

ASX RELEASE

23 June 2022

KAZIA EDUCATIONAL WEBINAR ON PAXALISIB IN CHILDHOOD BRAIN CANCER

Sydney, 23 June 2022 – Kazia Therapeutics Limited (NASDAQ: KZIA; ASX: KZA), an oncology-focused drug development company, is pleased to provide a presentation on paxalisib in childhood brain cancer, featuring Dr James Garner, Associate Professor Matt Dun and Dr John Friend. A copy of the webinar will be made available in the media section of our website.

<https://www.kaziatherapeutics.com/site/media-centre/overview>

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About Kazia Therapeutics Limited

Kazia Therapeutics Limited (NASDAQ: KZIA; ASX: KZA) is an oncology-focused drug development company, based in Sydney, Australia.

Our lead program is paxalisib, a brain-penetrant inhibitor of the PI3K / Akt / mTOR pathway, which is being developed to treat glioblastoma, the most common and most aggressive form of primary brain cancer in adults. Licensed from Genentech in late 2016, paxalisib commenced recruitment to GBM AGILE, a pivotal study in glioblastoma, in January 2021. Seven additional studies are active in various forms of brain cancer. Paxalisib was granted Orphan Drug Designation for glioblastoma by the US FDA in February 2018, and Fast Track Designation for glioblastoma by the US FDA in August 2020. In addition, paxalisib was granted Rare Pediatric Disease Designation and Orphan Designation by the US FDA for DIPG in August 2020, and Orphan Designation for AT/RT in June 2022.

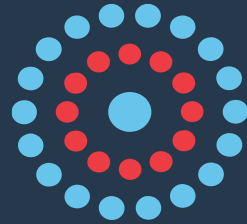
Board of Directors

Mr Iain Ross Chairman, Non-Executive Director
Mr Bryce Carmine Non-Executive Director
Mr Steven Coffey Non-Executive Director
Dr James Garner Chief Executive Officer, Managing Director

Kazia is also developing EVT801, a small-molecule inhibitor of VEGFR3, which was licensed from Evotec SE in April 2021. Preclinical data has shown EVT801 to be active against a broad range of tumour types and has provided compelling evidence of synergy with immunology agents. A phase I study commenced recruitment in November 2021.

For more information, please visit www.kaziatherapeutics.com or follow us on Twitter @KaziaTx.

This document was authorized for release to the ASX by James Garner, Chief Executive Officer, Managing Director.



KAZIA
THERAPEUTICS



Paxalisib in Childhood Brain Cancer

Educational Webinar

22 June 2022

Forward-Looking Statements

This presentation contains **forward-looking statements** within the meaning of the safe-harbor provisions of the Private Securities Litigation Reform Act of 1995. Such statements involve substantial risks and uncertainties, not all of which may be known at the time. All statements contained in this presentation, other than statements of historical fact, including statements regarding our strategy, research and development plans, collaborations, future operations, future financial position, future revenues, projected costs, prospects, plans, and objectives of management, are forward-looking statements. Not all forward-looking statements in this presentation are explicitly identified as such.

Many factors could cause the actual results of the Company to differ materially from the results expressed or implied herein, and you should not place undue reliance on the forward-looking statements. Factors which could change the Company's expected outcomes include, without limitation, our ability to: advance the development of our programs, and to do so within any timelines that may be indicated herein; the safety and efficacy of our drug development candidates; our ability to replicate experimental data; the ongoing validity of patents covering our drug development candidates, and our freedom to operate under third party intellectual property; our ability to obtain necessary regulatory approvals; our ability to enter into and maintain partnerships, collaborations, and other business relationships necessary to the progression of our drug development candidates; the timely availability of necessary capital to pursue our business objectives; and our ability to attract and retain qualified personnel; changes from anticipated levels of customer acceptance of existing and new products and services and other factors.

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In addition, the extent to which the COVID-19 outbreak continues to impact our workforce and our discovery research, supply chain and clinical trial operations activities, and the operations of the third parties on which we rely, will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration and severity of the outbreak, additional or modified government actions, and the actions that may be required to contain the virus or treat its impact.

