

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d)  
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): May 4, 2023

Chimerix, Inc.  
(Exact name of registrant as specified in its charter)

Delaware  
(State or other jurisdiction of  
incorporation)

001-35867  
(Commission File Number)

33-0903395  
(IRS Employer Identification No.)

2505 Meridian Parkway, Suite 100  
Durham, NC  
(Address of principal executive offices)

27713  
(Zip Code)

(919) 806-1074  
(Registrant's telephone number, including area code)

N/A  
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value \$0.001 per share	CMRX	The Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

**Item 2.02 Results of Operations and Financial Condition.**

On May 4, 2023, Chimerix, Inc. (the “Company”) announced our financial results for the three months ended March 31, 2023 in the press release attached hereto as Exhibit 99.1 and incorporated herein by reference.

**Item 7.01 Regulation FD Disclosure.**

On May 4, 2023, the Company also made available an updated corporate presentation (the “Presentation”) that the Company intends to use, in whole or in part, in meetings with investors, analysts and others. The Presentation can be accessed through the “Investors” section of the Company’s website. A copy of the Presentation is furnished as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated by reference herein.

The information in Item 2.02, Item 7.01 and the attached Exhibit 99.1 and 99.2 is being furnished and shall not be deemed “filed” for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that Section. The information in Item 2.02, Item 7.01 and the attached Exhibit 99.1 and 99.2 shall not be incorporated by reference into any registration statement or other document pursuant to the Securities Act of 1933, as amended.

**Item 9.01 Financial Statements and Exhibits.**

d) Exhibits

<u>Exhibit No.</u>	<u>Description</u>
99.1	<a href="#">Press Release of Chimerix, Inc. dated May 4, 2023.</a>
99.2	<a href="#">Chimerix, Inc. Corporate Presentation, dated May 4, 2023</a>
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

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**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**Chimerix, Inc.**

Date: May 4, 2023

By: /s/ Michael T. Andriole  
Name: Michael T. Andriole  
Title: Chief Business and Financial Officer



## **Chimerix Reports First Quarter 2023 Financial Results and Provides Operational Update**

*– European Union Study Authorization for Phase 3 ACTION Received, Reiterate First Efficacy Data Expected Early 2025 –*

*– Completion of ONC206 Dose Escalation Expected by First Half 2024 –*

*– Conference Call at 8:30 a.m. ET Today –*

**DURHAM, NC, May 4, 2023** -- Chimerix (Nasdaq:CMRX), a biopharmaceutical company whose mission is to develop medicines that meaningfully improve and extend the lives of patients facing deadly diseases, today reported financial results for the first quarter ended March 31, 2023 and provided an operational update.

"2023 is off to a strong start and has been highlighted by multiple presentations of data in support of our imipridone platform during the recent American Association for Cancer Research Annual Meeting (AACR) and our sponsorship at the Canadian Neuro-Oncology Meeting (CNO) this week," said Mike Sherman, Chief Executive Officer of Chimerix. "Dr. Carl Koschmann's ONC201 presentation at AACR marks the first known example of any therapy reversing the H3 K27 trimethyl loss (H3 K27me3-loss) seen in H3 K27M-mutant glioma patients. This shows that dordaviprone (ONC201) can reverse the epigenetic signature which is thought to be a defining characteristic of the disease. Recent literature suggests that reversing the H3 K27M mutation that increases H3 K27 trimethylation in established tumor models results in significant antitumor effects and prolongation of survival. This finding provides additional objective evidence of ONC201 biological activity in this patient population to complement the tumor response observed in the Phase 2 clinical studies. We have also recently completed multiple clinical pharmacology studies, the findings of which have been consistent with our expectations. These studies comprise key elements of a future new drug application (NDA) for ONC201 following positive data from the ACTION study. Our focus has been on accelerating every aspect possible of the Phase 3 ACTION study in order to expedite patient access to this potentially life-altering drug. To that end, we have now received authorization for the ACTION study from nine countries including the United States, the United Kingdom, South Korea, Israel and key markets across Western Europe, as our ramp of site activations continues."

"In addition, we are making good progress advancing the Phase 1 dose escalation studies for our second generation compound, ONC206. As these are open-label studies, in addition to the previously announced objective response observed to ONC206 monotherapy, we hope to identify additional signals of activity this year and look forward to completing dose escalation by first half of 2024," added Mr. Sherman.

### **ONC201 for Treatment of H3 K27M-Mutant Diffuse Glioma**

In April, Chimerix and along with collaborators presented multiple datasets related to the imipridone platform at the AACR Annual Meeting in Orlando, FL. Key results presented by collaborators at the University of Michigan demonstrated that H3 K27M-mutant glioma patients treated with ONC201 experienced a statistically significant reversal of the H3 K27me3-loss epigenetic signature throughout their tumor compared to patients who did not receive ONC201. Gliomas with the H3 K27M-mutation undergo H3 K27me3-loss, which is a negative prognostic variable among gliomas and thought to be a defining characteristic of the disease. Concordant findings were also reported in preclinical models that were mechanistically linked to specific metabolic changes induced in tumors by ONC201.

### **Ongoing Development of ONC206**

ONC206 is a second generation, potentially differentiated imipridone DRD2 antagonist and ClpP agonist, that has demonstrated monotherapy anti-cancer activity in pre-clinical models. ONC206 is currently being evaluated in Phase I dose escalation trials enrolling patients with advanced central nervous system tumors. In March 2023, the Company reported an investigator-assessed response that emerged during dose escalation in the PNOC study. The responder is a patient with recurrent glioblastoma without the H3K27M-mutation who received ONC206 monotherapy.

Preclinical work is ongoing that is designed to further elucidate the ONC206 mechanism of action, identify potential pharmacodynamic biomarkers, and assess the monotherapy efficacy profile of ONC206 in tumors that do not harbor the H3K27M mutation. These activities will inform data-driven clinical development plans.

### **First Quarter 2023 Financial Results**

Chimerix reported a net loss of \$21.4 million, or \$0.24 per basic and diluted share, for the first quarter of 2023. During the same period in 2022, Chimerix recorded a net loss of \$24.8 million, or \$0.28 per basic and diluted share.

