Chimerix Corporate Presentation

December 10, 2024

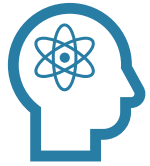
CHIMERIX

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, the possible regulatory path forward for dordaviprone, including the potential to seek accelerated approval, priority review, rare pediatric disease priority review vouchers and approval for marketing authorization; timing and consequences of a new drug application (NDA) submission to FDA; FDA's acceptance for filings; the timeline of related discussions with the FDA; the initial Prescription Drug User Fee Act (PDUFA) timing; the ability of dordaviprone to attain significant market acceptance among disease experts, patient advocates and their parents; the expected impact of dordaviprone on patients; 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, a priority review, rare pediatric disease priority review vouchers, and approval for marketing authorization; uncertainty on the response of regulators to including additional supportive data to be submitted in the NDA filing, including RANO 2.0 assessments, and uncertainty with respect to the initial potential PDUFA timing; risks related to the timing, completion and outcome of the Phase 3 ACTION study of dordaviprone; risks associated with repeating positive results obtained in prior preclinical or clinical studies in future studies; risks related to the clinical development of ONC206; risks associated with the potential market opportunity, funding and timing of future data readouts for our products; 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

Planned NDA submission in December 2024



Potential accelerated approval in Q3 2025

Imipridone pipeline progressing

Dordaviprone U.S. NDA submission planned for Dec '24, potential U.S. accelerated approval in 2025

- ✓ *No approved therapies currently in recurrent H3 K27M diffuse glioma, an invariably lethal Grade 4 glioma (World Health Org)*
- ✓ *Total addressable market exceeds $1Bn in U.S. (U.S. incidence >2,000 patients, ultra-orphan drug pricing)*
- ✓ *Patent protection thru 2037 (potential additional U.S. patent term extension)*
- ✓ *Front-line Ph 3 trial (ACTION study) substantial enrollment, active in >150 sites and 17 countries*
- ✓ *Application for Rare Pediatric Disease Priority Review Voucher (PRV) to be included in upcoming NDA*

ONC206 Recommended Phase 2 dose expected early 2025

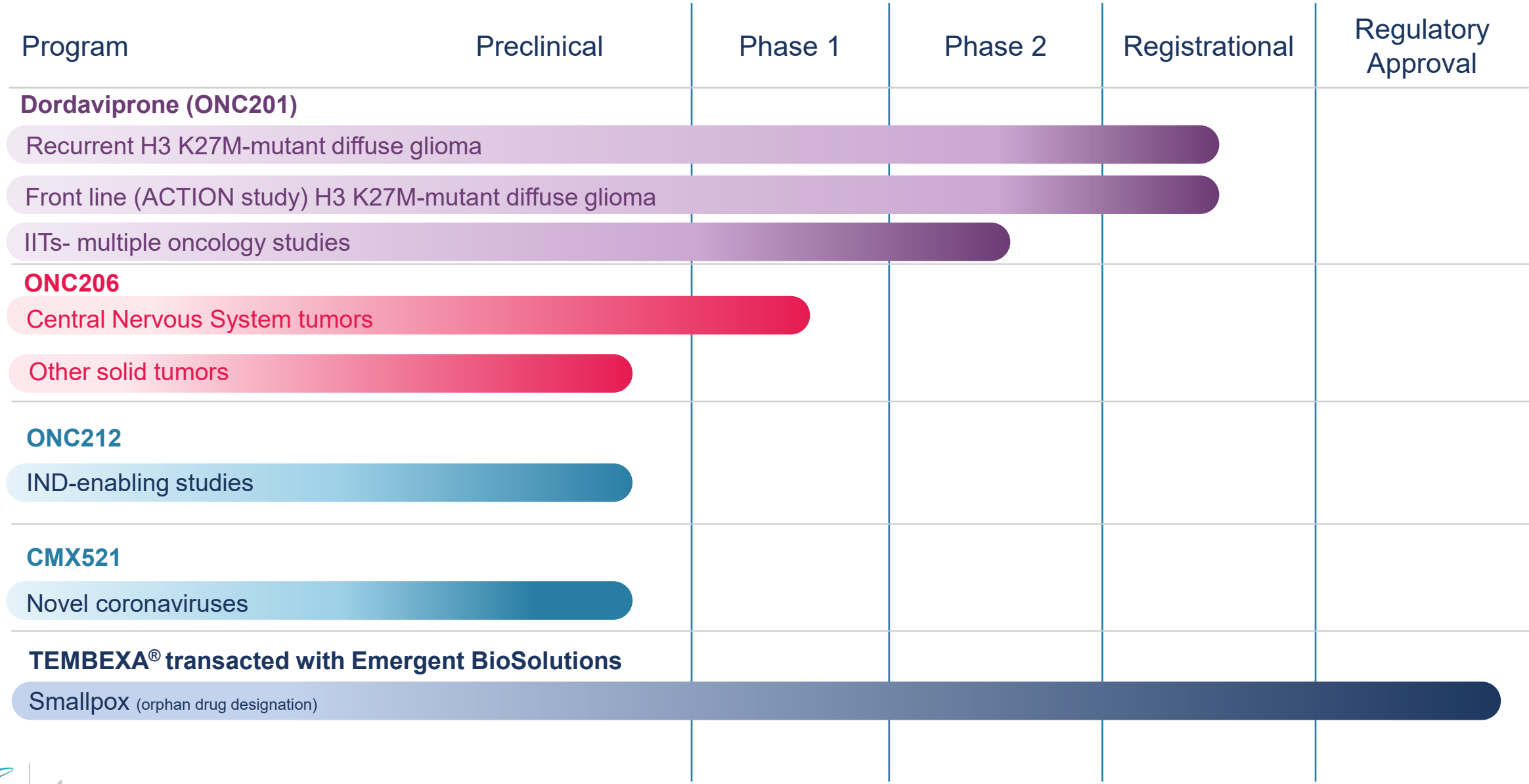
- ✓ *Pharmacokinetic data from dose escalation studies demonstrate dose proportionate exposure*
- ✓ *No unexpected safety events and no dose limiting toxicities to date*
- ✓ *Exhibits monotherapy activity in multiple non-clinical CNS models as well as tumors outside the CNS*

Positioned to accelerate growth from internal and/or external innovation

- ✓ *Robust business development search and evaluation process*

$152 million in capital to fund operations as of September 30, 2024

Deep Pipeline Across All Development Stages



Dordaviprone:
H3 K27M-mutant diffuse glioma

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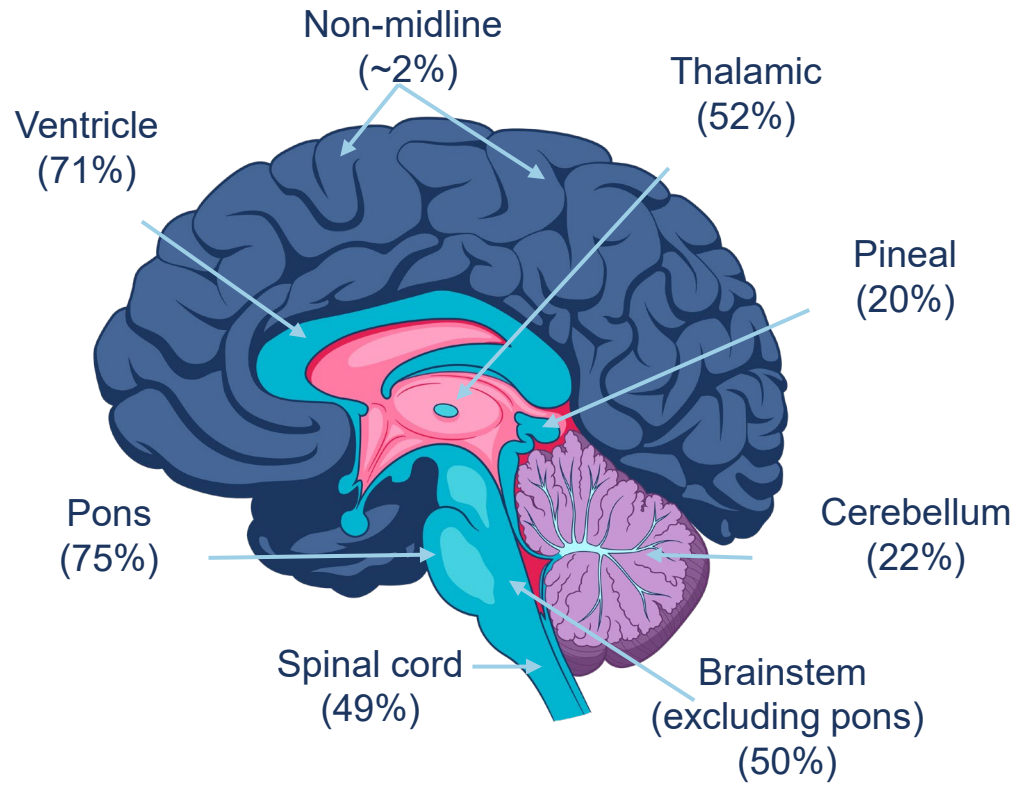
About H3 K27M-mutant Diffuse Glioma

