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): November 7, 2024

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

Delaware	**001-35867**	**33-0903395**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

2505 Meridian Parkway, Suite 100 **Durham, NC**	**27713**
(Address of principal executive offices)	(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 November 7, 2024, Chimerix, Inc. (the "Company") announced our financial results for the nine months ended September 30, 2024 in the press release attached hereto as Exhibit 99.1 and incorporated herein by reference.

Item 7.01 Regulation FD Disclosure.

On November 7, 2024, 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 Exhibits 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 Exhibits 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

Exhibit No.	Description
99.1	Press Release of Chimerix, Inc. dated November 7, 2024.
99.2	Chimerix, Inc. Corporate Presentation, dated November 7, 2024.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

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: November 7, 2024

By:	/s/ Michelle LaSpaluto
Name:	Michelle LaSpaluto
Title:	Chief Financial Officer

Chimerix Reports Third Quarter 2024 Financial Results and Provides Operational Update

– Phase 3 ACTION Study On-Track with First Interim Overall Survival Data Expected Third Quarter 2025 –

– IDMC Recommends Continuing Conduct of ACTION Study As-Is Following Preplanned Safety Review –

– Alignment with TGA to Submit Dordaviprone for Provisional Approval in Australia –

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

DURHAM, N.C., November 7, 2024 (GLOBE NEWSWIRE) -- Chimerix (NASDAQ:CMRX), a biopharmaceutical company whose mission it is to develop medicines that meaningfully improve and extend the lives of patients facing deadly diseases, today reported financial results for the third quarter ended September 30, 2024 and provided an operational update.

“We have sustained execution of the Phase 3 ACTION study and continue to be encouraged by the safety profile of dordaviprone following the Independent Data Monitoring Committee’s (IDMC) preplanned safety review which recommended continuing study conduct as-is, including at the more intense twice per week dose. Additionally, the Therapeutic Goods Administration (TGA) has granted orphan drug designation to dordaviprone, and we have alignment to file a New Drug Application (NDA) for Provisional Approval in Australia which we expect to occur in the coming months,” said Mike Andriole, Chief Executive Officer of Chimerix. “As we complete the dordaviprone NDA and look toward the balance of the year, we also expect to complete enrollment in a Phase 1 dose escalation study of ONC206 as we consider future development scenarios for this program.”

“In addition, we were delighted to announce the promotion of Dr. Josh Allen to the role of Chief Scientific Officer this quarter. Josh has been instrumental in the discovery and development of the imipridone class of compounds and expect his broad expertise in cancer biology and strong business acumen will underpin Chimerix early phase development for years to come,” added Mr. Andriole.

Dordaviprone (ONC201)

Dordaviprone, a first-in-class imipridone, has the potential to be the first treatment approved for H3 K27M-mutant diffuse glioma. It is an oral small molecule that crosses the blood-brain barrier and selectively binds to the mitochondrial protease ClpP and the dopamine receptor D2 (DRD2). Dordaviprone's unique mechanism of action includes alterations of key epigenetic modifications such as reversal of H3 K27me3-loss which is the hallmark of H3 K27M-mutant gliomas.

Dordaviprone is being evaluated in the Phase 3 ACTION trial that is currently enrolling H3 K27M-mutant diffuse glioma patients at over 145 sites in 15 countries. Chimerix expects interim OS data in the third quarter of 2025. For more information on the ACTION trial, please visit www.clinicaltrials.gov

Earlier this year, Chimerix initiated the evaluation process for dordaviprone to be considered for Provisional Registration in Australia. The Provisional Registration process is a three-step process which begins with a Pre-Submission Meeting evaluating current data, as well as other program features,

including the status of pivotal studies. The second step, the Provisional Determination Application, was approved during the third quarter 2024, as was the application for Orphan Drug Designation in Australia. The final step is the NDA submission for Provisional Registration which is expected to occur in the coming months with potential commercial availability as soon as year-end 2025.

ONC206

The imipridone ONC206 is a second generation ClpP agonist and DRD2 antagonist which also crosses the blood-brain barrier and is 10x more potent in vitro than dordaviprone. It has demonstrated monotherapy anti-cancer activity in vivo in central nervous system (CNS) tumor models, as well as in vivo solid tumors models outside of the CNS. The two Phase 1 dose escalation trials conducted in partnership with the Pacific Pediatric Neuro-Oncology Consortium (PNOC) and the National Institutes of Health (NIH) have enrolled over 80 pediatric and adult patients with unselected CNS tumors, with no dose limiting toxicity observed to date.

The safety profile of ONC206 has been consistent across both pediatric and adult populations, with the majority of treatment-related adverse events being mild to moderate, including fatigue, lymphocyte count decrease and vomiting. No significant change in the overall safety profile has been reported to date as dosing has escalated and intensified in frequency from once per week to twice per day on three consecutive days per week. Completion of enrollment in the remaining dose escalation cohorts is expected to occur in 2024.

Assessment of objective responses in patients where a monotherapy treatment effect can be reliably evaluated is ongoing in dose cohorts at or above target exposure thresholds. The company expects to assess any objective responses in the first half of 2025, allowing sufficient time for response onset and confirmation in current and future dose cohorts.

Additionally, ONC206 nonclinical studies remain ongoing to identify candidate oncology indications and biomarkers to inform future development plans.

Corporate

In September 2024, Chimerix promoted Joshua E. Allen, PhD, to the role of Chief Scientific Officer after previously serving as Chief Technology Officer. Dr. Allen co-discovered the anti-cancer activity of ONC201 and co-invented the imipridone class of compounds. He has continuously advanced the research and development of dordaviprone from academic discovery to its registration program, along with the creation and clinical introduction of biologically distinct derivatives. He received his Ph.D. in Biochemistry and Molecular Biophysics from the University of Pennsylvania. Several research publications, patents, grants, and awards reflect his scientific and entrepreneurial efforts in oncology, including recognition on the Forbes 30 under 30 list. Prior to joining Chimerix, Dr. Allen served as Chief Scientific Officer at Oncoceutics.

Third Quarter 2024 Financial Results

Chimerix reported a net loss of $22.9 million, or $0.26 per basic and diluted share, for the third quarter of 2024. During the same period in 2023, Chimerix recorded a net loss of $24.0 million, or $0.27 per basic and diluted share.