Research and development expenses decreased to \$18.8 million for the first quarter of 2023, compared to \$19.0 million for the same period in 2022.

General and administrative expenses increased to \$5.7 million for the first quarter of 2023, compared to \$5.6 million for the same period in 2022.

Chimerix's balance sheet at March 31, 2023 included \$246.1 million of capital available to fund operations, approximately 88.6 million outstanding shares of common stock and no outstanding debt.

### **Conference Call and Webcast**

Chimerix will host a conference call and live audio webcast to discuss first quarter 2023 financial results and provide a business update today at 8:30 a.m. ET. To access the live conference call, please dial 646-307-1963 (domestic) or 800-715-9871 (international) at least five minutes prior to the start time and refer to conference ID 8594205.

A live audio webcast of the call will also be available on the Investors section of Chimerix's website, [www.chimerix.com](http://www.chimerix.com). An archived webcast will be available on the Chimerix website approximately two hours after the event.

### **About the Phase 3 ACTION Study**

The ACTION study is a worldwide, randomized, double-blind, placebo-controlled, multicenter study of ONC201 designed to enroll 450 newly diagnosed diffuse glioma patients whose tumor harbors an H3 K27M-mutation. Treatment with ONC201 begins shortly after completion of radiation therapy. Participants are randomized 1:1:1 to receive 625mg of ONC201 once per week (the Phase 2 dosing regimen), 625mg twice per week on two consecutive days or placebo. The dose is scaled by body weight for pediatric patients. Overall survival (OS) will be assessed for efficacy at three alpha-allocated timepoints: two interim assessments by the Independent Data Monitoring Committee (IDMC) at 164 events and 246 events, respectively, and a final assessment at 327 events. The final Progression Free Survival analysis will be performed after 286 events, with progression assessed using RANO HGG criteria by blinded independent central review (BICR).

## About Chimerix

Chimerix is a biopharmaceutical company with a mission to develop medicines that meaningfully improve and extend the lives of patients facing deadly diseases. The Company's most advanced clinical-stage development program, ONC201, is in development for H3 K27M-mutant glioma.

## Forward-Looking Statements

This press release contains 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 probability of success of the Phase 3 ACTION study, the potential filing and approval of and NDA for ONC201 and subsequent commercial opportunity, the implications of the monotherapy radiographic partial response observed during ONC206 dose escalation; the ability to reproduce clinical and pre-clinical findings, and projections regarding funding and timing of future data readouts. Among the factors and risks that could cause actual results to differ materially from those indicated in the forward-looking statements are risks related to the timing, completion and outcome of the Phase 3 ACTION study of ONC201; risks associated with repeating positive results obtained in prior preclinical or clinical studies in future studies; risks related to the clinical development of ONC206; 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.

## CONTACTS:

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**CHIMERIX, INC.**  
**CONSOLIDATED BALANCE SHEETS**  
(in thousands, except share and per share data)  
(unaudited)

	March 31, 2023	December 31, 2022
<b>ASSETS</b>		
Current assets:		
Cash and cash equivalents	\$ 15,951	\$ 25,842
Short-term investments, available-for-sale	198,801	191,492
Accounts receivable	668	1,040
Prepaid expenses and other current assets	9,330	9,764
Total current assets	224,750	228,138
Long-term investments	31,322	48,626
Property and equipment, net of accumulated depreciation	267	227
Operating lease right-of-use assets	1,848	1,964
Other long-term assets	346	386
Total assets	\$ 258,533	\$ 279,341
<b>LIABILITIES AND STOCKHOLDERS' EQUITY</b>		
Current liabilities:		
Accounts payable	\$ 2,847	\$ 3,034
Accrued liabilities	13,584	17,381
Total current liabilities	16,431	20,415
Loan fees	125	250
Lease-related obligations	1,666	1,819
Total liabilities	18,222	22,484
Stockholders' equity:		
Preferred stock, \$0.001 par value, 10,000,000 shares authorized at March 31, 2023 and December 31, 2022; no shares issued and outstanding as of March 31, 2023 and December 31, 2022	—	—
Common stock, \$0.001 par value, 200,000,000 shares authorized at March 31, 2023 and December 31, 2022; 88,583,567 and 88,054,127 shares issued and outstanding as of March 31, 2023 and December 31, 2022, respectively	89	88
Additional paid-in capital	975,254	970,535
Accumulated other comprehensive loss, net	(231)	(337)
Accumulated deficit	(734,801)	(713,429)
Total stockholders' equity	240,311	256,857
Total liabilities and stockholders' equity	\$ 258,533	\$ 279,341

**CHIMERIX, INC.**  
**CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS**  
(in thousands, except share and per share data)  
(unaudited)

	<b>Three Months Ended March 31,</b>	
	<b>2023</b>	<b>2022</b>
<b>Revenues:</b>		
Contract and grant revenue	\$ 234	\$ —
Licensing revenue	49	15
Total revenues	283	15
Cost of goods sold	—	114
Gross profit	283	(99)
<b>Operating expenses:</b>		
Research and development	18,822	19,040
General and administrative	5,679	5,632
Total operating expenses	24,501	24,672
Loss from operations	(24,218)	(24,771)
<b>Other income:</b>		
Interest income and other, net	2,846	4
Net loss	(21,372)	(24,767)
<b>Other comprehensive loss:</b>		
Unrealized gain (loss) on debt investments, net	106	(52)
Comprehensive loss	\$ (21,266)	\$ (24,819)
<b>Per share information:</b>		
Net loss, basic and diluted	\$ (0.24)	\$ (0.28)
Weighted-average shares outstanding, basic and diluted	88,294,624	87,088,804

# Chimerix Corporate Presentation

Q2 2023



## Forward-Looking Statements

This presentation contains 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 probability of success of the Phase 3 ACTION study, the potential filing and approval of an NDA for ONC201 and subsequent commercial opportunity, the implications of the monotherapy radiographic partial response observed during ONC206 dose escalation; the ability to reproduce clinical and pre-clinical findings, and projections regarding funding and timing of future data readouts. Among the factors and risks that could cause actual results to differ materially from those indicated in the forward-looking statements are risks related to the timing, completion and outcome of the Phase 3 ACTION study of ONC201; risks associated with repeating positive results obtained in prior preclinical or clinical studies in future studies; risks related to the clinical development of ONC206; 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.