- **Highly aggressive** and classified as WHO Grade 4
- U.S. incidence >2,000 - most frequently occurs in **children and young adults**[1]
- **Surgical resection limited** due to location
- Effective treatment limited to radiotherapy, invariably recurs
- **No approved therapies** for H3 K27M-mutant glioma currently
- Median overall survival approximately 1 year[2] from diagnosis and 5.1 months[3] from recurrence

H3 K27M-mutant Patients by Tumor Location (rate of positivity)[4]



[1]ZS Associates, ONC201 Opportunity Assessment – Epidemiology Assumptions, October 31, 2024
[2]Vuong et al, Frontiers in Oncology March 2022.
[3] Company-sponsored natural disease history study. 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)
[4] see slide 18 for supporting references

We Believe Extensive Program Progress Supports New Drug Application Seeking U.S. FDA Accelerated Approval

Recent program milestones include:

- **Substantial enrollment** of the Phase 3 ACTION study
- 50-patient primary efficacy analysis using multiple response criteria, including the most recently established response criteria for glioma, **Response Assessment in Neuro Oncology (RANO) 2.0**
- Responders had **consistent findings in other measures of clinical benefit**, including reduction in corticosteroid dose, improvement in performance status, and longer survival
- Additional clinical data sets and patient narratives **supportive of the primary efficacy analysis** observed to date
- Clinical and nonclinical demonstration that dordaviprone **reverses the central hallmark of H3 K27M-mutant diffuse glioma: H3 K27 trimethyl loss**
- A comprehensive safety database of glioma patients treated with dordaviprone which supports a **favorable benefit/risk profile** observed to date
- **Comprehensive clinical pharmacology and Chemistry, manufacturing, and controls (CMC)** studies

Eligibility for Primary Efficacy Analysis Aligned With FDA

Objective

- To evaluate monotherapy efficacy of dordaviprone in recurrent H3 K27M-mutant diffuse midline glioma by dual-reader blinded independent central review (BICR) in first 50 subjects who meet the following eligibility criteria agreed to with U.S. FDA

Eligibility

- Age ≥2yo and received dordaviprone under studies ONC006, ONC013, ONC014, ONC016, or ONC018
- Diffuse glioma with a known H3K27M 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 dordaviprone dose:
  - Radiation: 90 days
  - Temozolomide: 23 days / Antibodies (e.g., bevacizumab): 42 days / Other anticancer therapies: 28 days
- Baseline Performance Status ≥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

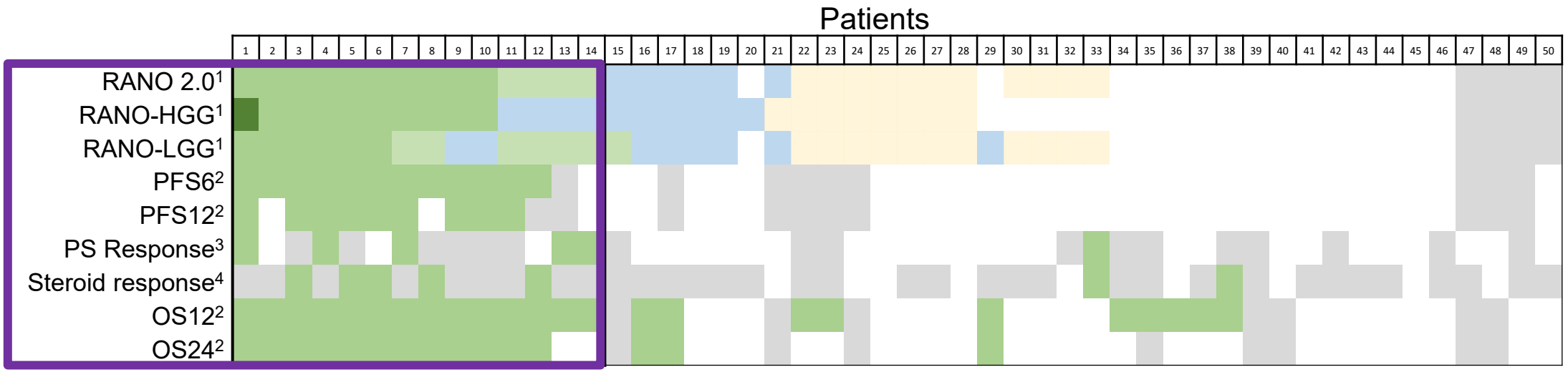
Primary Efficacy Analysis in Recurrent H3 K27M-mutant DMG by dual reader BICR

n=50	RANO 2.0	RANO-HGG	RANO-LGG
Objective Response Rate, n (%) [95% CI]	**14 (28.0) [16.2-42.5]**	**10 (20.0) [10.0-33.7]**	**13 (26.0) [14.6-40.3]**
Complete Response	0	1 (2.0)	0
Partial Response	10 (20.0)	9 (18.0)	6 (12.0)
Minor Response	4 (8.0)	NA	7 (14.0)
Stable Disease	6 (12.0)[1]	10 (20.0)	8 (16.0)
Not Evaluable	11 (22.0)	8 (16.0)[2]	11 (22.0)[3]
Progressive Disease	15 (30.0)	18 (36.0)	14 (28.0)
Not Applicable	4 (8.0)	4 (8.0)	4 (8.0)
Disease Control Rate, n (%) [95% CI]	20 (40.0) [26.4-54.8]	20 (40.0) [26.4-54.8]	21 (42.0) [28.2-56.8]
Median Time to Response, months [range]	4.6 [1.6-15.9]	8.3 [1.9-15.9]	3.6 [1.6-17.8]
Median Duration of Response, months, [95% CI]	10.4 [7.4-15.4]	11.2 [3.8-NR]	10.4 [3.6-12.7]
Overall Survival, months, median [95% CI]		14.0 [8.0-26.1]	
12-month survival estimate, [95% CI]		57.5% [41.7-70.5]	
24-month survival estimate, [95% CI]		37.6% [23.2-51.9]	

1.Includes one patient with unconfirmed response by RANO 2.0.
2.Five overall radiographic SD accompanied by increase in corticosteroids; three overall radiographic PD accompanied by decrease in corticosteroids.
3.Eight overall radiographic SD accompanied by increase in corticosteroids; three overall radiographic PD accompanied by decrease in corticosteroids.

Primary Efficacy Analysis 'Heatmap' Reflects RANO Responses Associated with Other Measures of Clinical Benefit

RANO 2.0 response as a time varying covariate was significantly associated with OS in a multivariate Cox Proportional Hazards model (HR [95% CI]: 0.22 [0.08 to 0.58]; p=0.0024)