Research and development expenses increased to $19.6 million for the third quarter of 2024, compared to $17.4 million for the same period in 2023.

General and administrative expenses decreased to $5.2 million for the third quarter of 2024, compared to $9.3 million for the same period in 2023. This decrease is due to a one-time non-cash expense related to historical equity grants recognized during the 2023 period.

Chimerix's balance sheet at September 30, 2024 included $152.4 million of capital available to fund operations, approximately 89.9 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 third quarter 2024 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 6580777. A live audio webcast of the call will also be available on the Investors section of Chimerix's website, www.chimerix.com. An archived webcast will be available on the Chimerix website approximately two hours after the event.

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, dordaviprone (ONC201), is in development for H3 K27M-mutant diffuse glioma. The Company is conducting Phase 1 dose escalation studies of ONC206 to evaluate safety and PK data.

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, expectations regarding interim OS data from the ACTION study, plans for Provisional Registration and commercialization in Australia, expectations regarding completion of enrollment and assessment of responses in the ONC206 dose escalation trials, and the characteristics and development of ONC206. 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 ability to obtain and maintain accelerated approval; 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 our clinical candidates; 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.

CONTACT:

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will@sternir.com

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

	September 30, 2024	December 31, 2023
ASSETS		
Current assets:		
Cash and cash equivalents	$ 23,645	$ 27,661
Short-term investments, available-for-sale	112,585	155,174
Accounts receivable	155	4
Prepaid expenses and other current assets	4,517	6,271
Total current assets	140,902	189,110
Long-term investments	16,201	21,657
Property and equipment, net of accumulated depreciation	281	224
Operating lease right-of-use assets	1,089	1,482
Other long-term assets	195	301
Total assets	$ 158,668	$ 212,774
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 5,340	$ 2,851
Accrued liabilities	16,904	15,592
Total current liabilities	22,244	18,443
Line of credit commitment fee	—	125
Lease-related obligations	644	1,177
Total liabilities	22,888	19,745
Stockholders’ equity:		
Preferred stock, $0.001 par value, 10,000,000 shares authorized at September 30, 2024 and December 31, 2023; no shares issued and outstanding as of September 30, 2024 and December 31, 2023	—	—
Common stock, $0.001 par value, 200,000,000 shares authorized at September 30, 2024 and December 31, 2023; 89,936,053 and 88,929,300 shares issued and outstanding as of September 30, 2024 and December 31, 2023, respectively	90	89
Additional paid-in capital	996,389	988,457
Accumulated other comprehensive gain, net	258	7
Accumulated deficit	(860,957)	(795,524)
Total stockholders’ equity	135,780	193,029
Total liabilities and stockholders’ equity	$ 158,668	$ 212,774

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2024	**2023**	**2024**	**2023**
Revenues:				
Contract and grant revenue	$ 26	$ 11	$ 155	$ 271
Licensing revenue	—	—	—	49
Total revenues	26	11	155	320
Operating expenses:				
Research and development	19,646	17,396	56,918	53,144
General and administrative	5,173	9,304	15,252	19,431
Total operating expenses	24,819	26,700	72,170	72,575
Loss from operations	(24,793)	(26,689)	(72,015)	(72,255)
Other income:				
Interest income and other, net	1,914	2,703	6,582	8,321
Net loss	(22,879)	(23,986)	(65,433)	(63,934)
Other comprehensive loss:				
Unrealized gain (loss) on debt investments, net	466	188	251	(288)
Comprehensive loss	$ (22,413)	$ (23,798)	$ (65,182)	$ (64,222)
Per share information:				
Net loss, basic and diluted	$ (0.26)	$ (0.27)	$ (0.73)	$ (0.72)
Weighted-average shares outstanding, basic and diluted	89,701,117	88,620,666	89,531,017	88,500,813

Chimerix Corporate Presentation

November 7, 2024

CHIMERIX

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, expectations regarding interim OS data from the ACTION study, expectations regarding completion of enrollment and assessment of responses in the ONC206 dose escalation trials, the characteristics and development of our product candidates, our ability to successfully commercialize our current and future product candidates, the potential for royalty and milestone revenue from strategic collaborations, and projections regarding the potential market opportunity, funding and timing of future data readouts for our products. 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 ability to obtain and maintain accelerated approval; 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 and key catalysts

Ph 3 ACTION study actively enrolling | **Significant commercial potential** | **Corporate capability and financial flexibility**

Dordaviprone Ph 3 trial enrolling - interim OS data expected in third quarter 2025

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

- ✓ *No approved therapies targeting H3 K27M diffuse glioma, an area of high unmet medical need*
- ✓ *First in class mechanism of action with clinical validation*
- ✓ *Patent protection thru 2037 (potential additional US patent term extension)*

ONC206 now dosing within the expected therapeutic range

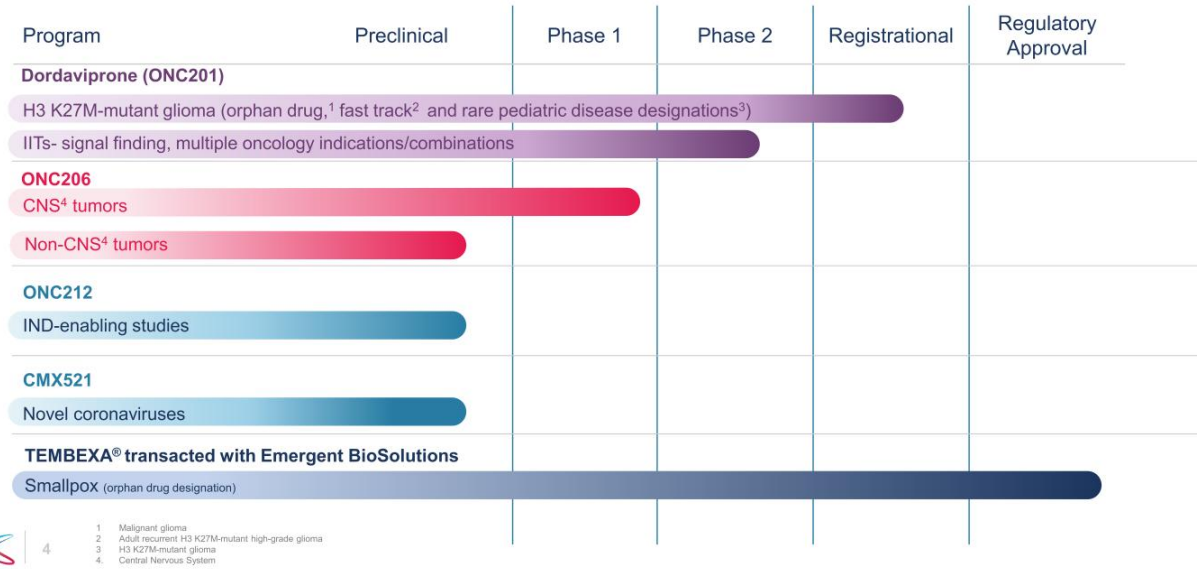
- ✓ *Pharmacokinetic data from dose escalation studies demonstrate dose proportionate exposure*
- ✓ *No unexpected safety events and no dose limiting toxicities to date*
- ✓ *Exhibits monotherapy activity in multiple non-clinical CNS models as well as tumors outside the CNS*