## Investment highlights



### High probability of success for Phase 3 ACTION study of ONC201

- Phase 2 study designed to isolate single agent activity in difficult treatment setting
- Durable responses associated with OS and other forms of clinical benefit
- Numerous independent and natural disease history studies support potential survival advantage
- Genetically selected patient population limits patient heterogeneity



### Low barriers to commercial potential for ONC201

- Terminal disease with no effective therapeutic options
- High awareness for program within neuro-oncology community
- U.S. patent exclusivity through at least 2037
- Global revenue potential of ~\$750m in first indication alone



### Corporate capability and financial flexibility

- Leadership team successfully executed large scale studies and regulatory approvals
- Strong balance sheet fully funds ACTION study and potential ONC206 catalysts
- Opportunity for continued non-dilutive TEMBEXA milestones and royalties adds flexibility
- Track record of objectivity in creating paths to capture value

# Deep pipeline across all development stages



4.

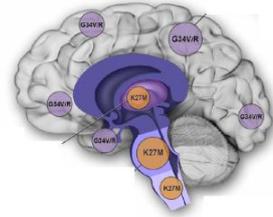
1. Malignant glioma
2. Adult recurrent H3 K27M-mutant high-grade glioma
3. H3 K27M-mutant glioma
4. Central Nervous System
5. Rapidly Emerging Antiviral Drug Development Initiative

**ONC201 (dordaviprone)  
Phase 2 Efficacy  
Analysis**



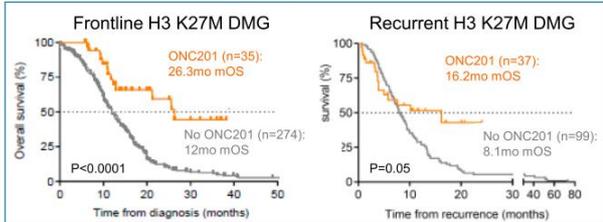
## H3 K27M-mutant diffuse glioma: high unmet need

- H3 K27M mutation is predominantly found among diffuse midline gliomas (DMGs) in young adults and children
- Frontline radiotherapy remains standard of care with transient benefit; resection often not feasible
- DMGs harboring the H3 K27M mutation are WHO Grade IV; historically invariably lethal
- Studies consistently indicate longer OS of ONC201-treated glioma patients relative to diverse external controls



Histone H3 Mutations in CNS Tumors<sup>1</sup>

### External analysis reported at SNO 2022<sup>2</sup>



<sup>1</sup> Lulla RR et al. Sci Adv. 2016;2(3):e1501354

<sup>2</sup> Sunjong Ji, B.S. et al. "Clinical efficacy and predictive biomarkers of ONC201 in H3 K27M-mutant diffuse midline glioma", Society of Neuro-oncology 2022

<sup>3</sup> The median OS was 5.1 months for the subset of patients with H3 K27M-mutant diffuse glioma excluding DIPG, CSF dissemination, spinal or leptomeningeal disease (N=12), OS at 12 mos was 25.0%, OS at 24 mos was 16.7%

### Company Sponsored Studies

	Natural Disease History: Recurrent H3 K27M and/or DMG <sup>3</sup> (n=43)	ONC201 Phase 2: Recurrent H3 K27M DMG (n=50)
Median OS,mo (95% CI)	5.1 (3.9-7.7)	13.7 (8-20.3)
OS @ 12mo (95% CI)	23.6% (11.7-37.9)	57% (41-70)
OS @ 24mo (95% CI)	11.1% (3.3-24.2)	35% (21-49)

## **Phase 2 efficacy for ONC201 in recurrent H3 K27M DMG**

- ONC201 monotherapy exhibited durable, clinically meaningful efficacy in recurrent H3 K27M-mutant DMG
  - Overall Response Rate (ORR) of 30% (95% CI: 18 - 45%) by RANO HGG and/or LGG dual reader BICR
  - RANO-HGG criteria assessed by dual reader BICR
    - ORR 20% (95% CI: 10 – 34%)
    - Median Duration of Response (DOR) 11.2 months (95% CI: 3.8 – not reached)
    - Median time to response 8.3 months (range 1.9 – 15.9)
    - Disease control rate 40% (95% CI: 26 – 55%)
    - PFS at 6 months 35% (95% CI: 21 – 49%); PFS at 12 months 30% (95% CI: 17 – 44%)
  - RANO-LGG criteria assessed by dual reader BICR
    - ORR 26% (95% CI: 15 – 40%)
  - Overall survival
    - 12 months: 57% (95% CI: 41 – 70%)
    - 24 months: 35% (95% CI: 21 – 49%)
- Improvements observed in performance status and reduction in corticosteroid use
- All SAEs considered not related to ONC201 by sponsor

## **FDA-aligned criteria for Phase 2 efficacy analysis to isolate ONC201 single agent activity**

### **Objective**

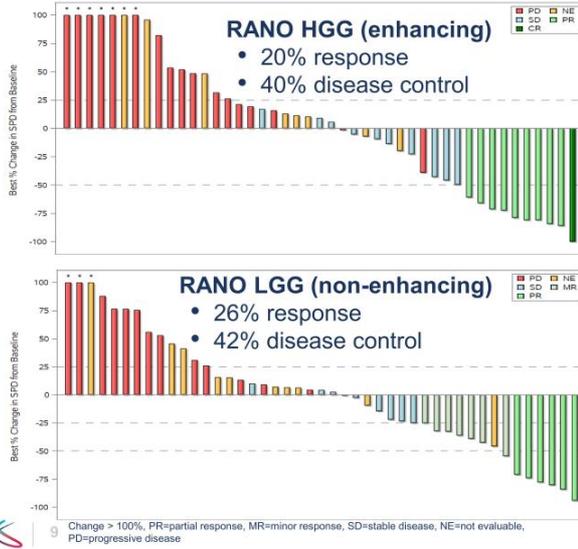
- To evaluate monotherapy efficacy of ONC201 in recurrent H3 K27M-mutant diffuse midline glioma