Legend

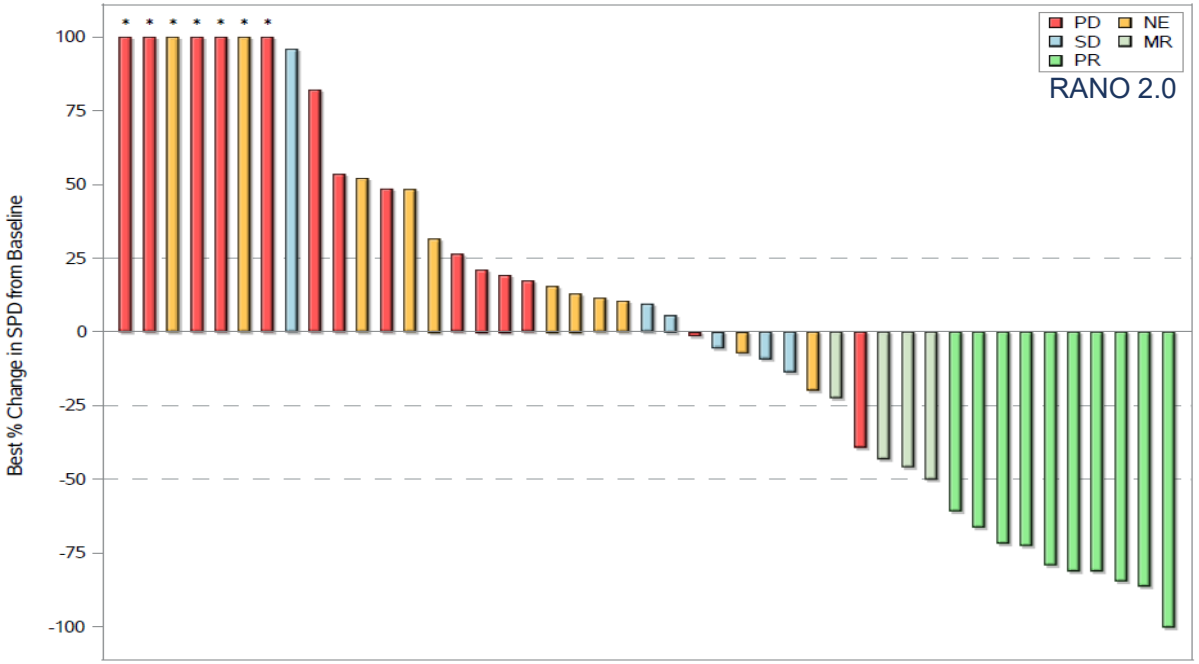
RANO[1]	Complete response	Partial response	Minor Response	Stable Disease	Not Evaluable	Progressive Disease	Not Applicable
PFS6 / PFS12 / OS12 / OS24[2]	Yes	No	Censored				
Performance Status Response[3]	Yes	No	Unevaluable				
Steroid Response[4]	Yes	No	Unevaluable				

[1]Best overall response by RANO criteria assessed by BICR. Not evaluable if PD with decreasing steroids or SD with increasing steroids. Not applicable if no post-baseline assessments.
[2]Progression free-survival ≥ 6 months / 12 months by RANO 2.0 criteria assessed by BICR; Overall survival ≥ 12 months / 24 months. Patients censored if not progressed/alive at last assessment/follow-up prior to cutoff.
[3]Performance status response defined as increase in KPS/LPS compared with baseline, while also having stable or reduced corticosteroid use. Increase must be confirmed at the next analysis timepoint. Patients with baseline KPS/LPS ≤80 were evaluable for this analysis.
[4]Corticosteroid response defined as ≥50% reduction in average daily steroid dose compared with baseline or reduction ≤2 mg with stable or improved KPS/LPS. Reduction must be confirmed at the next analysis timepoint. Corticosteroids were converted into a dexamethasone equivalent dose. Patients receiving ≥4mg dexamethasone at baseline were evaluable for this analysis.

28% ORR by RANO 2.0 Evaluates Enhancing and Non-Enhancing Disease

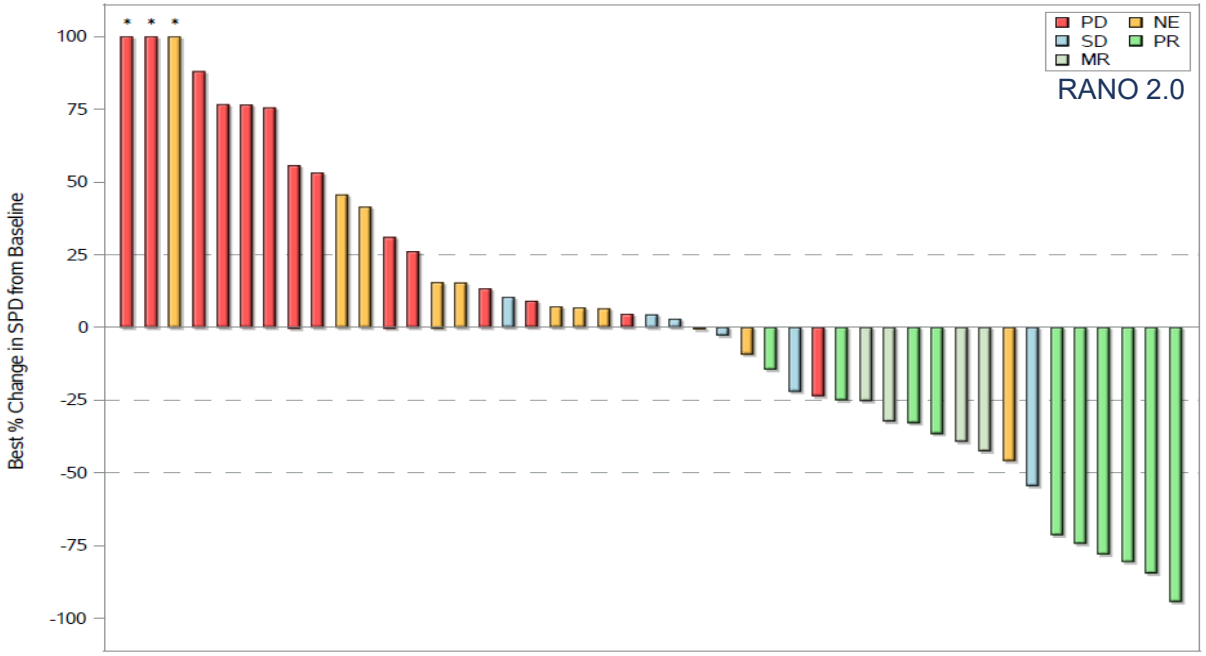
Reflects Only Enhancing Disease

MRI type: T1 post-contrast[1]



Includes Non-Enhancing Disease

MRI type: T2/FLAIR[1]



[1] 50-patient primary efficacy analysis in recurrent H3 K27M-mutant DMG by dual-reader BICR: Chimerix internal analysis as of December 9, 2024

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

Robust Dordaviprone Clinical Pharmacology and Safety Assessment Supported Favorable Benefit/Risk Profile

Clinical Pharmacology Studies n=245

- Dordaviprone 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.
- Dordaviprone 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.

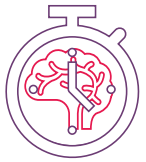
1. Based on available data from dordaviprone Investigator brochure, version 11, AEs are prior to initiation of other anticancer therapy

Dordaviprone FDA Designations

Rare Pediatric Disease Designation for treatment of H3 K27M mutant glioma

- Upcoming NDA to include an application for a Rare Pediatric Disease Priority Review Voucher[1]

Orphan Drug Designation



Fast Track Designation

1. Should the Company be awarded a Priority Review Voucher and thereafter sell such Priority Review Voucher to a third party, 50% of the net proceeds from such sale would be payable to the former security holders of Oncoceutics, Inc., pursuant the Agreement and Plan Merger, dated January 7, 2021.

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

Key Patient Inclusion

- H3 K27M-mutant diffuse glioma[1]
- Radiation therapy recently completed
- KPS ≥ 70 at time of randomization
- Stable steroid dose
- No prior bevacizumab
- No temozolomide within three weeks

Treatment

- Dordaviprone twice weekly (625mg ONC201 day 1 + day 2)
- Dordaviprone weekly (625mg ONC201 day 1 + placebo day 2)
- Placebo (Placebo day 1 + placebo day 2)

Endpoints

- Primary: Overall Survival
- PFS (alpha-allocated)
- Secondary: steroid response, performance status, QoL, neurologic function

1. Excludes DIPG and spinal tumors

We Believe the ACTION Study 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