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*

$152 million in capital to fund operations as of September 30, 2024, no debt

Deep pipeline across all development stages



1 Malignant glioma
2 Adult recurrent H3 K27M-mutant high-grade glioma
3 H3 K27M-mutant glioma
4. Central Nervous System

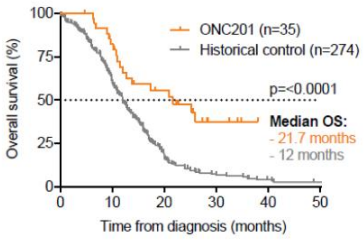
Dordaviprone(ONC201)
Phase 2 Data Analysis

CHIMERIX

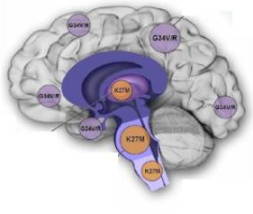
Dordaviprone data suggests potential to address high unmet need

- 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
- Consistently longer OS of dordaviprone treated H3 K27M DMG patients across:
  - Diverse external controls (historical, trials)
  - Sensitivity analysis (early event censoring)
  - Isolated tumor locations (thalamus, brainstem)

Frontline H3 K27M DMG[2]



Histone H3 Mutations in CNS Tumors[1]



Recurrent H3 K27M DMG[3]

	Natural Disease History[4] (n=43)	ONC201 Phase 2 (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)

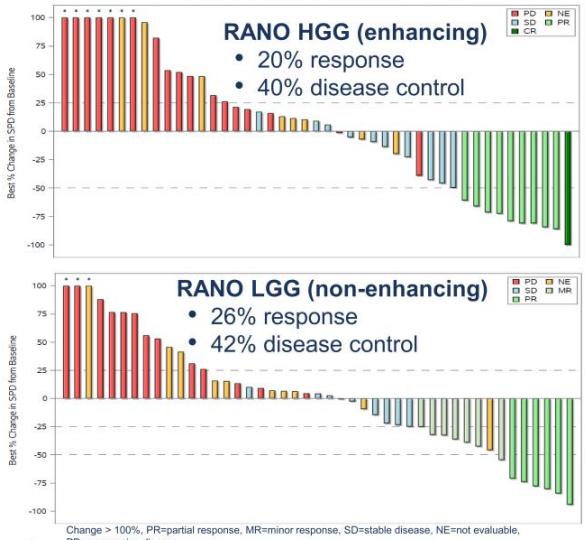
[1] Lulla RR et al. Sci Adv. 2016;2(3):e1501354
[2] Koschmann, Carl et al, "Clinical efficacy of ONC201 in H3 K27M-mutant diffuse midline glioma is driven by disruption of integrated metabolic and epigenetic pathways", Cancer Discovery, Aug 16, 2023
[3] In company sponsored studies
[4] The median OS 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%

Dordaviprone phase 2 efficacy in recurrent H3 K27M Diffuse Midline Glioma (DMG)

- Dordavirprone 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 Serious Adverse Events considered not related to dordaviprone by sponsor

Dordaviprone waterfall plot – 30% RANO HGG / LGG response

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



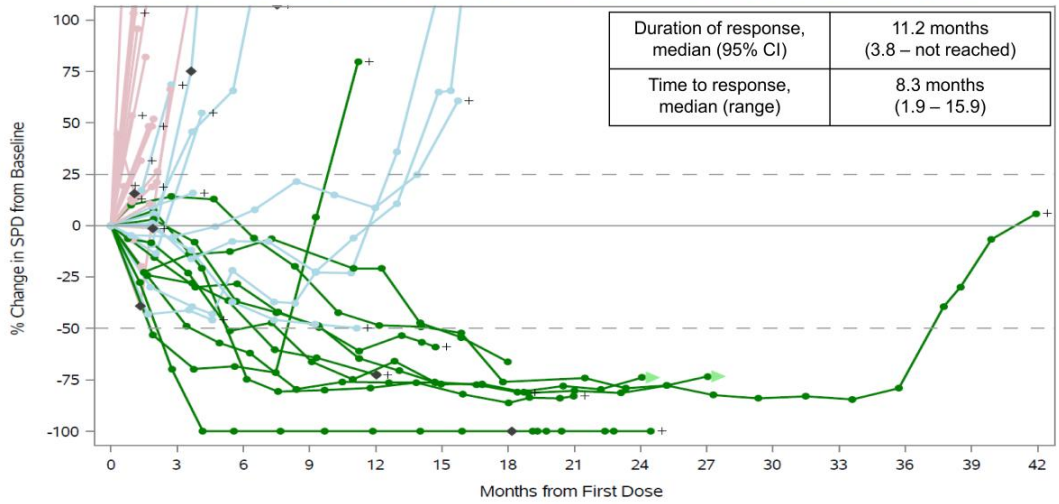
Change > 100%, PR=partial response, MR=minor response, SD=stable disease, NE=not evaluable, PD=progressive disease