### **Eligibility**

- Age  $\geq 2$ yo and received ONC201 under studies ONC006, ONC013, ONC014, ONC016, or ONC018
- Diffuse glioma with a known H3 K27M mutation and involvement of a midline structure of the brain
- Progressive and measurable disease on contrast-enhanced brain MRI by RANO-High Grade Glioma (HGG) criteria
- Prior therapy with at least radiation
- Washouts prior to first ONC201 dose:
  - Radiation: 90 days
  - Temozolomide: 23 days / Antibodies (e.g., bevacizumab): 42 days / Other anticancer therapies: 28 days
- Baseline Performance Status  $\geq 60$
- Corticosteroids stable or decreasing for at least 3 days prior to baseline scan
- Excluded: DIPG, primary spinal tumors, atypical and non-astrocytic hist., leptomeningeal spread, CSF dissemination

## ONC201 waterfall plot – 30% RANO HGG / LGG response

ONC201 Ph 2 Efficacy Analysis by BICR in Recurrent H3  
K27M-mutant Diffuse Midline Glioma



- Strict selection criteria to ensure responses attributable to single agent treatment
- Responses require both imaging and clinical criteria
- Dual reader blinded independent central review (BICR)
- Growing consensus that assessment of enhancing and non-enhancing disease (RANO-HGG and RANO-LGG criteria) is needed for diffuse midline glioma

## RANO-HGG responses observed across age groups

### Responses by age group:

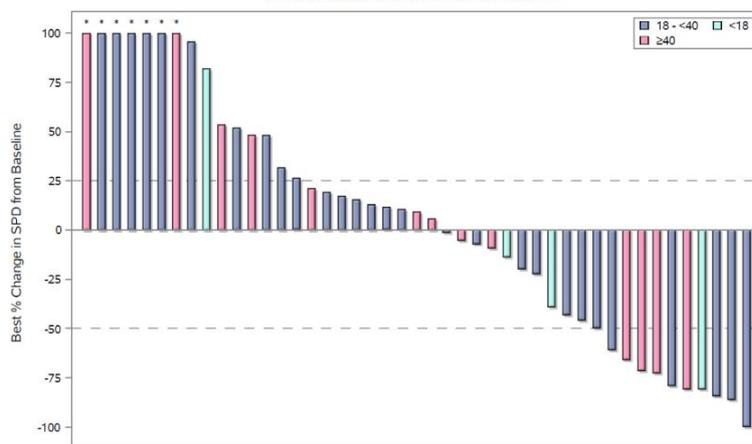
<18 years: 1/4 (25%)

18-40 years: 5/32 (16%)

≥40 years: 4/14 (29%)

RANO-HGG response of 8-year-old subject suggests activity in this population

ONC201 Ph 2 Efficacy Analysis by BICR in Recurrent H3 K27M-mutant Diffuse Midline Glioma



\* Change > 100%, SPD=sum of products of perpendicular diameters (target enhancing lesions per BICR)  
Only patients with measurable target enhancing lesions at both baseline and post-baseline are included.

## RANO HGG response correlation to performance status (PS) supports early-line trial

Predictably, patients with higher PS were more likely to respond to treatment

100: 1/2 (50%)

90: 4/14 (29%)

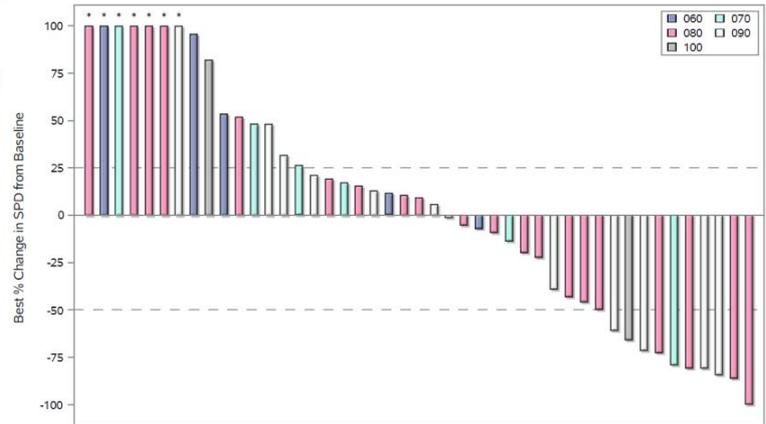
80: 4/20 (20%)

70: 1/7 (14%)

60: 0/7 (0%)

Supports hypothesis that treating earlier in disease course may enhance efficacy

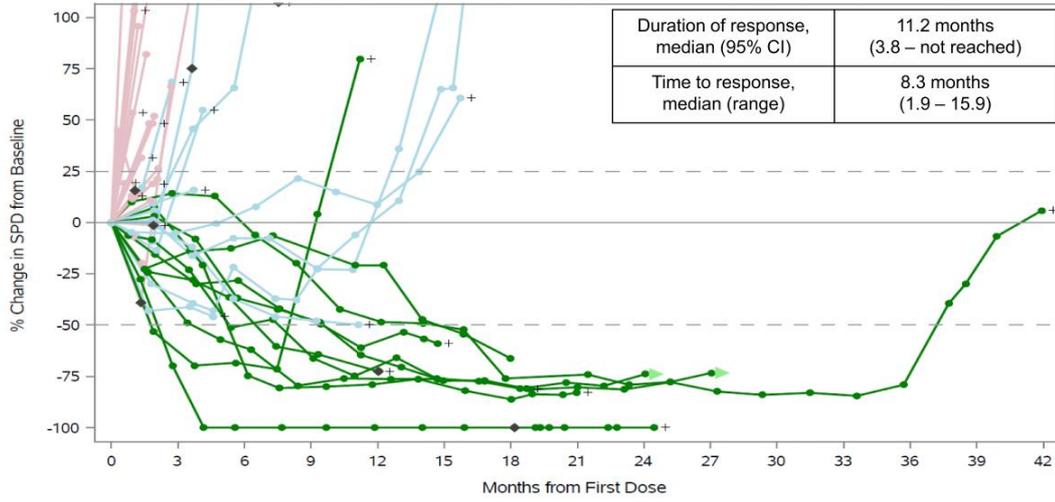
ONC201 Ph 2 Efficacy Analysis by BICR in Recurrent H3 K27M-mutant Diffuse Midline Glioma



\* Change > 100%, SPD=sum of products of perpendicular diameters (target enhancing lesions per BICR). Only patients with measurable target enhancing lesions at both baseline and post-baseline are included.