Any forward-looking statements contained in this presentation speak only as of the date this presentation is made, and we expressly disclaim any obligation to update any forward-looking statements, whether because of new information, future events or otherwise.



Dr James Garner

Chief Executive Officer

Kazia Therapeutics Limited



Associate Professor Matt Dun

Group Leader, Cancer Research
Signalling Group

Hunter Medical Research Institute
University of Newcastle, Australia



Dr John Friend

Chief Medical Officer

Kazia Therapeutics Limited

Agenda

- Strategic considerations in development of drugs for childhood brain cancer
Dr James Garner
- Emerging data for paxalisib in DIPG
Associate Professor Matt Dun
- Emerging data for paxalisib in AT/RT
Dr John Friend
- Overview of Kazia's childhood brain cancer program
Dr John Friend
- Closing Comments + Q&A

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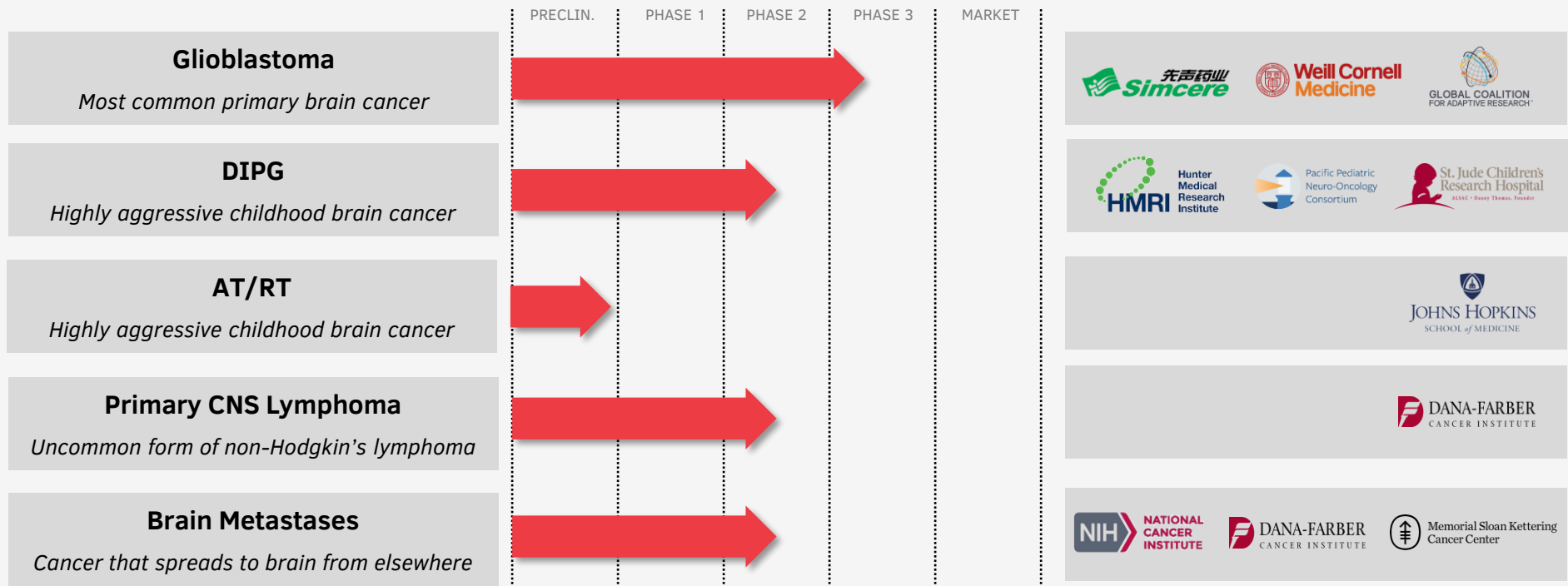
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Childhood brain cancer is emerging as a critical element of the paxalisib development program

