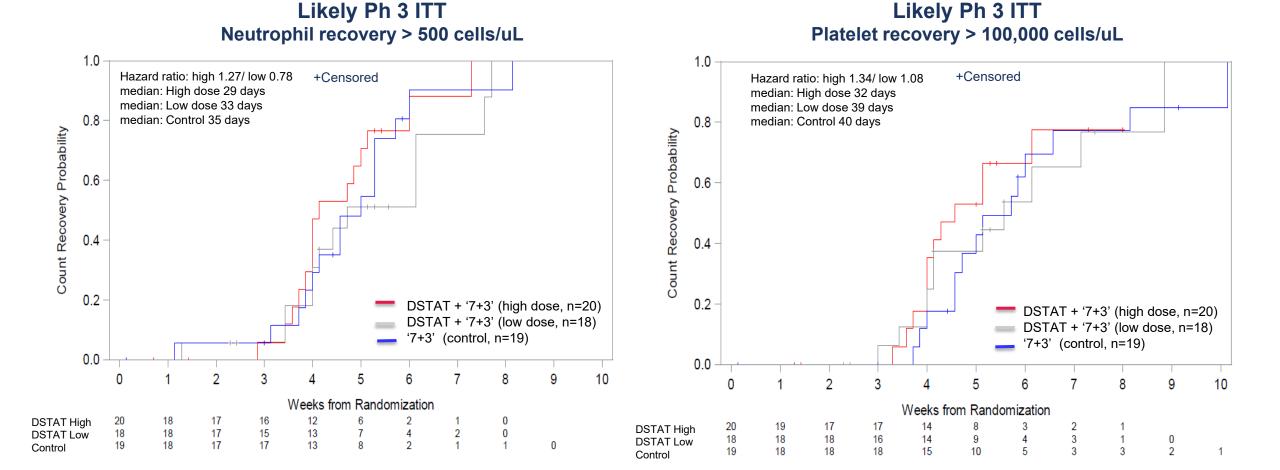
Complete Response (CR) or Complete Response without complete hematologic recovery (CRi)

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

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

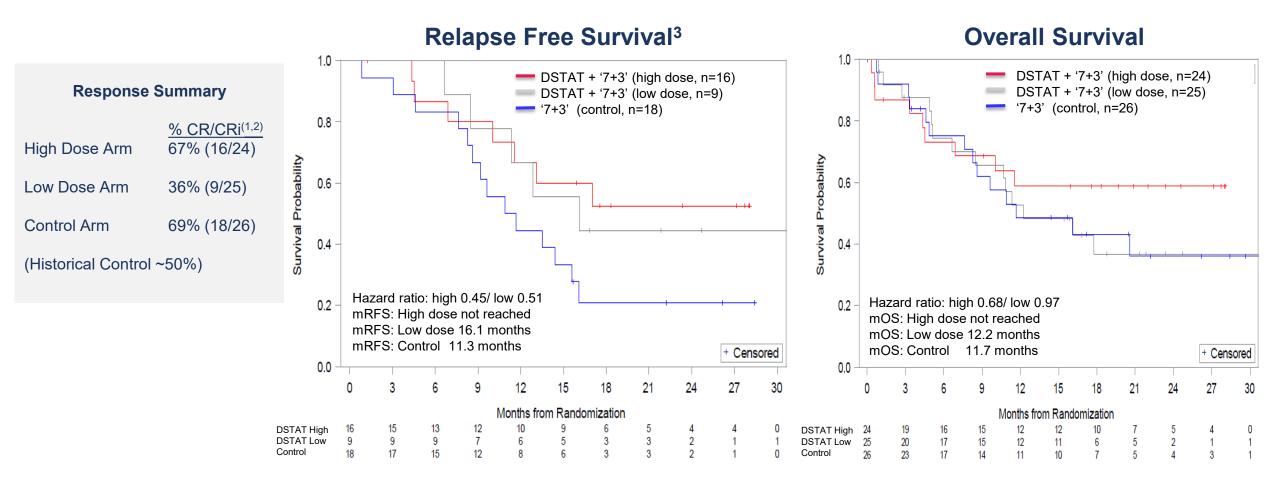
### **DSTAT** may not delay hematologic recovery, may accelerate

Median days to neutrophil and platelet recovery reduced by 17% and 20%, respectively on high dose



### Full ITT population outperforms standard 7+3 chemo

RFS and OS benefit in full ITT Ph 2 population



1. Complete Response (CR) or Complete Response without complete hematologic recovery (CRi)

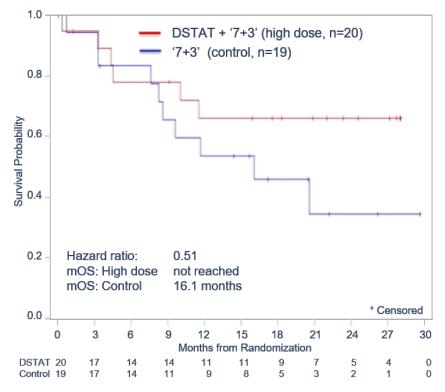
2. Confirmed with post day 14 (D14) bone marrow (BM) biopsy and less than 5% blasts. If no post D14 was performed, the D14 BM biopsy was used to determine response.