Arrillaga-Romany, et al, Journal of Clinical Oncology, Feb 2024

- Strict selection criteria to ensure responses attributable to single agent treatment
- RANO requires both confirmed radiographic response and other forms of clinical benefit (eg no increase in steroid utilization, no deterioration in performance status, et al)
- Assessments done by dual reader blinded independent central review (BICR)
- Growing consensus that assessment of enhancing and non-enhancing disease (RANO-HGG and RANO-LGG criteria) is clinically relevant for diffuse midline glioma

Clinically meaningful and durable RANO-HGG responses

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



Duration of response, median (95% CI)	11.2 months (3.8 – not reached)
Time to response, median (range)	8.3 months (1.9 – 15.9)

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
Arrillaga-Romany, et al, Journal of Clinical Oncology, Feb 2024

Dordaviprone safety

Clinical Pharmacology Studies n=245

- ONC201 was well tolerated at various dose levels (125 mg to 750 mg).
- The majority of treatment-related adverse events across the clinical pharmacology studies were Grade 1 (mild) and transient.
- Most common treatment-related AEs were grade 1 nausea and dizziness.
- ONC201 clinical pharmacology program includes:
  - Dose-escalation, food-effect, & formulation evaluation
  - Thorough QT Study
  - Drug-drug interaction (DDI) studies: Strong CYP3A4 inhibitor and Proton-pump inhibitor studies
  - Renal impairment study
  - Hepatic impairment study
  - Mass balance study
  - Formulation Bioequivalence studies

Glioma Patient Studies

Treatment-related Adverse Events in >5%

Treatment-related Adverse Events, Integrated Safety Data Set, (N=422 glioma patients) [1]	Related TEAEs	
	All grades	Grade ≥ 3
Any Treatment-related AE	51.4%	9.7%
Fatigue	18.5%	1.7%
Nausea	14.5%	0
Vomiting	10.4%	0.9%
Lymphocyte count decreased	8.1%	1.9%
Headache	6.6%	0
ALT increased	6.4%	0.7%
White blood cell count decreased	5.5%	0.2%

Only 10 patients (2.4%) experienced a treatment-related AE that led to study drug modification or discontinuation.

1. Based on available data from ONC201 Investigator brochure, version 11

Dordaviprone Phase 3 ACTION Study Summary

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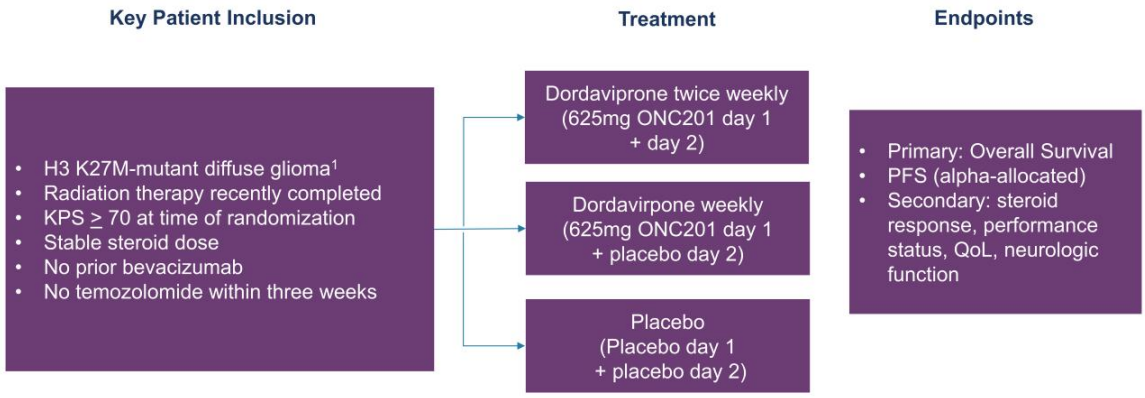
Pivotal Phase 3 ACTION trial design

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.



1. Excludes DIPG and spinal tumors

Design provides multiple paths for success

Interim data expected in third quarter of 2025

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

First OS[1] Interim
- ~164 events
- Success at HR[3]~0.52

PFS by RANO HGG[2]
- ~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

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

Dordaviprone Market Opportunity Assessment

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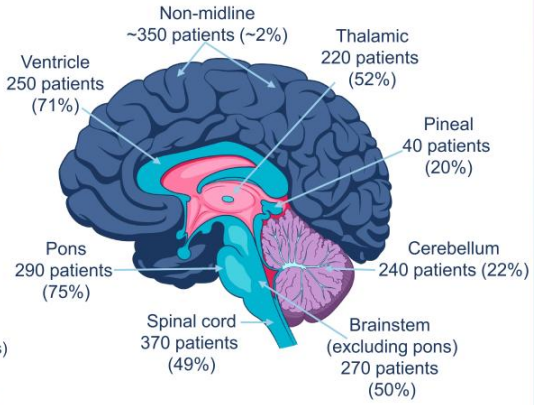
Approximately 21,000 gliomas reported in the U.S. each year, affecting all locations in the brain[1]

- **~40%** of 4,000+ ***midline gliomas*** are expected to harbor the H3 K27M mutation[2]
- **~2%** of 17,000+ ***non-midline gliomas*** are expected to harbor the H3 K27M mutation[2]
- Each year it is estimated that **~2,000** patients are affected by H3 K27M-mutant glioma in the U.S;
  ~5,000 patients in the top seven global markets
  (by extrapolation of the estimated US incidence rate to the top seven markets)
- No approved therapies specifically for H3 K27M mutant glioma

Estimated # of U.S. H3 K27M+ Patients by Tumor Location (rate of positivity)[2]