# Clinically meaningful and durable RANO-HGG responses

ONC201 Phase 2 Efficacy Analysis by BICR in Recurrent H3 K27M-mutant Diffuse Midline Glioma



SPD=sum of products of perpendicular diameters (target enhancing lesions per BICR)  
 Only patients with measurable target enhancing lesions by BICR at baseline and with post-baseline evaluations are included.  
 Three patients did not have on-treatment monotherapy MRIs available for BICR; one patient censored prior to first on-treatment MRI ; one patient did not have measurable target lesion.

## ONC201 safety

### Healthy Adult Dose Escalation Study<sup>1</sup> Incidence of ONC201-Related Adverse Events (AE)

	125 mg N=33	375 mg N=15	625 mg N=45
Any treatment-related AE	36.0%	20.0%	53.0%
Grade 1	36.0%	20.0%	53.0%
Grade 2	0	0	0
Grade 3-5	0	0	0

- In addition to healthy adult dose escalation study above, clinical pharmacology studies included: food-effect, safety pharmacology, special populations, and drug-drug interaction studies
- Treatment-related AEs were generally Grade 1 and transient across the clinical pharmacology program.
- The most commonly reported treatment-related events were mild dizziness, headache and nausea.

### Treatment-related Adverse Events in ≥ 3% Glioma Patients

Treatment-related Adverse Events, Integrated Safety Data Set, (N=211 glioma patients) <sup>2</sup>	Related TEAEs	
	All grades	Grade > 3
Any Treatment-related AE	55.5%	11.8%
Fatigue	21.8%	2.8%
Nausea	20.4%	0
Vomiting	14.2%	0.5%
Headache	8.5%	0.5%
Lymphocyte count decreased	6.6%	0.5%
Decreased appetite	5.7%	0
White blood cell count decreased	4.7%	0.5%
ALT increased	4.3%	0.5%
Hypophosphataemia	4.3%	0
Neutrophil count decreased	3.8%	0.5%
Anaemia	3.3%	0
Diarrhea	3.3%	0



## RANO responses correspond with survival & clinical benefit

ONC201 Ph 2 Efficacy Analysis by BICR in Recurrent H3 K27M-mutant DMG

- No deaths were reported in patients who experienced a RANO-HGG response 24 months<sup>2</sup>
- RANO response strongly associated with reduction in steroid use and improvement in performance status

	All patients	RANO HGG Responders	RANO HGG and/or LGG Responders
N	50	10	15
PFS at 12 months (number of patients censored)	30% <sup>1</sup>	90% (0)	67% (2)
OS at 24 months (number of patients censored) <sup>2</sup>	35% <sup>1</sup>	80% (2)	53% (5)
Corticosteroids response <sup>3</sup> (number of patients evaluable)	47% (15)	100% (4)	100% (5)
Performance status response <sup>4</sup> (number of patients evaluable)	21% (34)	60% (5)	67% (9)

1. Kaplan-Meier median Progression-Free Survival or Overall Survival

2. Censored patients include those who are lost to follow-up or have withdrawn prior to the time point, as well as those who have not yet reached the time point. These patients are counted in the denominator but not counted as survivors (i.e., imputed as failure)

3. Corticosteroid response:  $\geq 50\%$  reduction in average daily corticosteroid dose compared to baseline with stable or improved KPS/LPS. Must be confirmed at next analysis timepoint. Corticosteroids converted into a dexamethasone equivalent dose. Baseline  $\geq 4\text{mg}$  dexamethasone at baseline were evaluable.

4. Performance status response: increase in KPS/LPS compared to baseline with stable or reduced corticosteroid use. Must be confirmed at next analysis timepoint. Baseline KPS/LPS  $\leq 80$  were evaluable.



## Strong rationale for phase 3 success relative to recent GBM trials

Experimental Agent	Ph2 Design	Biomarker	Response criteria	Confounded by anti-angiogenic pseudo response	ORR	Duration of response	6 month PFS	Approved?
<b>ONC201– Ph2 rDMG</b>	Single agent	H3 K27M	RANO BICR	No	20-30%	11.2	35%	To be determined
<b>Temodal<sup>®</sup></b> temozolomide	Single agent	-	Levin	No	5%	?	21%	Yes (OS)
<b>AVASTIN<sup>®</sup></b> bevacizumab	Various	-	Various	Yes	20-70%	4-6	18-50%	Yes (AA per ORR, PFS)
<b>Cediranib</b>	Single agent	-	MacDonald	Yes	27%	?	26%	No
<b>Rindopepimut</b>	Combo + Avastin	EGFRv3	RANO	Yes	30%	7.8	28%	No
<b>Depatuxizumab mafodotin</b>	Single agent	-	RANO	No	7%	6.7	29%	No
<b>Enzastaurin</b>	Combo + Avastin	-	RANO	Yes	22%	?	21%	No