Paxalisib
Small molecule, highly potent, brain-penetrant inhibitor of PI3K / mTOR

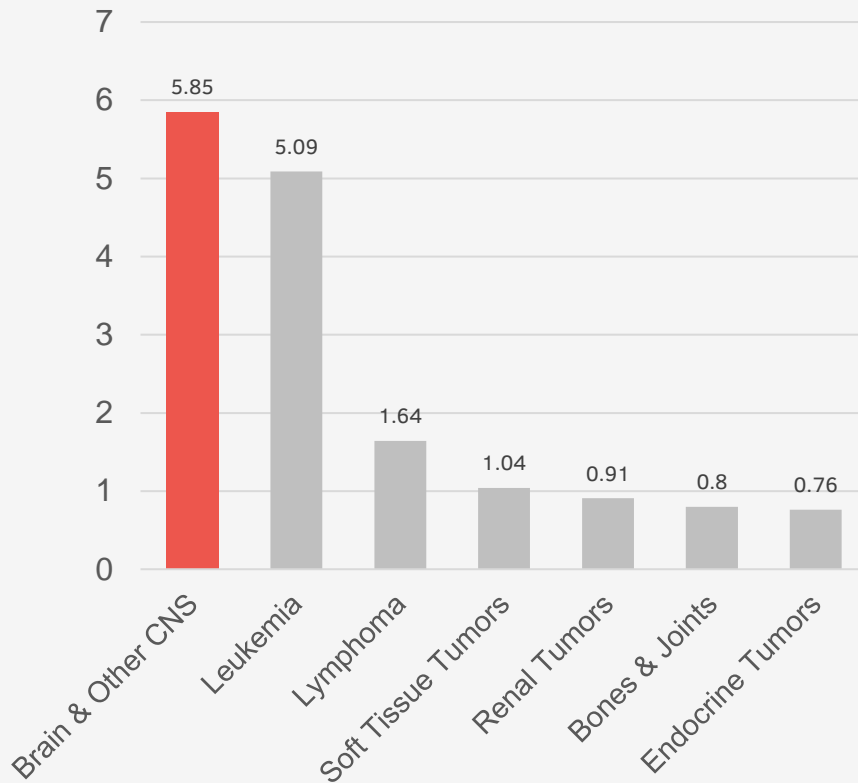
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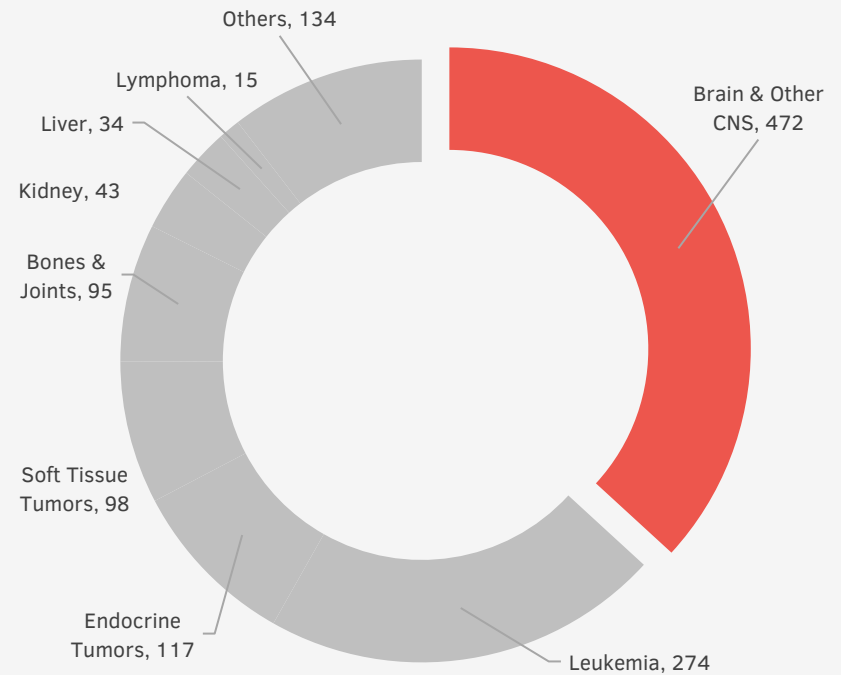