(1) Ostrom QT, et al. *Neuro Oncol*. 2022;24(Suppl 5):v1-v95; **(2)** Patient numbers and percentages are estimates (weighted avg per sample size) derived from a review of the literature from (2012-2023): (Aihara K, et al. *Neuro Oncol*. 2014;16(1):140-6; Feng J, et al. *Hum Pathol*. 2015;46(11):1626-32; Solomon DA, et al. *Brain Pathol*. 2016;26(5):569-80;Ryall S, et al. *Acta Neuropathol Commun*. 2016;4(1):93; Aboian MS, et al. *AJNR Am J Neuroradiol*. 2017;38(4):795-800; Wang L, et al. *Hum Pathol*. 2018;78:89-96; Castel D, et al. *Acta Neuropathol Commun*. 2018;6(1):117; Karremann M, et al. *Neuro Oncol*. 2018;20(1):123-131; Aboian MS, et al. *AJNR Am J Neuroradiol*. 2019;40(11):1804-1810; Dorfer C, et al. *Acta Neurochir (Wien)*. 2021;163(7):2025-2035; Sievers P, et al. *Neuro Oncol*. 2021;23(1):34-43; Mackay A, et al. *Cancer Cell*. 2017;32(4):520-537 e5; Huang T, et al. *Oncotarget*. 2018;9(98):37112-37124; Schreck KC, et al. *J Neurooncol*. 2019;143(1):87-93; Chiba K, et al. *World Neurosurg*. 2020;134:e530-e539; Mukasa A, et al. *Neuro Oncol*. 2014;16(Suppl 3):iii9-iii10; Castel D, et al. *Acta Neuropathol*. 2015;130(6):815-27; Khuong-Quang DA, et al. *Acta Neuropathol*. 2012;124(3):439-47; Roux A, et al. *Neuro Oncol*. 2020;22(8):1190-1202; Giagnacovo M, et al. *Childs Nerv Syst*. 2020;36(4):697-704; Wu G, et al. *Nat Genet*. 2014;46(5):444-450; Wu G, et al. *Nat Genet*. 2012;44(3):251-3; Taylor KR, et al. *Nat Genet*. 2014;46(5):457-461; Saratsis AM, et al. *Acta Neuropathol*. 2014;127(6):881-95; Erker C, et al. *Neuro Oncol*. 2022;24(1):141-152; Buczkowicz P, et al. *Acta Neuropathol*. 2014;128(4):573-81; Daoud EV, et al. *J Neuropathol Exp Neurol*. 2018;77(4):302-311; Chai RC, et al. *Acta Neuropathol Commun*. 2020;8(1):40; Yi S, et al. *Neurosurgery*. 2019;84(5):1072-1083; Gessi M, et al. *Acta Neuropathol*. 2015;130(3):435-7; Alvi MA, et al. *Mod Pathol*. 2019;32(9):1236-1243; Crotty EE, et al. *J Neurooncol*. 2020;148(3):607-617; Dono A, et al. *J Clin Neurosci*. 2020;82(Pt A):1-8; Akinduro OO, et al. *J Neurosurg Spine*. 2021;35(6):834-843; Nakata S, et al. *Brain Tumor Pathol*. 2017;34(3):113-119; Nomura M, et al. *Acta Neuropathol*. 2017;134(6):941-956; Eschbacher KL, et al. *Am J Surg Pathol*. 2021;45(8):1082-1090; D'Amico RS, et al. *J Neurooncol*. 2018;140(1):63-73; Korshunov A, et al. *Acta Neuropathol*. 2015;129(5):669-78; Albaidula A, et al. *Neuro Oncol*. 2017;19(10):1327-1337.)

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

- No approved therapies for H3 K27M mutant glioma, dordaviprone is the leading program targeting this mutation globally
- Potential market opportunity ~$750 million
- Approximately 5,000 patients in top seven markets[1]
- Ultra-orphan indication drug pricing
- H3 K27M mutations most often in children / young adults
- 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)

1. By extrapolation of the estimated US incidence rate to the top seven markets

Potential for imipridones beyond brain tumors

Results of Phase II Study of dordaviprone (ONC201) in Neuroendocrine Tumors at the Cleveland Clinic[1]

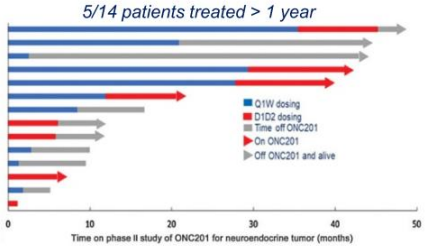
- Single agent responses in PCPG: adrenal-related tumors with high malignant DRD2 expression
- Investigator initiated trial at Cleveland Clinic in a heavily refractory and pretreated patient population (n=14)

Prior local treatments, N	
Surgery only	2 (14.3%)
Surgery + radiotherapy (RT)	3 (21.4%)
Surgery + chemotherapy	3 (21.4%)
RT + chemotherapy	1 (7.1%)
Surgery + RT+ chemotherapy	5 (35.7%)

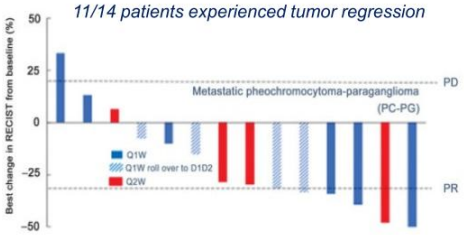
Sites of meastasis, N (%)	
Lymph nodes	11 (78.6%)
Lung	6 (42.9%)
Liver	2 (14.3%)
Bone	13 (92.9%)
Other	0 (0.0%)

- Superior tolerability and administration profiles relative to SOC therapies

5/14 patients treated > 1 year



11/14 patients experienced tumor regression



1. https://aacrjournals.org/clincancerres/article/28/9/1773/694456/Phase-II-Study-of-ONC201-in-Neuroendocrine-Tumors

Dordaviprone Mechanism of Action

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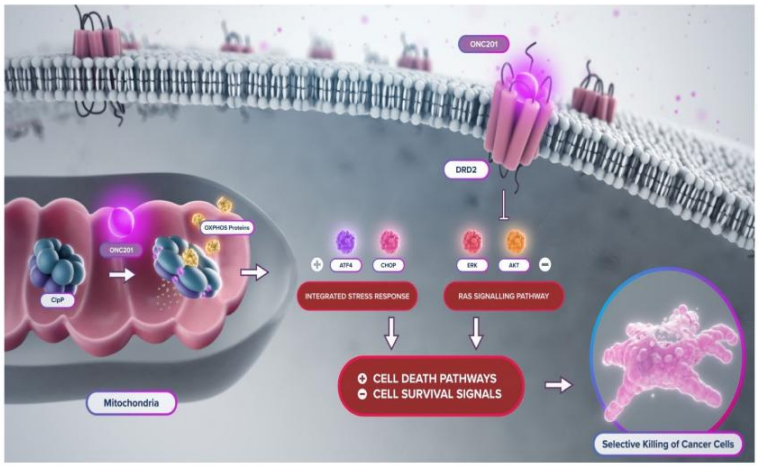
Dordaviprone directly engages ClpP and DRD2