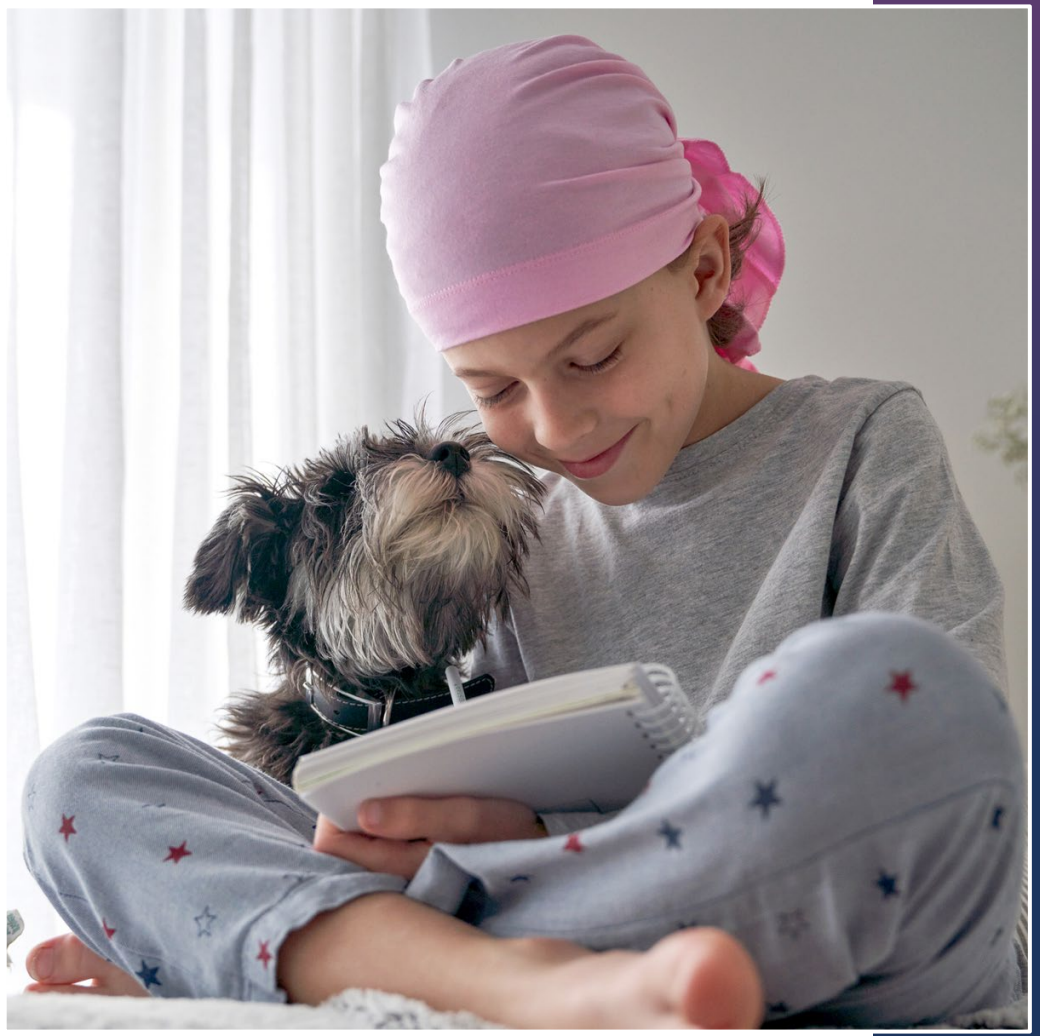
Final OS

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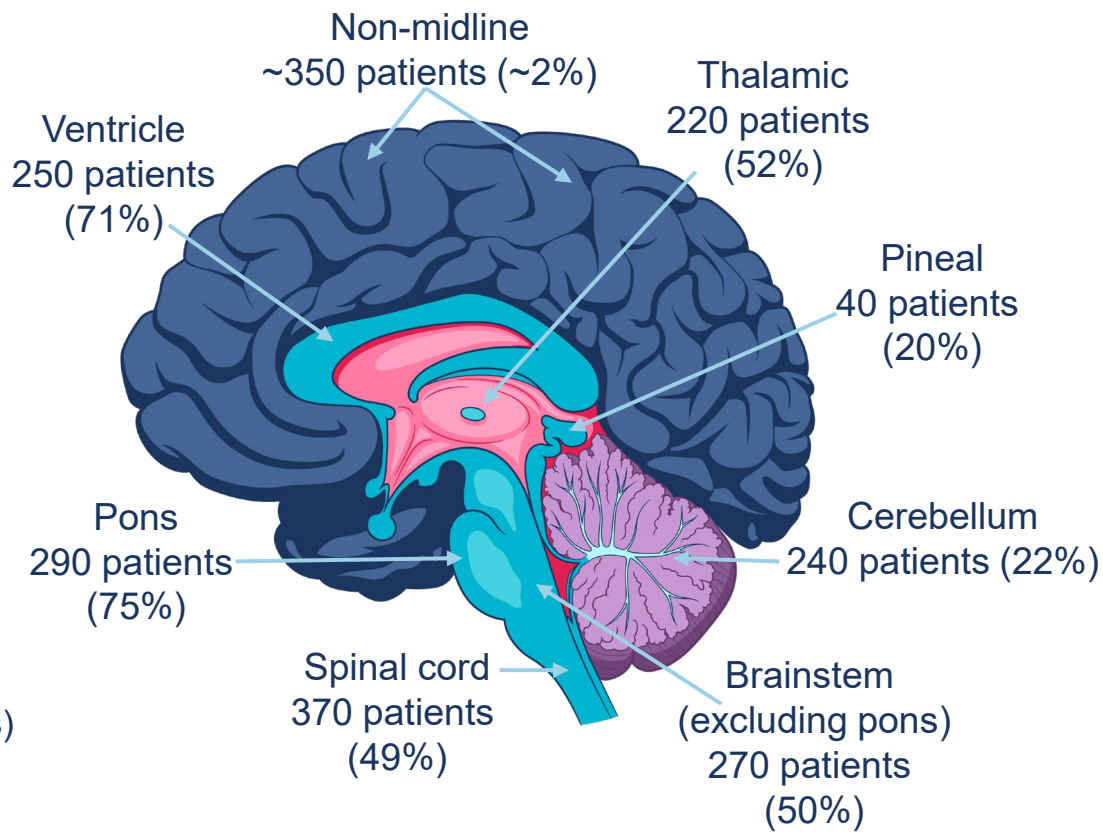
Approximately 21,000 gliomas reported in the U.S. each year, affecting all locations in the brain[1]

- **~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;[3]
  ~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 currently

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):1072-1081; 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; Aibaidula A, et al. *Neuro Oncol*. 2017;19(10):1327-1337.) (3) ZS Associates, ONC201 Opportunity Assessment – Epidemiology Assumptins, October 31, 2024

Commercial Platform Expected to be Ready for Launch by Q3 2025, if NDA is Granted

Unmet Need

- ✓ Lethal condition with limited treatment options
- ✓ Predominately affects children and young adults
- ✓ >2,000 US patients

Access & Pricing

- ✓ Ultra-Orphan pricing
- ✓ Protected Class status
- ⚙ Payer Engagement

Functional Expertise

- ✓ Commercial Operations
- ✓ Analytics & Insights
- ✓ Pricing & Access
- ✓ Distribution & Services
- ⚙ Marketing
- ⚙ Sales

Patient Services & Distribution

- ⚙ Third Party Logistics
- ⚙ Specialty Pharmacy
- ⚙ Industry leading patient services