Brain cancer is the most common malignancy of childhood, representing about one third of childhood cancer deaths

Average Annual Age-Adjusted Incidence (cases / 100,000 people; 2014-2018)

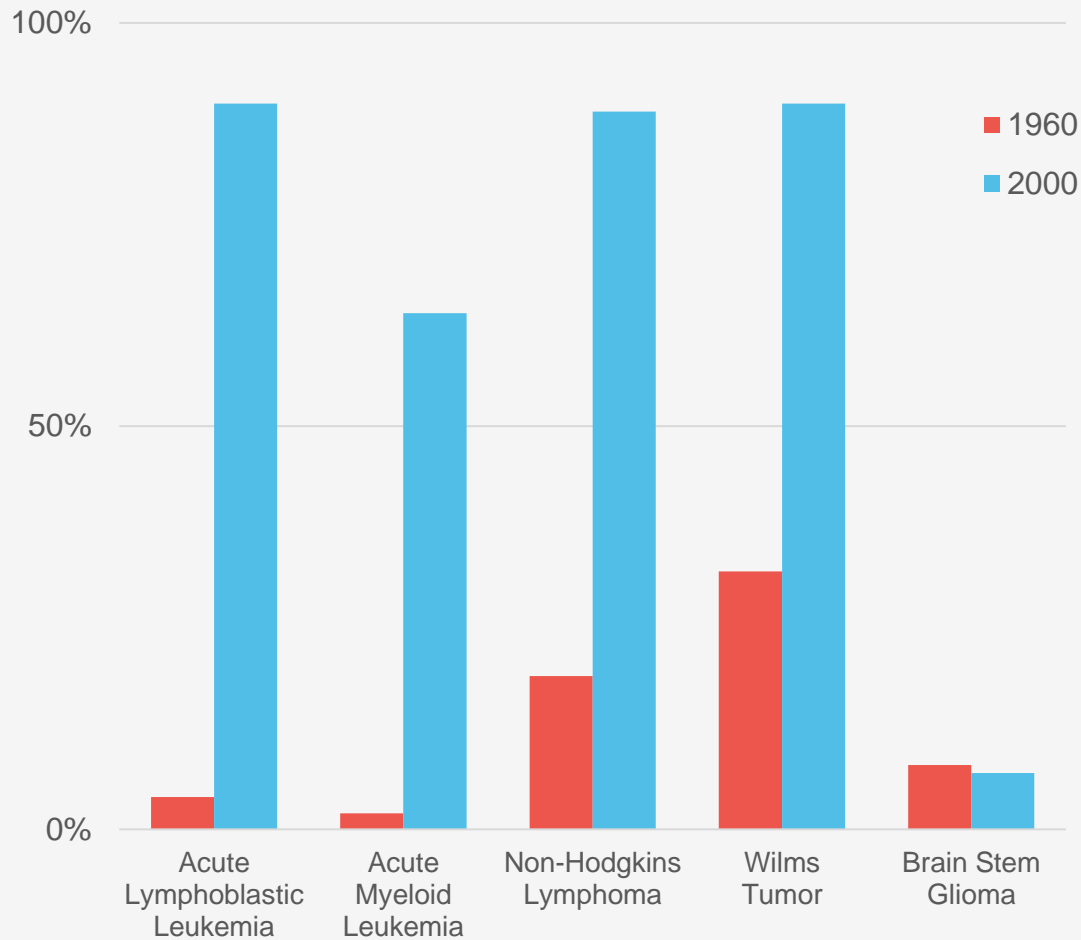


Mortality (estimated absolute number of cases in US; 2020)



Source: CBTRUS; CDC; Ages 0-14 shown

Prognosis of childhood brain cancer, especially DMGs, has improved little in recent decades