Dordaviprone upregulates integrated stress response, inactivates Akt/ERK, and selectively induces tumor cell death



- Dordaviprone can selectively induce apoptosis in cancer cells by altering the activity of two protein targets
- ClpP agonism
  - Dordaviprone modifies ClpP conformation to increase degradation of mitochondrial proteins important for metabolism, epigenetics, and cancer cell viability
- DRD2 antagonism
  - DRD2 is a G protein-coupled neuroreceptor that regulates Ras signaling
  - Dordaviprone antagonizes DRD2, inhibiting Ras signaling pathways

ClpP=caseinolytic protease P; OXPHOS=oxidative phosphorylation; DRD2=Dopamine receptor D2; ATF4=activating transcription factor 4; CHOP=C/EBP-homologous protein; ERK=extracellular-regulated kinase;

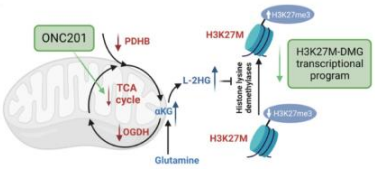
Mechanism and frontline clinical efficacy in H3 K27M DMG

CANCER DISCOVERY

RESEARCH ARTICLE | AUGUST 16 2023

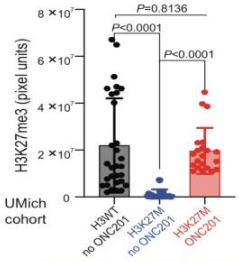
Clinical efficacy of ONC201 in H3K27M-mutant diffuse midline gliomas is driven by disruption of integrated metabolic and epigenetic pathways

Mitochondrial effects reverse H3 K27me3-loss hallmark of H3 K27M



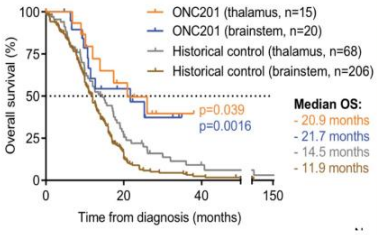
Provides ClpP connection to H3 K27M
Anchors MOA directly to targeting H3 K27M

H3 K27me3-loss reversal evident in ONC201-treated H3 K27M patients



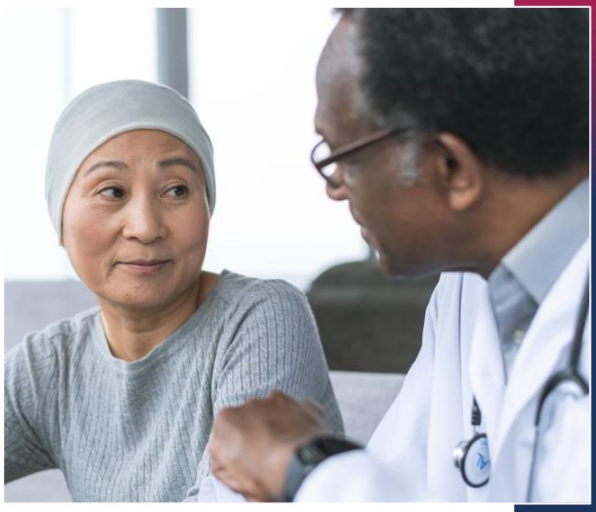
Increased confidence in Ph3 dose

Front-line ONC201 following RT survival benefit



Extends documented benefit to front-line, pediatrics, and brainstem

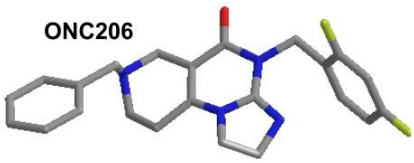
ONC206

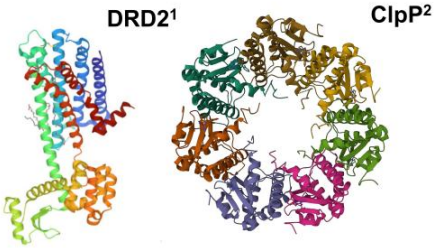


CHIMERIX

ONC206: second generation oral brain penetrant ClpP agonist + DRD2 antagonist

- 10x higher in vitro potency relative to dordaviprone
- Monotherapy efficacy across multiple preclinical models of Central Nervous System (CNS) and non-CNS tumors
  - Tumor regression in patient-derived xenografts
- Oral dose escalation trials with intensified dosing are nearing completion in CNS cancers





1. PDB 6CM4
2. PDB 6DL7

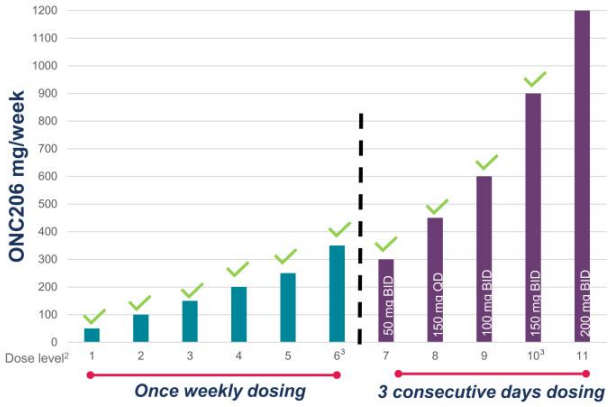
ONC206 Phase 1 dose escalation and intensification to expected therapeutic range in CNS cancer patients[1,2]

Expect to complete enrollment of dose escalation in 2024

- 83 patients enrolled
[Adults (n=30); Peds (n=53)]

-Biologically active concentrations achieved with ***continuing escalation at intensified dose frequency***

- Well-tolerated with intensified dose frequency at exposures achieving ***efficacy in vivo***



Eligibility Criteria

All CNS tumors

Received SOC therapies

No limit on prior recurrences

1. In partnership with Nation al Institutes of Health (NIH)
2. In partnership with Pacific Pediatric Neuro-Oncology Consortium (PNOC)
3. In adults only