Patient Advocacy

- ✓ Collaborative engagements

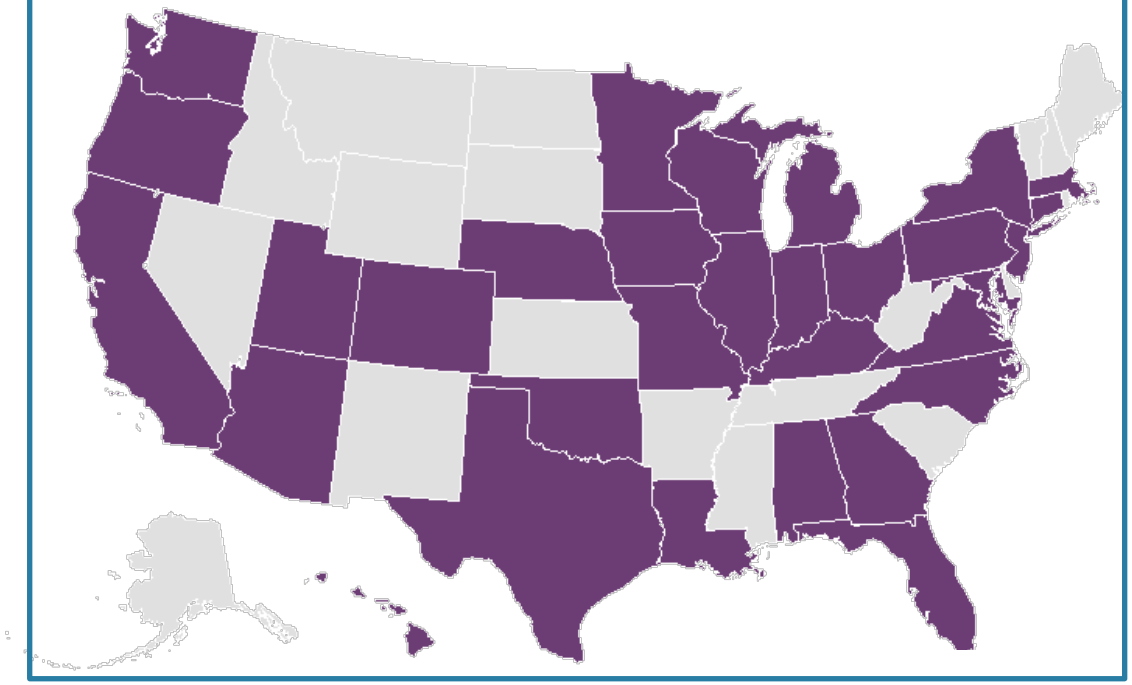
⚙ Work initiated

Launch Plan Will Be Enabled by a Focused and Agile Commercial Infrastructure

Leveraging brand equity and deep expertise within the Neuro-oncology community

66 U.S. ACTION sites and 25 U.S. EAP sites

Strong support and pre-launch engagement from Neuro-Oncology Centers of Excellence



U.S. sites active as of December 9, 2024

- **Specialized account teams** embracing the patient community
- Focused efforts on **concentrated centers** of excellence and KOLs
- **Optimized promotional effort** throughout the neuro-oncology ecosystem
- **Data-driven approach** to drive investments and maximize effectiveness
- **Scalable and flexible** infrastructure to ensure long-term sustainability

Dordaviprone Mechanism of Action

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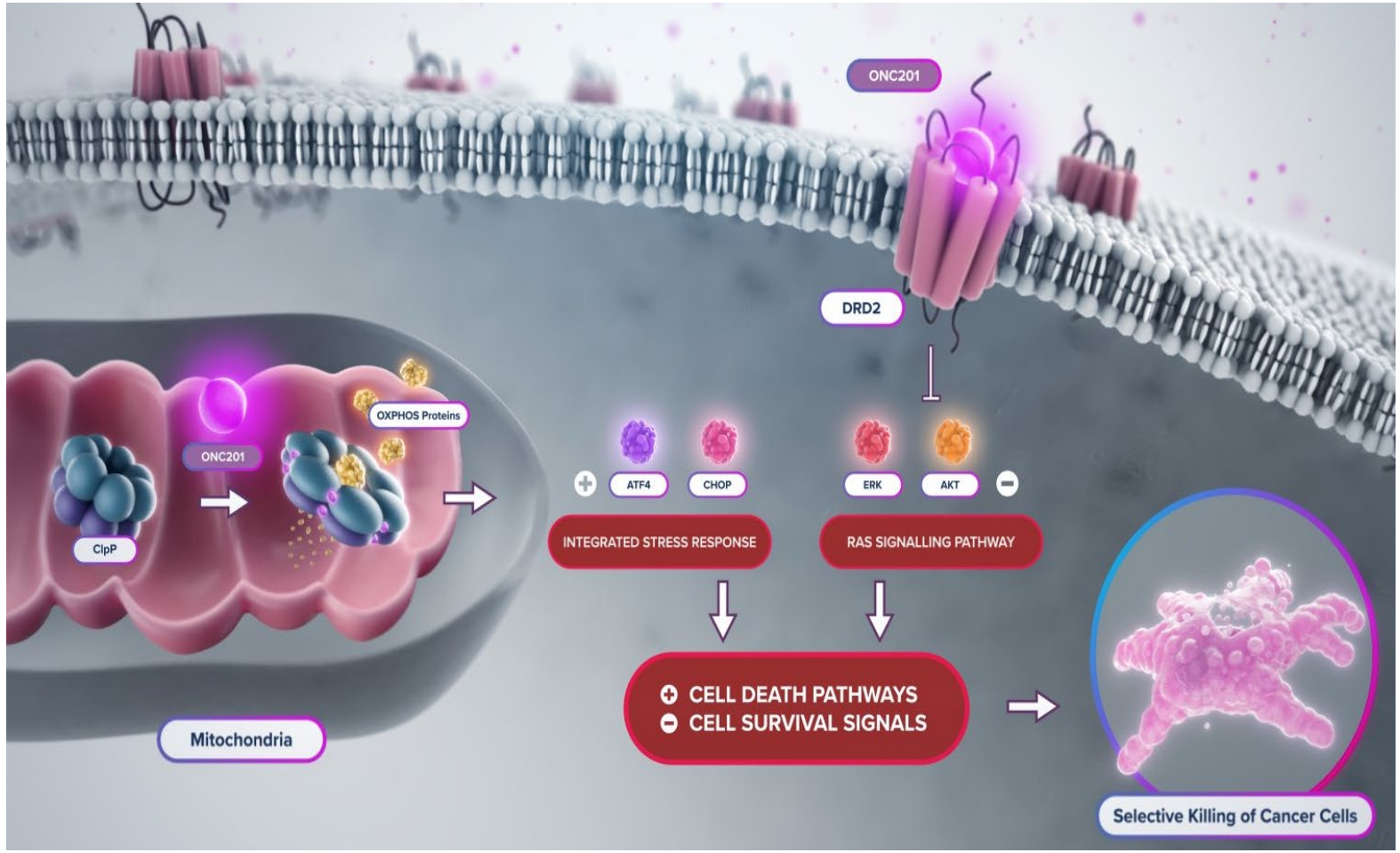
Dordaviprone Directly Engages ClpP and DRD2

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[1]
- 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

1. https://pubmed.ncbi.nlm.nih.gov/38386699/.

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;

Dordaviprone Reverses Central Hallmark of H3 K27M-mutant Diffuse Glioma

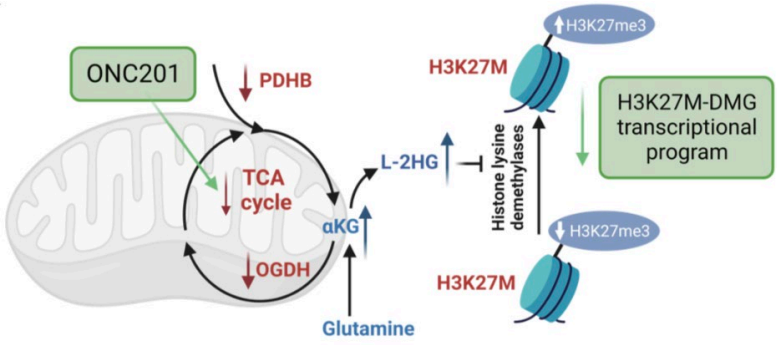
CANCER DISCOVERY

Volume 13, Issue 11

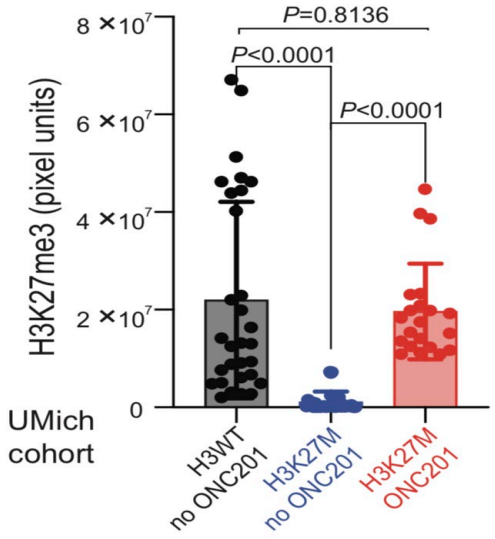
1 November 2023

Venneti S., et al

Mitochondrial effects of dordaviprone reverse H3 K27me3-loss



Statistically significant H3 K27me3-loss reversal in dordaviprone-treated H3 K27M diffuse glioma patients



https://aacrjournals.org/cancerdiscovery/article/13/11/2370/729854/Clinical-Efficacy-of-ONC201-in-H3K27M-Mutant