FDA-Approved Drug Therapies

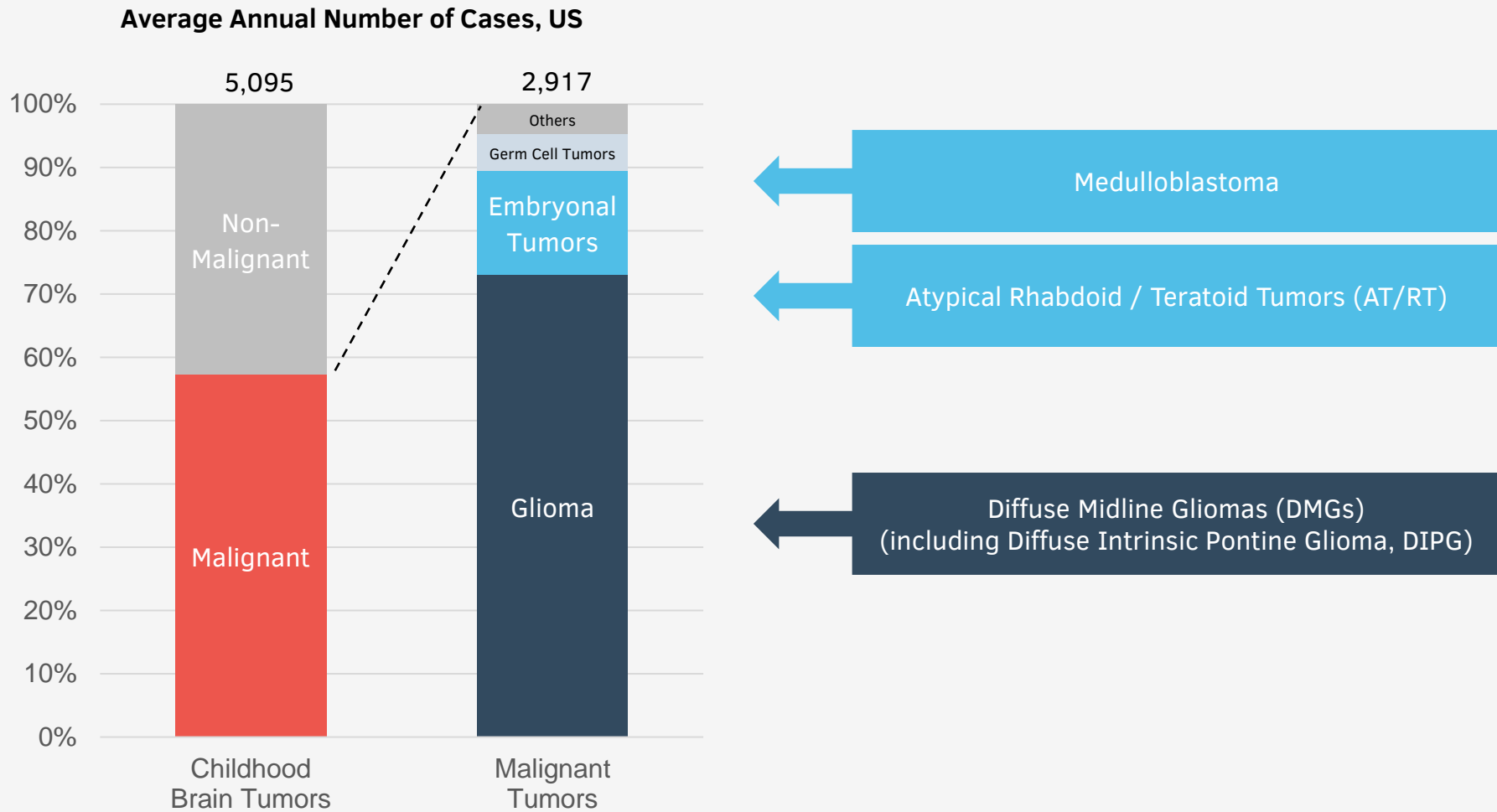
Diffuse Midline Gliomas Nil

Atypical Teratoid / Rhabdoid Tumors Nil

Medulloblastoma Nil