3. Relapse-Free Survival (RFS) is survival without relapse following induction success (CR/CRi)

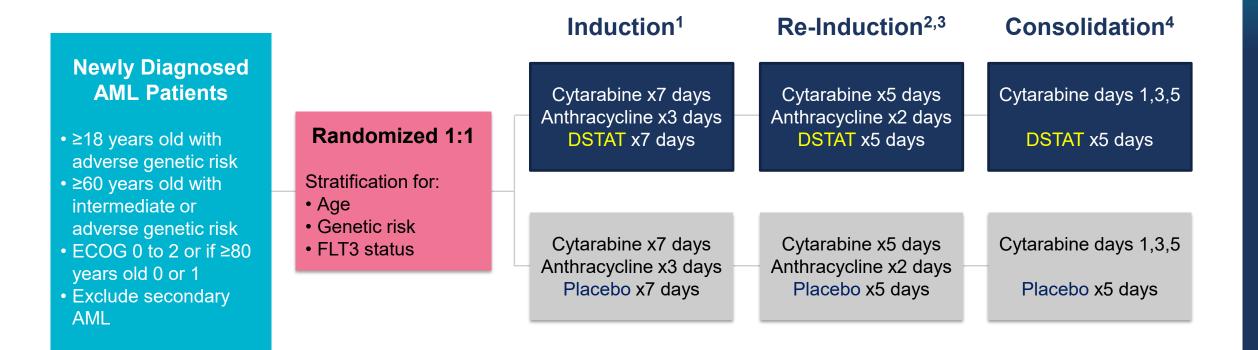
## **Currently Enrolling DASH AML Ph 3 trial design**

- 570 newly diagnosed adults with AML, fit for intensive chemotherapy
- Double-blind, placebo-controlled, randomized 1:1
  - DSTAT plus standard induction/consolidation chemotherapy ("7+3")
  - Placebo plus standard induction/consolidation chemotherapy ("7+3")
- FLT-3 positive subjects able to receive midostaurin
- Primary endpoints: overall survival and event free survival
- Secondary endpoints:
  - Minimal Residual Disease (MRD), Time to hematologic recovery, Response (CR, CR+CRi) and EFS with composite CR (CR+CRi)
- Early efficacy analysis: 80 evaluable patients
  - CR and MRD evaluated
  - Recent publications support predictive power MRD for OS, DFS
  - Data unblinded and published unless extraordinary benefit observed

#### Phase 2 Overall Survival of Target Ph 3 ITT Population



### **DASH Phase 3 treatment plan**



1. Cytarabine and DSTAT are given as continuous IV infusions

2. Patients age 18-59 receive cytarabine x7 days, anthracycline x3 days and DSTAT or Placebo for 7 days

3. Patients may proceed to HCT instead of consolidation chemotherapy

4. Re-induction if day 14 bone marrow shows persistent disease (≥5% blasts)

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### **Early assessment to confirm mechanism**

- Propose early assessment cohort of n=80 evaluable<sup>1</sup> patients for MRD status<sup>2</sup>
- MRD and CR are early indicators of potential OS and EFS advantage
- Patients continue to enroll during assessment
- Most likely unblind to assess and report data<sup>3</sup>
- Key benefits:
  - Confirmation of mechanism driving Phase 2 durable responses and OS
  - Prudent investment trigger
  - Ongoing reporting of cohort as data matures (including EFS and OS)
- IDMC discretion to maintain blinding if advantage is exceptional
  - Example: both CR and MRD advantage >20pp
- Allows for limited investment prior to proof of MRD advantage

1. Evaluable patients include those who have valid MRD results following induction or re-induction, discontinue due to AE or die during induction or re-induction

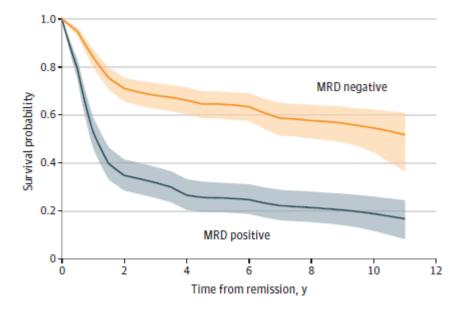
2. Following induction or re-induction if applied

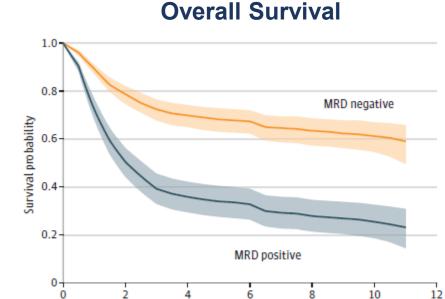
3. Data from early assessment would be excluded from final analysis if unblinded