ONC206

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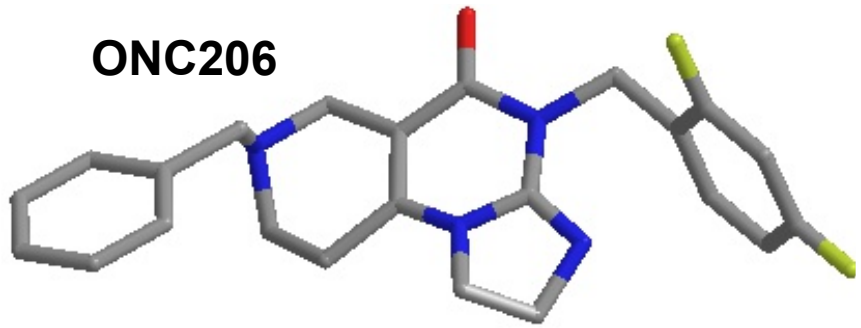
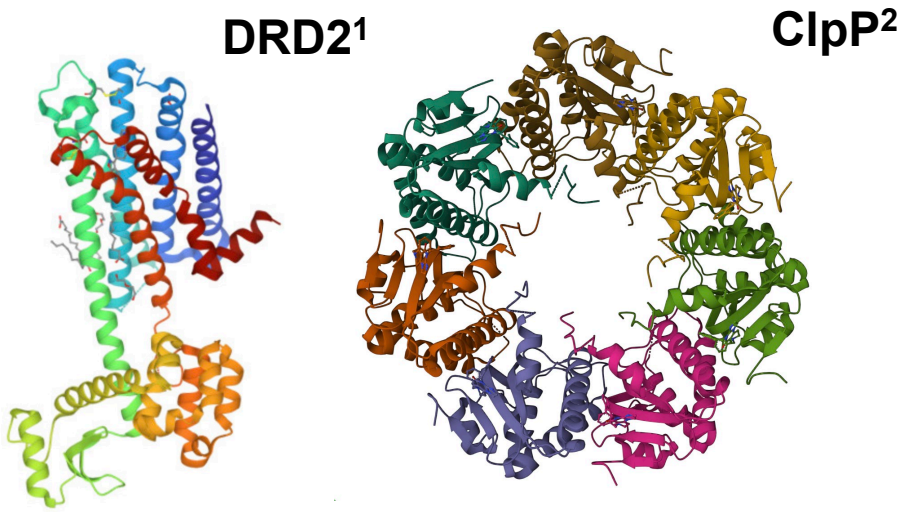
ONC206: Second Generation Oral Brain Penetrant ClpP Agonist + DRD2 Antagonist

- 10x higher in vitro potency relative to dordaviprone
- Monotherapy efficacy data observed 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 nearing completion in CNS cancers

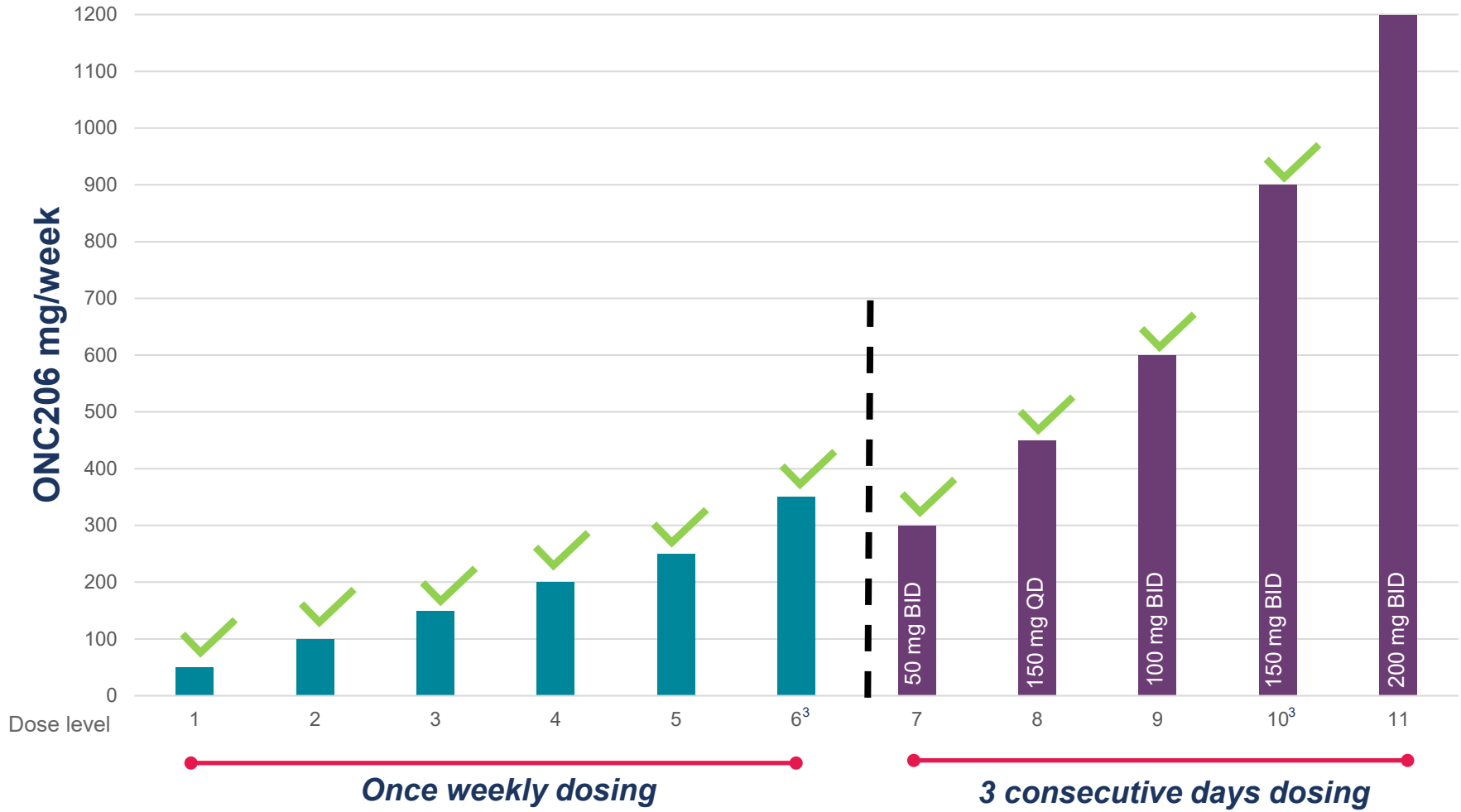




1. PDB 6CM4
2. PDB 6DL7

ONC206 Ph 1 Dose Escalation in Unselected CNS Tumors Enrolling Final Cohort[1,2]

Recommended Phase 2 Dose Expected Early 2025



Broad Eligibility Criteria

- Unselected CNS patients to accelerate collection of safety and PK data
- Received prior therapies
- Does not require response-evaluable disease
- Late stage patients with 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 Appears Well-Tolerated in Adult and Pediatric Patients to Date

	Related AEs[1] Integrated Data Set N=100	
	All grades	Grade ≥ 3
Any Treatment-related AE	**49%**	**2%**
Fatigue	21%	1%
Vomiting	14%	0%
Lymphocyte count decreased	9%	0%
Headache	8%	0%
Nausea	8%	0%
White blood cell decrease	7%	0%
Neutrophil count decreased	6%	0%
Diarrhea	5%	0%
ALT increased	5%	1%

Data cutoff : 02Dec2024

- Majority of treatment-related adverse events (TRAEs) are mild to moderate in severity
- Most frequent TRAEs are fatigue, vomiting and lymphopenia
  - 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 data observed in adults and pediatrics

1. Adverse Events evaluable for safety. Data extraction from Adult study and Pediatric study as of Dec 2, 2024; preliminary data

ONC206 Dose Escalation and Intensification Appears Well-Tolerated 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=12	200mg QW N=18	250mg QW N=14	350 mg QW N=3[3]	50mg BID; TIW N=9	150mg QD; TIW N=14	100mg BID; TIW N=6	150mg BID; TIW N=3[3]	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%	58%	56%	57%	67%	44%	43%	17%	33%	
Grade 1	60%	45%	50%	39%	50%	67%	33%	36%	17%	33%	
Grade 2	30%	45%	42%	33%	43%	33%	11%	21%	0%	33%	
Grade 3	0%	9%	8%	0%	0%	0%	0%	0%	0%	0%	
Grade 4/5	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	

Enrolling

1. Adverse Events. Data extraction from Adult study and Pediatric study as of 02Dec2024, preliminary data
2. Weight-based dosing utilized in pediatric patients <60 kg
3. Adults only