Source: Adamson PC, *CA Cancer J Clin.* 2015;65:212–220

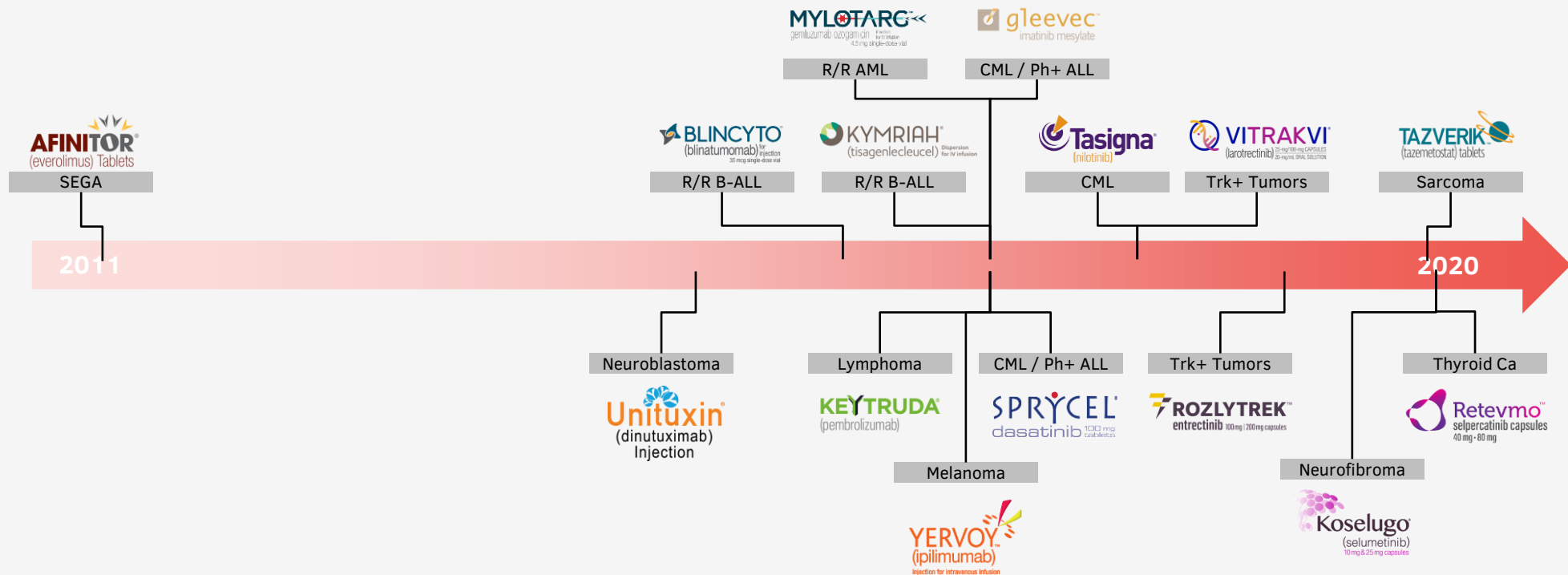
Childhood brain cancer comprises a diverse range of pathologies