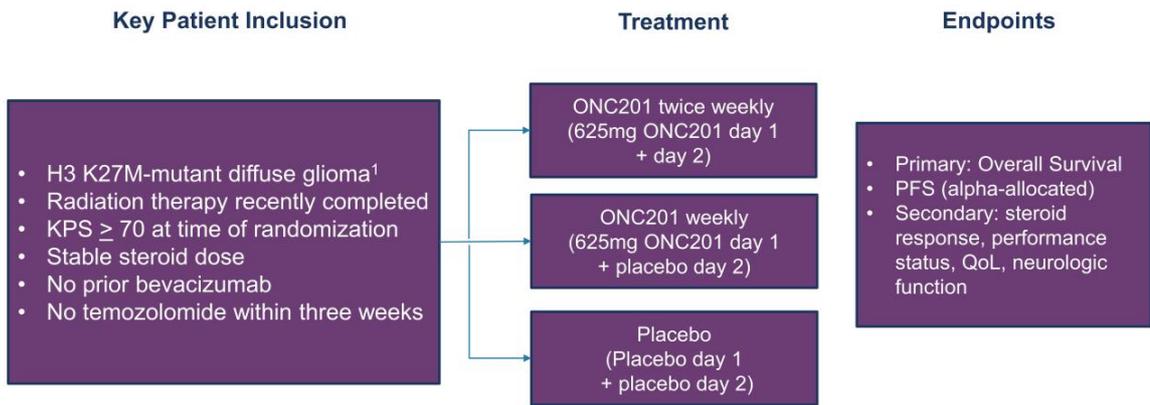
WKA Yung, et al, British Journal Cancer, Aug 8, 2000; Teri Kreisl, et al, Journal Clinical Oncology, 2009, Feb 10;27(5):740-5; Tracy Batchelor, et. al., Journal of Clinical Oncology, vol28, issue 17, Jun 10, 2010; David Reardon, et al, Clin Cancer Research Apr 2020; 26(7):1586-1594; Martin van den Bent, et al, Cancer Chemo & Pharma, 26 Oct 2017 80, 1209-1217; Yazmin Odia, et al, Journal Neuro-Oncology 127, 127-125 (2016)

## ONC201 Phase 3 ACTION Study Summary



## Pivotal Phase 3 ACTION trial design

Now enrolling, a randomized, double-blind, placebo-controlled, multicenter international study in 450 newly diagnosed diffuse glioma patients whose tumor harbors an H3 K27M-mutation.



## Multiple unique aspects to ONC201 data support translation to phase 3 success

### Isolated, durable single agent activity

- Responses not confounded by combination treatments
- Responses were gradual, durable, and multi-focal
- Responses observed via most stringent criteria in blinded assessment

### Consistency across multiple endpoints

- Responses highly associated with other forms of clinical benefit
- PFS and OS favorable to historical benchmarks
- Multiple separate analyses suggest longer survival of patients who received ONC201

### Enhanced activity not required, but likely

- Earlier setting associated with higher response rate (performance status, tumor volume)
- Addition of higher-dose study arm
- Biomarker selection supports patient homogeneity

## Design provides multiple paths for success

Interim data expected in early 2025 and final data in 2026

Independent comparisons for each ONC201 arm versus control will be made at each timepoint.

### First OS<sup>(1)</sup> Interim

- ~164 events
- Success at HR<sup>(3)</sup>=0.52

### PFS by RANO HGG<sup>(2)</sup>

- ~286 events
- Success at HR=0.68

### Second OS Interim

- ~246 events
- Success at HR=0.64

### Final OS

- ~327 events
- Success at HR=0.73

Powering assumptions 0.65 expected HR for OS and 0.60 expected HR for PFS

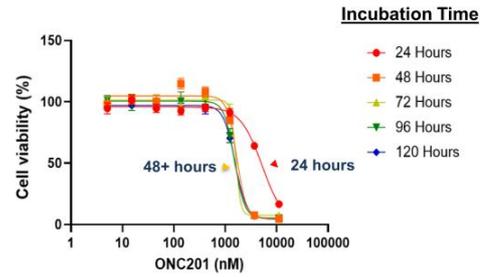


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1. Overall Survival (OS)
2. Progression-free survival (PFS). PFS may provide valuable data for regulatory discussions.
3. Hazard Ratio

## Potential to increase ONC201 efficacy with dose schedule

- Once per week ONC201 dosing effective as monotherapy in Phase 2 studies
- Twice per week dosing on two consecutive days expected to increase duration of therapeutic exposure
  - Increased exposure time can increase glioma sensitivity to ONC201 in vitro
  - Generally well tolerated in Phase 1 without dose limiting toxicity or AEs leading to dose modification
- Phase 3 ACTION study will evaluate once per week and twice per week dosing schedules at 625mg (or body weight equivalent)



# ONC201 Market Opportunity Assessment



## H3 K27M-mutant glioma: rapid ramp to peak revenue expected

- No approved therapies for H3 K27M mutant glioma, ONC201 is the leading program targeting this mutation globally
- Potential market opportunity ~\$750 million
- Approximately 5,000 patients in top seven markets
- Ultra-orphan indication drug pricing
- H3 K27M mutations most often in children / young adults (little exposure to Medicare)
- Low barriers to adoption
  - No effective alternative therapies
  - High unaided awareness among neuro-oncologists
  - Mutation routinely identified by existing diagnostics
  - Longer-term, potentially combinable with other glioma therapies
- Patent protection for lead indication into 2037 - potential U.S. patent term extension (up to five years)