ONC206 Patient Exposures with Intensified Dosing Exceeded Exposures Associated with Nonclinical Efficacy

- ***Cmax*** exceeded IC50 in diverse CNS and non-CNS solid tumor cell lines[2]
- ***AUC*** exceeded 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[5]	**900**	Pending		
	200 mg; BID/TIW	***1200***	*Open to enrollment*		

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 and Preclinical Efficacy

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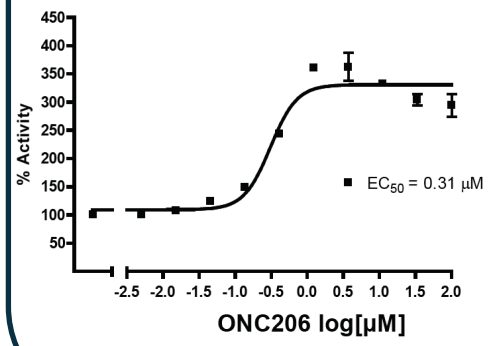
ONC206 Is a Second Generation Dual ClpP Agonist/DRD2 Antagonist

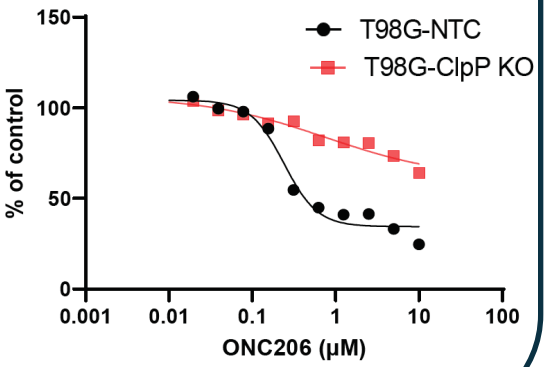
- ClpP and DRD2 are direct binding targets that **control mitochondrial and pro-survival functions**, respectively, in a range of human cancers
- ClpP agonism and DRD2 antagonism occurs at **nanomolar concentrations**
- **Anti-cancer activity** is dependent on ClpP and/or DRD2 depending on tumor type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

ClpP

ClpP catalytic activity is stimulated by ONC206[1]

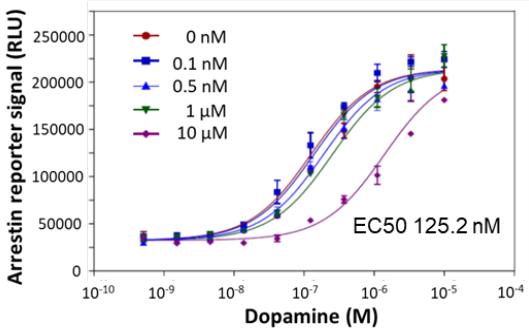


ClpP-dependent in vitro activity of ONC206 in T98G high grade glioma cells[1]

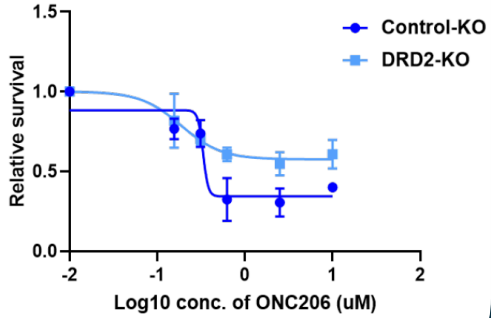


DRD2

DRD2 signaling is inhibited by ONC206 [2]



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



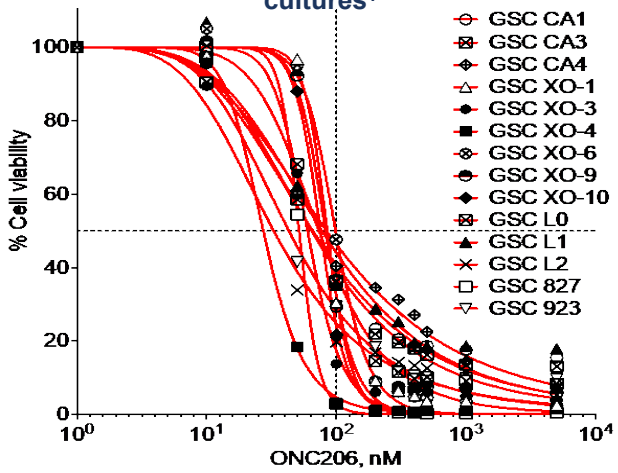
1. Maranto et al, AACR Brain Cancer Conference 2023
2. Prabhu et al, AACR 2020
3. Hu et al, Cancers 2020;

ONC206 Exhibits Monotherapy Activity in Multiple CNS Cancer Models

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

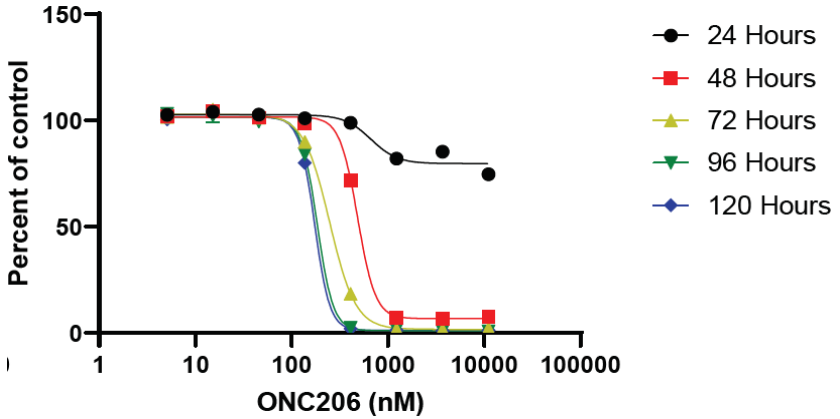
Nanomolar IC50

Patient-derived high-grade glioma cultures[1]



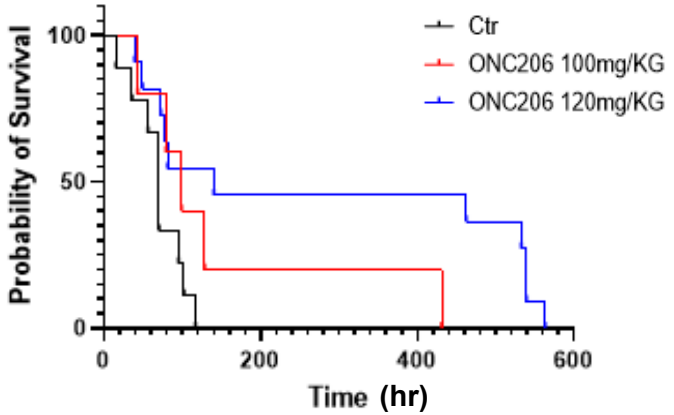
Efficacy data enhanced with duration

High-grade glioma SF8628 cells[2]



Efficacy enhanced with dose

Transgenic SHH (SmoA1) **Medulloblastoma** Model[3]



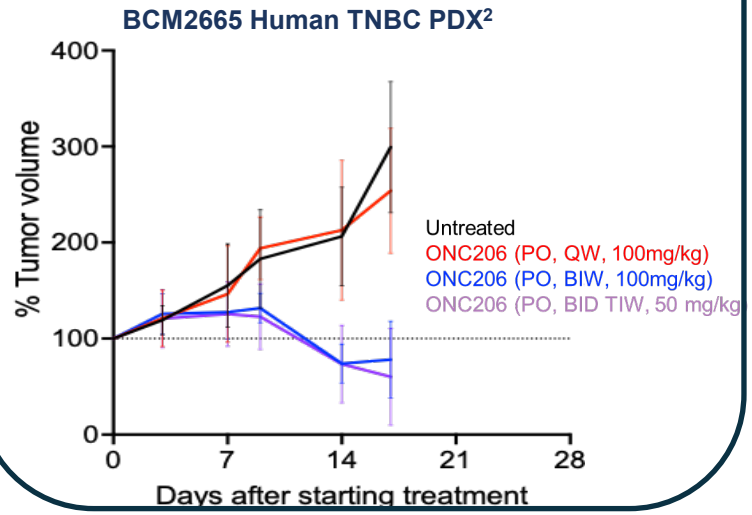
1. Jung et al, SNO 2017
2. Maranto et al, AACR Brain Cancer Conference 2023
3. Tzaridis et al, AACR 2024