## **MRD** negativity is associated with superior DFS and OS

80 Patient Assessment likely strong predictor of success

- Meta-analysis of 81 studies (>11,000 patients) links MRD negativity with superior OS and disease-free survival (DFS)
- Results independent of age, subtype, time of assessment or detection method
- Average HR for achieving MRD activity was 0.37 for DFS and 0.36 for OS





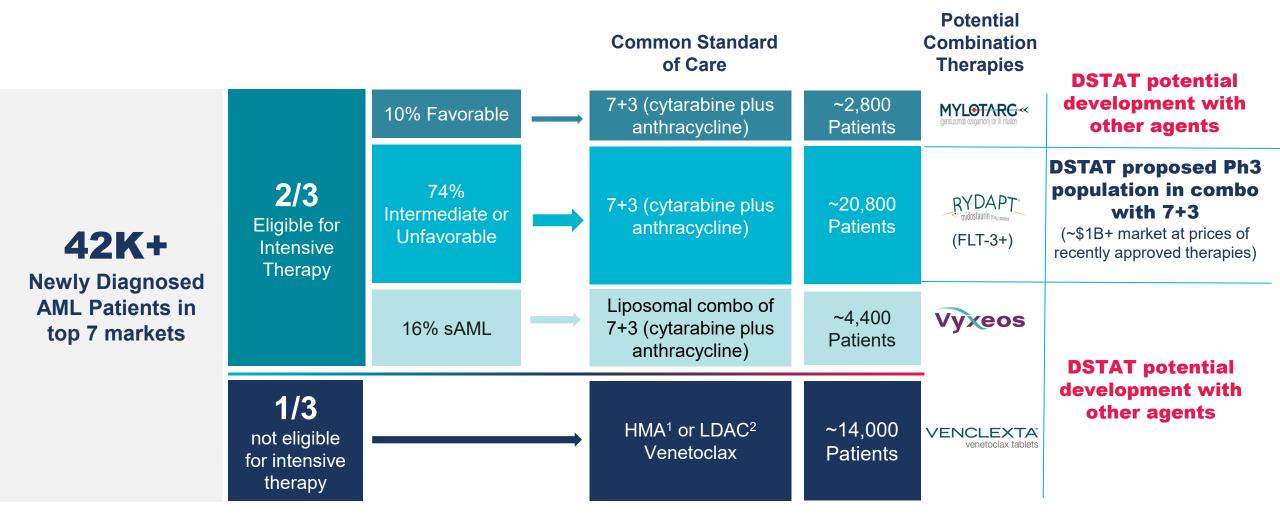
Time from start of therapy, y

#### **Disease-free Survival**

36 Short, et al. JAMA Oncology, October 8,2020

## Significant commercial opportunity and potential to expand

Phase 3 design may position DSTAT as standard of care for up to ~20,800 patients



371.Hypomethylating agents2.Low dose cytarabine

# **Corporate Update**





## **Financial summary**

Dollars (millions)	June YTD 2021
R&D	\$ 25.7
G&A	8.5
Acquired in process R&D	82.9
Total operating expenses	117.1
Net income(loss)	(115.2)
Ending Cash balance	\$ 139.6
Shares outstanding	86.2

- Several levers available for additional capital:
  - Expected significant non-dilutive proceeds from potential TEMBEXA® stockpiling in 2021
  - Global rights to most programs
  - Several 2021 catalysts provides additional optionality

## Major, near-term paths to value

- TEMBEXA® approved for the treatment of smallpox June 4, 2021
  - Satisfies mandate for 2<sup>nd</sup> countermeasure for strategic national stockpile
  - Potential \$80-\$100m annual cash flow next 5-12 years
- Synergistic acquisition of precision oncology platform
  - Efficacy analysis by blinded independent central review of ONC201 data in 2021 (recurrent H3 K27M mutant glioma)
  - Opportunities for new indications and pipeline expansion with the imipridone program
- DSTAT development in front-line AML
  - Phase 3 DASH-AML, enrolling with an early assessment on the first 80 evaluable patients for MRD status

### **Execution focused on multiple catalysts in 2021**

#### **TEMBEXA**®

- ✓ FDA approved TEMBEXA® June 2021
- Potential for \$100m BARDA procurement of TEMBEXA® into the strategic national stockpile
- Potential for procurement of international government sales of TEMBEXA®

#### ONC201 ONC206 ONC212

- Efficacy analysis by BICR of ONC201 registration cohort
- ONC201 pre-NDA meeting preparations
- Continued enrollment of ONC206 dose escalation studies
- IND preparations for ONC212

#### DSTAT

#### AML: ✓ Initiated Ph3 study, DASH AML

# Chimerix Corporate Presentation