ONC206 is appears well-tolerated in adult and pediatric patients to date

	Related AEs[1] Integrated Data Set N=77	
	All grades	Grade ≥ 3
Any Treatment-related AE	**60%**	**5%**
Fatigue	26%	1%
Lymphocyte count decreased	16%	3%
Vomiting	17%	0%
Bilirubin increased	6%	0%
Diarrhea	6%	0%
Headache	9%	0%
Nausea	9%	0%
ALT increased	5%	1%
Neutrophil count decreased	6%	0%
White blood cell decrease	6%	0%

Data cutoff : 08July2024[2]

- Majority of treatment-related adverse events (TRAEs) are mild to moderate in severity
- Most frequent TRAEs are fatigue, lymphopenia, and vomiting
  - Occur in a minority of patients
  - Typical AEs in advanced CNS tumors
- No substantial changes in the AE profile as a function of dose or frequency
- Similar safety profile in adults and pediatrics

1. Adverse Events evaluable for safety,. Data extraction from Adult study and Pediatric study (PNOC Arms A and D) as of July2024
2. To date no additional SAE's in patients dosed after July 8th 2024 data cut-off

ONC206 dose escalation and increased dose frequency well-tolerated in adult and pediatric patients to date

Majority of treatment related AEs[1] are mild to moderate in severity with fatigue most common

Incidence of ONC206-Related AEs[1]

	50mg QW N=10	100mg QW N=11	150mg QW N=11	200mg QW N=11	250mg QW N=10	350 mg QW N=3[3]	50mg BID; TIW N=9	150mg QD; TIW N=9	100mg BID; TIW N=3[3]	150mg BID; TIW	200mg BID; TIW
	Weekly Dosing						Multi-day/ week dosing				
Weekly Dose[2]	**50 mg**	**100 mg**	**150 mg**	**200 mg**	**250 mg**	**350 mg**	**300 mg**	**450 mg**	**600 mg**	**900 mg**	**1200mg**
Treatment-related AE, all grades	60%	73%	64%	64%	80%	67%	44%	44%	**0%**	*Enrolled[4]*	*To Be Enrolled*
Grade 1	60%	64%	55%	64%	70%	67%	33%	44%	**0%**		
Grade 2	33%	45%	45%	45%	60%	33%	11%	33%	**0%**		
Grade 3	10%	18%	9%	**0%**	**0%**	**0%**	**0%**	**0%**	**0%**		
Grade 4/5	**0%**	**0%**	**0%**	**0%**	**0%**	**0%**	**0%**	**0%**	**0%**		

1. Adverse Events. Data extraction from Adult study and Pediatric study (PNOC Arms A and D) as of July2024
2. Weight-based dosing utilized in pediatric patients <60 kg
3. DL6 and DL9 data in adults only
4. Adults only

ONC206 patient exposures with intensified dosing exceed exposures associated with nonclinical efficacy

Patient Exposures in Expected Therapeutic Range:

- ***Cmax*** exceeds IC50 in diverse CNS and non-CNS solid tumor cell lines[2]
- ***AUC*** exceeds plasma exposures in nonclinical solid tumor models demonstrating efficacy[3]
  - Favorable tumor/ tissue: plasma ratios in target organs of nonclinical models[4]
  - adrenals ~7x, uterus ~6x, lung ~6x, prostate ~4x, CNS ~2x
- Intensified dosing increased ***time above IC50*** to >24hr while being well-tolerated
- Continued dose escalation expected to further enhance duration of exposure to biologically active concentration

Relative PK Data from ongoing studies[1]

	Dose Level; Frequency	Weekly Dose (mg)	Cmax > IC50[2]	Weekly AUC > in vivo model[3]	Time above IC50[2]
Once- Weekly Dosing	**50 mg; QW**	**50**	0.8x	0.2x	0 hr
	150 mg; QW	**150**	>3x	0.6x	3 hr
	200 mg; QW	**200**	>7x	1.5x	7 hr
	350 mg; QW	**350**	>9x	2.4x	17 hr
Multi-day/ Week Dosing	**50 mg; BID/TIW**	**300**	0.8x	0.9x	0 hr
	150mg; QD/TIW	**450**	>4x	2.0x	19 hr
	100mg; BID/TIW	**600**	>2x	3.4x	28 hr
	150 mg; BID/TIW	**900**	**Enrolled[5]**		
	200 mg; BID/TIW	***1200***	***To be enrolled***		

1. PK summary based on adult data; pediatric PK in DL 1-7 have been similar to adult
2. Average IC50 of 562 nM across 1088 cancer cell lines representing 25 tumor types
3. In vivo models include High-grade glioma (50 mg/kg QW), medulloblastoma (50 mg/kg BID TIW, 100 mg/kg and 120 mg/kg QW, 100 mg/kg BIW), endometrial (125 mg/kg QW, 100 mg/kg BIW), ovarian (125 mg/kg QW), TNBC (100 mg/kg BIW, 50 mg/kg BID TIW), hepatocellular (80 mg/kg BIW), cholangiocarcinoma (50 mg/kg QW) and SCLC (50 mg/kg BID TIW). Average AUC in positive nonclinical models ~5000 ng*hr/mL .
4. Mean AUC tissue:plasma ratio in single oral dose healthy mouse study
5. Adults only

ONC206 Mechanism of Action

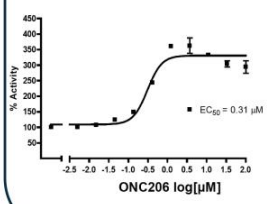
CHIMERIX

ONC206 is a second generation dual ClpP agonist/DRD2 antagonist

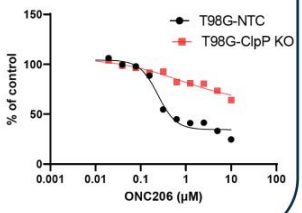
- ClpP and DRD2 are direct binding targets that control mitochondrial and prosurvival functions, respectively, in a range of human cancers
- ClpP agonism and DRD2 antagonism occurs at nanomolar concentrations
- Anti-cancer activity is dependent on ClpP and/or DRD2 depending on tumor type
- Downstream effects of engaging ClpP/DRD2 in vitro and in vivo include altered mitochondrial metabolism, integrated stress response, bioenergetics, MYC expression, Akt/ERK signaling and apoptosis [1-4]

ClpP

ClpP catalytic activity is stimulated by ONC206[1]