Monotherapy Results & Tolerability of ONC206 in Several Non-CNS Solid Tumors

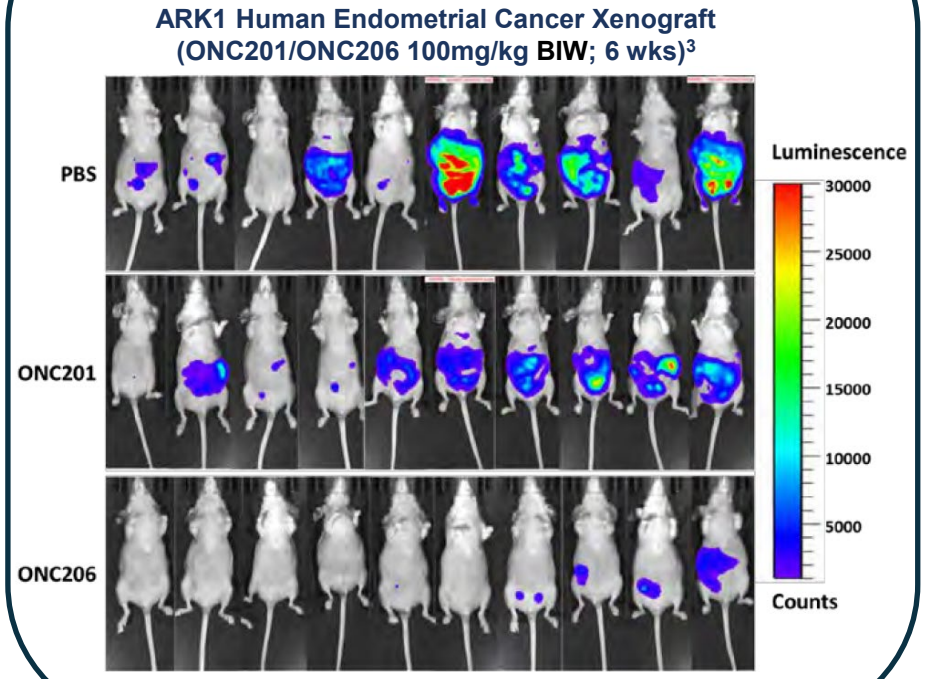
pheochromocytoma, triple-negative breast (TNBC)[2], endometrial[3], cholangiocarcinoma[1], ovarian[4], hepatocellular cancer[5], small cell lung cancer

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

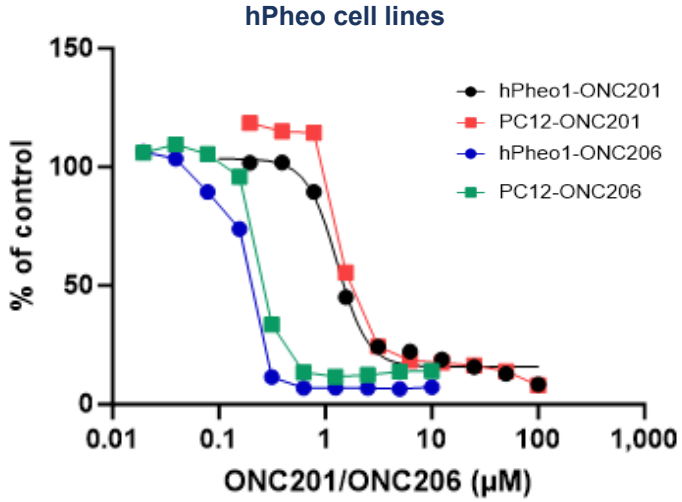
Tumor Regressions with Increased Dose Frequency



Enhanced in vivo results



Enhanced in vitro results in PCPG cell lines



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

Potential for Imipridones Beyond Brain Tumors

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

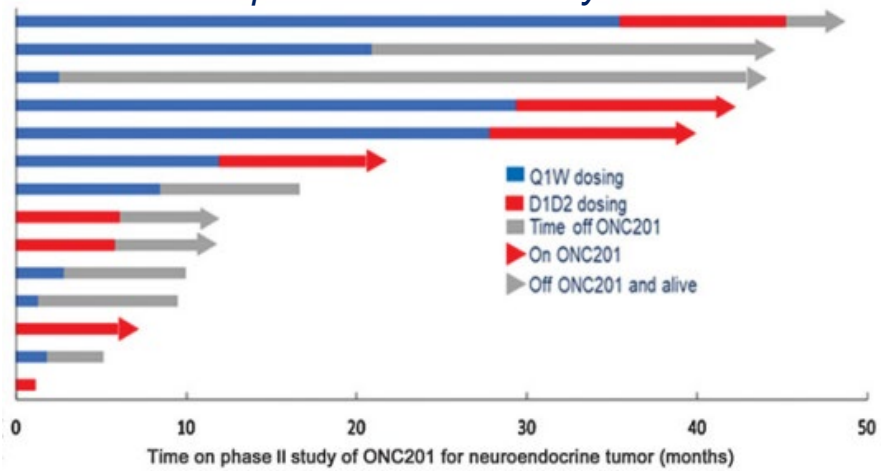
- Single agent responses in Pheochromocytoma and Paraganglioma (PCPG): adrenal-related tumors with high malignant DRD2 expression
- Investigator initiated trial at Cleveland Clinic in a heavily refractory and pretreated patient population (n=14)

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%)

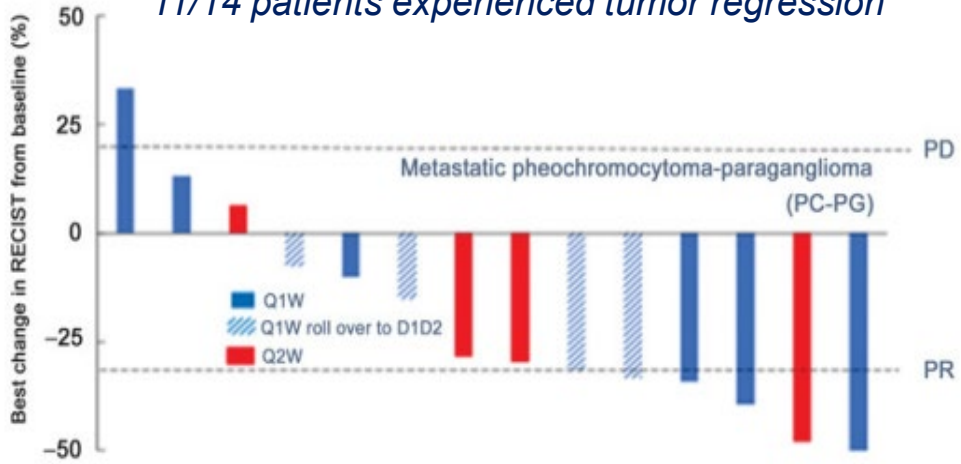
Sites of meastasis, N (%)	
Lymph nodes	11 (78.6%)
Lung	6 (42.9%)
Liver	2 (14.3%)
Bone	13 (92.9%)
Other	0 (0.0%)

- 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

TEMBEXA® Deal Term Summary

TEMBEXA is an internally-developed anti-viral program approved by FDA in 2021 and divested to Emergent in an asset sale agreement in 2022.

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

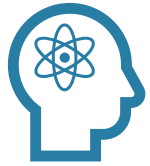
Terms summary:

- $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

Planned NDA submission in December 2024



Potential accelerated approval in Q3 2025

Imipridone pipeline progressing

Dordaviprone U.S. NDA submission planned for Dec '24, potential U.S. accelerated approval in 2025

- ✓ *No approved therapies currently in recurrent H3 K27M diffuse glioma, an invariably lethal Grade 4 glioma (World Health Org)*
- ✓ *Total addressable market exceeds $1Bn in U.S. (U.S. incidence >2,000 patients, ultra-orphan drug pricing)*
- ✓ *Patent protection thru 2037 (potential additional U.S. patent term extension)*
- ✓ *Front-line Ph 3 trial (ACTION study) substantial enrollment, active in >150 sites and 17 countries*
- ✓ *Application for Rare Pediatric Disease Priority Review Voucher (PRV) to be included in upcoming NDA*

ONC206 Recommended Phase 2 dose expected early 2025

- ✓ *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*

Positioned to accelerate growth from internal and/or external innovation

- ✓ *Robust business development search and evaluation process*

$152 million in capital to fund operations as of September 30, 2024

Chimerix Corporate Presentation

CHIMERIX