## Regulatory designations



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

EU - ODD for treatment of glioma



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

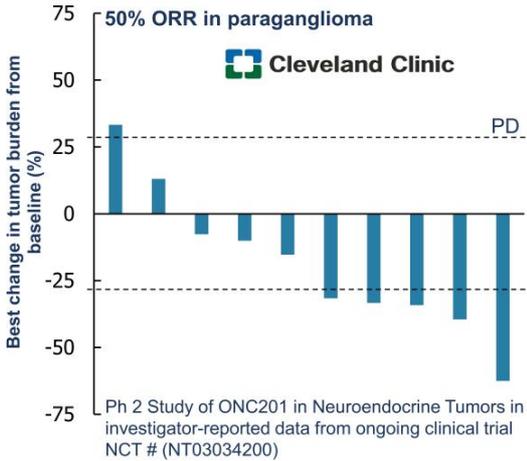


Rare Pediatric Disease Designation for treatment of H3 K27M mutant glioma

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



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



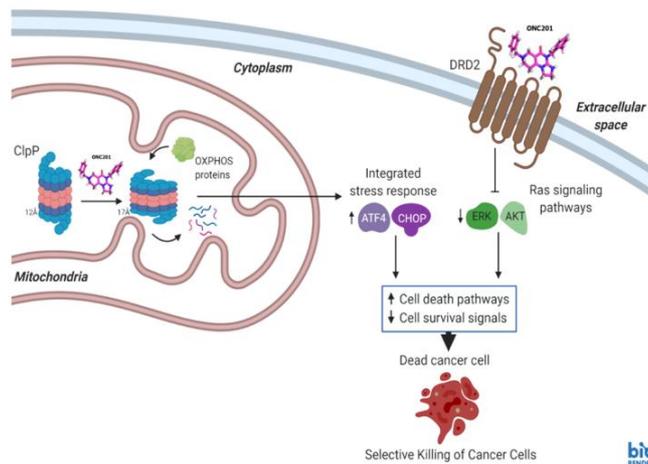
- Single agent responses in Ph 2 neuroendocrine trial of ONC201 observed in subset (paraganglioma)
- Paraganglioma are adrenal-related tumors with elevated DRD2 expression
- Five patients have been treated > 1 year
- Fewer short-term and potential long-term toxicities than other paraganglioma therapies

## ONC201 Mechanism of Action



## ONC201 directly engages DRD2 and ClpP

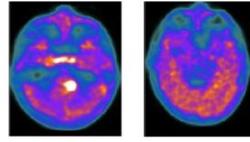
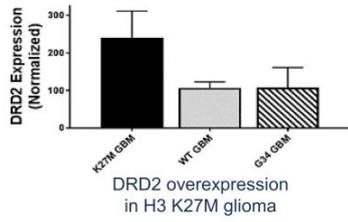
ONC201 upregulates integrated stress response, inactivates Akt/ERK, selectively inducing tumor cell death



- 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

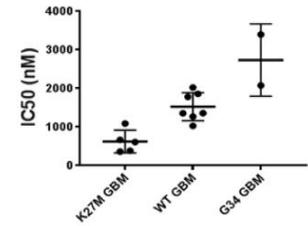
# H3 K27M glioma primed for ONC201 sensitivity

DRD2 pathway inhibited by ONC201 is enriched in H3 K27M glioma



18F-DOPA PET  
H3 K27M glioma often located in dopamine-rich environment

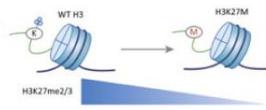
H3 K27M is hypersensitive to ONC201



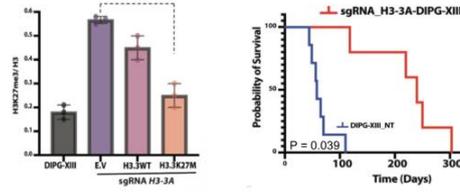
Ex vivo high grade glioma growth sensitivity to ONC201 by H3 status

# H3 K27M central characteristic reversed by ONC201

H3 K27M causes loss of global H3 K27 trimethylation (H3 K27me3-loss)

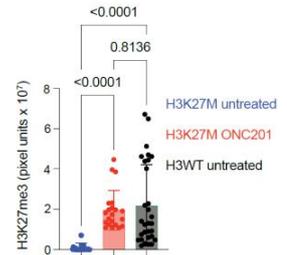


Removal of H3 K27M mutation results in reversal H3 K27me3-loss and prolonged OS in glioma models



CRISPR-Cas9 deletion of H3 K27M (left) specifically increases H3 K27me3 and (right) prolongs OS

ONC201 reverses H3 K27me3-loss in H3 K27M glioma patients' tumors

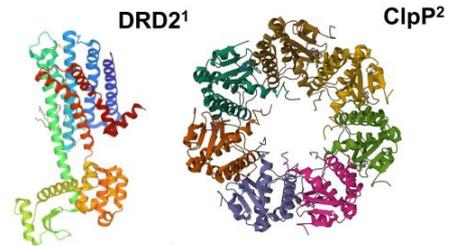
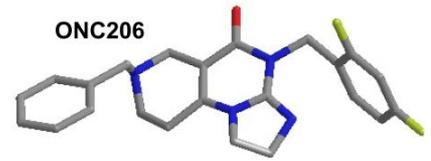


**ONC206**

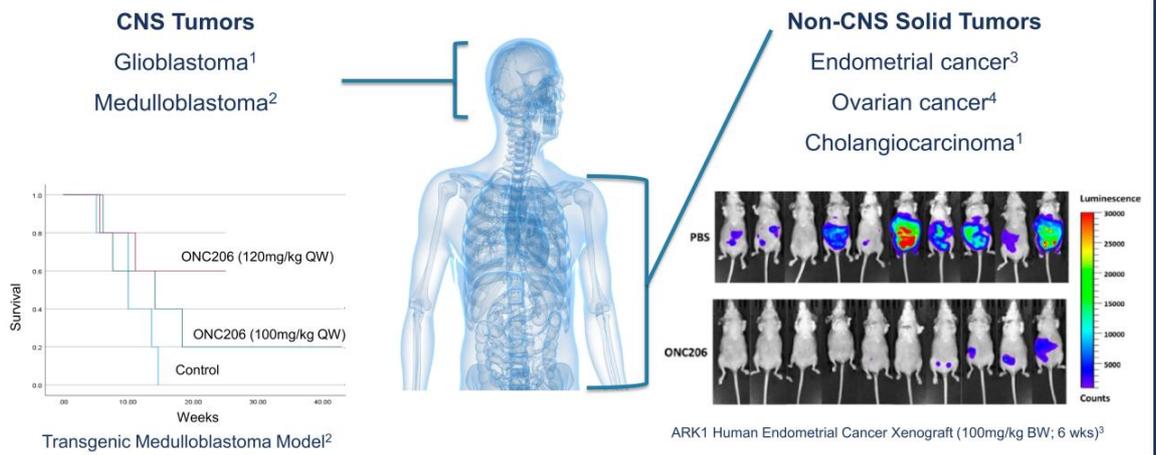


## ONC206: oral brain penetrant DRD2 antagonist + ClpP agonist

- Second generation imipridone designed to expand to new indications
- Efficacy in cell culture, xenograft and transgenic central nervous system (CNS) and other tumor models
- Oral dose escalation trials ongoing in CNS cancers
- Monotherapy response reported by investigator in early dose escalation cohort for a patient in recurrent non-H3 K27M GBM
  - Dordaviprone responses amongst CNS tumors exclusively in H3K27M gliomas