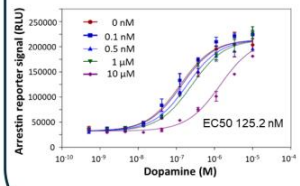


ClpP-dependent in vitro activity of ONC206 in T98G high grade glioma cells[1]

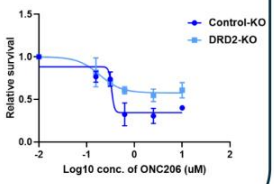


DRD2

DRD2 signaling is inhibited by ONC206 [2]



DRD2-dependent in vitro activity of ONC206 in endometrial cancer ARK2 cells [3]



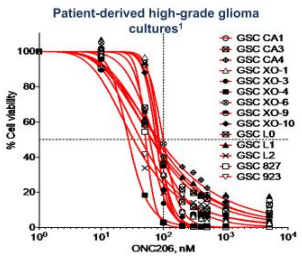
1. Maranto et al, AACR Brain Cancer Conference 2023
2. Prabhu et al, AACR 2020
3. Hu et al, Cancers 2020;
4. Batsios et al, bioRxiv 2024
5. Baek et al, SABCS 2023
6. Hu et al, Cancers 2020;
7. Ishida et al, Clin Can Res 2018

ONC206 exhibits monotherapy activity in multiple CNS cancer models

- Nanomolar activity across CNS tumors, including high-grade glioma and medulloblastoma
- In vitro and in vivo data demonstrates enhanced efficacy with increasing dose and sustained exposure
- Tumor regression and survival extension in transgenic and patient-derived medulloblastoma models

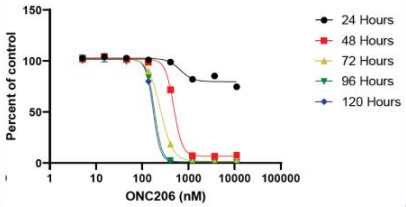
Nanomolar IC50

Patient-derived high-grade glioma cultures[1]



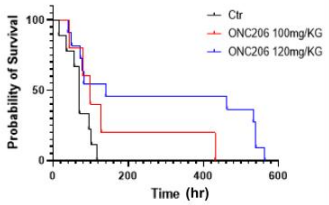
Efficacy enhanced with duration

High-grade glioma SF8628 cells[2]



Efficacy enhanced with dose

Transgenic SHH (SmoA1) Medulloblastoma Model[3]



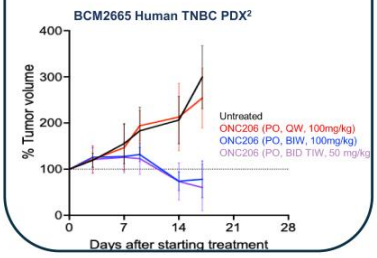
1. Jung et al, SNO 2017
2. Maranto et al, AACR Brain Cancer Conference 2023
3. Tzaridis et al, AACR 2024

ONC206 shows monotherapy efficacy & tolerability in several non-CNS solid tumors

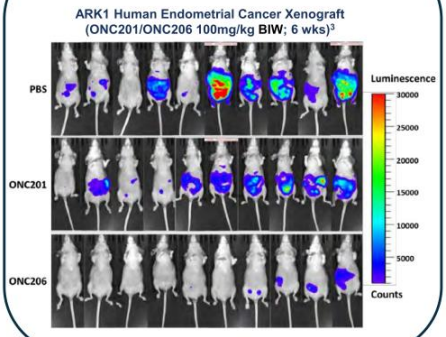
pheochromocytoma, triple-negative breast (TNBC)[2], endometrial[3], cholangiocarcinoma[1], ovarian[4], hepatocellular cancer[5], small cell lung cancer

- Broadly active across 1088 cancer cell lines representing 25 tumor types with an average IC50 of 562 nM [1]
- In vivo efficacy improves with dose intensification in chemo-refractory TNBC, including tumor regressions[2]
- Improved efficacy relative to ONC201 in endometrial cancer[3]

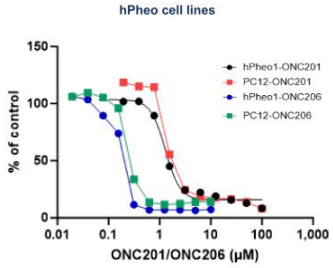
Tumor Regressions with Increased Dose Frequency



Enhanced in vivo efficacy



Enhanced in vitro efficacy in human PCPG cell line



1. Prabhu et al, AACR 2020
2. Baek et al, SABCS 2023
3. Hu et al, Cancers 2020
4. Tucker et al, American Journal of Cancer Research, 2022
5. Cao et al, Neoplasia 2024

Ongoing pipeline development

- ONC212 GPR132 + ClpP agonist
  - GLP-tox studies complete, potential to advance to IND, work performed with support from academic grants
  - Preclinical studies are ongoing to evaluate additional oncology indications and predictive biomarkers for ONC212 for clinical development
- CMX521 broad spectrum coronavirus preclinical activity
  - Developed thru Phase 1 in norovirus
  - Monotherapy efficacy in mouse-adapted SARS-CoV-2-MA10 model across multiple endpoints
  - $2m grant to fund research collaboration with University of North Carolina/READDI[1]

1. Rapidly Emerging Antiviral Drug Development Initiative

Corporate Update

CHIMERIX

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

Investment highlights and key catalysts

Ph 3 ACTION study actively enrolling

Significant commercial potential

Corporate capability and financial flexibility

Dordaviprone Ph 3 trial enrolling - interim OS data expected in third quarter 2025

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

- ✓ *No approved therapies targeting H3 K27M diffuse glioma, an area of high unmet medical need*
- ✓ *First in class mechanism of action with clinical validation*
- ✓ *Patent protection thru 2037 (potential additional US patent term extension)*

ONC206 now dosing within the expected therapeutic range

- ✓ *Pharmacokinetic data from dose escalation studies demonstrate dose proportionate exposure*
- ✓ *No unexpected safety events and no dose limiting toxicities to date*
- ✓ *Exhibits monotherapy activity in multiple non-clinical CNS models as well as tumors outside the CNS*

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*

$152 million in capital to fund operations as of September 30, 2024, no debt

Chimerix Corporate Presentation