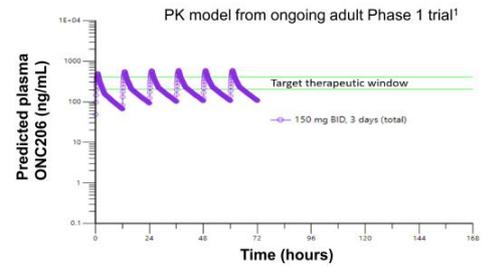
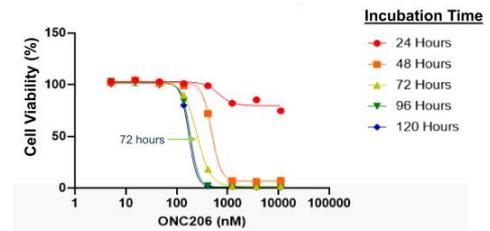
# ONC206 monotherapy active in models of CNS and other cancers



## Dose intensification expected to enhance therapeutic exposure

- Consecutive day dosing may increase therapeutic response
  - In vitro data demonstrates enhanced efficacy with 72 hour sustained exposure
  - Toxicology data enables safe escalation to more prolonged exposures
- PK models from ongoing adult Phase 1 trial data suggest a therapeutic and safe exposure possible with twice daily, three times weekly dosing

HGG in vitro response to ONC206 enhanced with exposure time



## ONC206 dose escalation: pediatric and adult CNS tumors

- Monotherapy dose escalation trials enrolling in parallel for adult and pediatric CNS tumors
- Response reported by investigator from early cohort (100mg QW) without H3 K27M mutation
  - 18-year-old patient with recurrent temporal lobe glioblastoma
  - Regression on MRI & metabolic reduction via PET imaging, continuing on therapy over 10 months
  - Details to be presented at future medical conference



National Institutes  
of Health



PACIFIC PEDIATRIC  
NEURO-ONCOLOGY  
CONSORTIUM

## ~30,000 new cases of GBM annually in the top 7 markets; >\$2Bn market opportunity

- GBM is a rapidly progressive disease with low survival rates, few drug approvals last 25 years:
  - Temozolomide (TMZ) approved 1999
  - Bevacizumab approved 2009
- Existing therapies rarely offer durable effect
  - 3-year survival from diagnosis



- Chimerix retains global operational rights to ONC206<sup>2</sup>
- Worldwide market opportunity exceeds \$2Bn
  - TMZ revenue peaked at approximately \$1.4 billion in 2009, prior to going generic
    - o Inflation adjusted peak: > \$2.5Bn
  - New GBM therapy: 50% penetration at average price of contemporary oncology drug approvals exceeds \$2Bn

# Preclinical Development

## ONC212 and CMX521

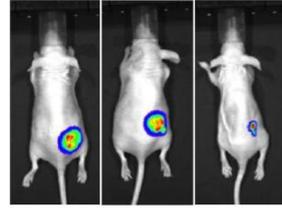


## ONC212: GPR132 + ClpP Agonist

- Distinct molecular target (GPR132) and efficacy profile relative to ONC201/ONC206
- Efficacy in preclinical models of advanced cancers
- GLP-tox studies complete, potential to advance to IND
- Partnerships established for early-stage clinical trials with Brown University and MD Anderson Cancer Center

### Pancreatic cancer model shows the potential of ONC212<sup>1</sup>

Vehicle    ONC201    ONC212

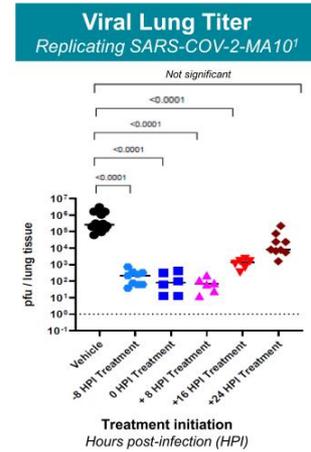




## CMX-521: anti-SARS-CoV-2 preclinical activity

- Ribonucleoside analog that is a viral polymerase inhibitor
  - Inhaled nebulized liquid aerosol formulation; minimal systemic exposure
- Monotherapy efficacy in mouse-adapted SARS-CoV-2-MA10 model across multiple endpoints
  - Lung viral titer
  - Viral RNA parallel viral lung titer (plaque forming unit)
  - Clinical scoring (animal health)
  - Lung pathology
  - Animal weight loss

**\$2 million grant to fund prodrug formulations that could enable oral administration with improved lung delivery**



## Corporate Update



## TEMBEXA® deal term summary

Emergent BioSolutions is an experienced biodefense company collaborating with government agencies to protect public health

### Terms summary:

- \$238 million received upfront at closing in Q3 2022
- Up to an additional \$124 million in potential BARDA procurement milestones
- 20% royalty on future U.S. gross profit with volumes above 1.7 million courses of therapy
- 15% royalty of all international gross profit
- Up to an additional \$12.5 million in development milestones

# TEMBEXA®

brincidofovir

10 mg/mL oral suspension | 100 mg tablets



## Financial strength supports development through key catalysts



**\$246 million cash balance at March 31, 2022, no debt**

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**Fully funded Ph 3 program with multiple potential paths to approval**

First-Line H3 K27M-mutant diffuse glioma – The ACTION Study

- ✓ Trial initiated November 2022
- ✓ Interim OS data expected early 2025, full OS data expected 2026

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**ONC206 in early dose escalation studies at NIH and PNOG**

- ✓ Confirmed response in Non-H3 K27M recurrent glioblastoma patient

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**Early-stage pipeline leverages external capital**

- ✓ Pre-clinical programs potential to advance to clinic or partner (ONC212, CMX521)
- ✓ Robust business development search and evaluation process

# Chimerix Corporate Presentation