Source: CBTRUS; Ages 0-19 shown

Childhood cancers are becoming an area of focus for the pharmaceutical industry

Pediatric Cancer Drug Approvals by FDA, 2010-2020



Regulatory agencies encourage and, increasingly, require paediatric development

| | | |
|--|--|--|
| FDA  | Best Pharmaceuticals for Children Act (2002) | <ul style="list-style-type: none">• Allows FDA to request sponsors to provide pediatric data, but fulfilment is voluntary• 6 month patent extension for drugs completing PSP successfully |
| FDA  | Pediatric Research Equity Act (2003) | <ul style="list-style-type: none">• Requires sponsors to provide pediatric assessment for any adult indications seeking NDA |
| FDA  | RACE for Children Act (2017) | <ul style="list-style-type: none">• Requires sponsors to submit a Pediatric Study Plan if target of the drug is on a Relevant Molecular Target List [<i>PI3K inhibitors are listed</i>]• 6 month patent extension for drugs completing PSP successfully |
| EMA  | Regulation (EC) No 1901/2006 of the European Parliament and of the Council (2016) | <ul style="list-style-type: none">• Requires sponsors to submit a Pediatric Investigational Plan, which must be complete by time of marketing authorisation• 6 month patent extension for drugs completing PIP successfully |
| FDA  | Creating Hope Act (2012) | <ul style="list-style-type: none">• Creates priority review vouchers, which are fungible and can be traded• Unituxin (denutuximab) pPRV sold for \$350M |

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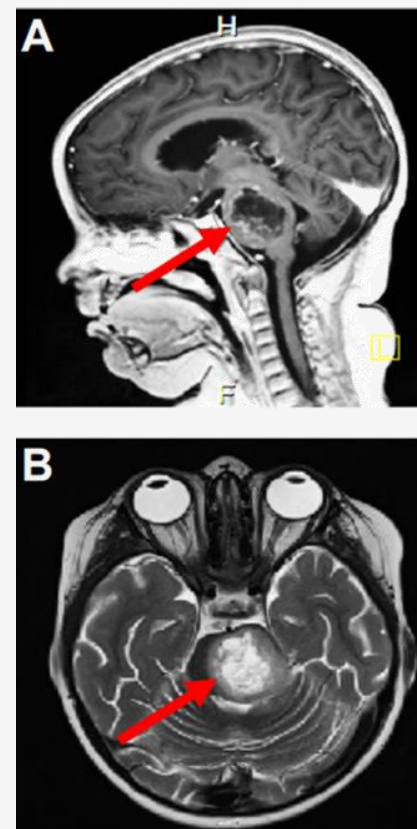
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What is DIPG?

- Most aggressive paediatric cancer with median overall survival of ~9-11 months and no long term survivors
- Located in the pontine region of the brain, which is responsible for life-essential functions, including cardiac and respiratory control
- Current treatment is radiotherapy, which only extends survival by ~3 months; surgical resection is highly dangerous

Effective new therapies for the treatment of DIPG are desperately needed



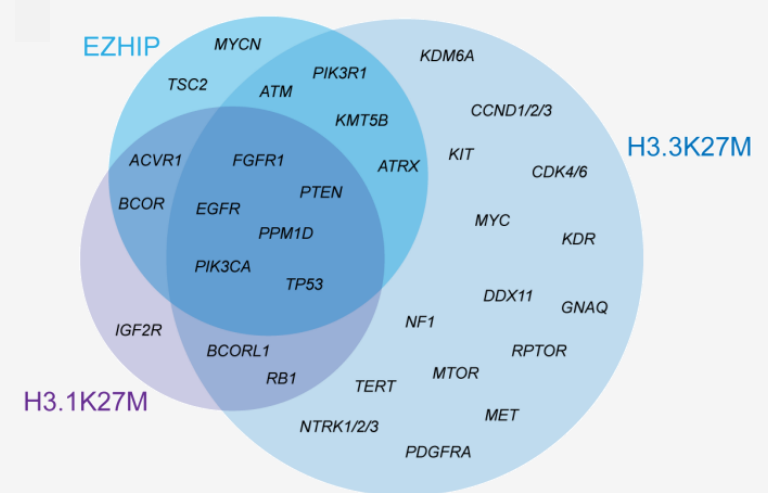
Magnetic resonance imaging (MRI) of DIPG.
A. Sagittal and B. Axial MRI show high signal intensity at red arrow.

Josephine Dun – March 2019

DIPG is genetically heterogenous

- 80-90% of DIPG cases harbour a lysine-to-methionine (K-to-M) mutation in histone 3 (H3) at amino acid 27 (H3K27M), and this may be considered the defining genetic alteration of DIPG
- Additional mutations are necessary to drive glioma formation:
Proliferative genes: ACVR1, PDGFRA, PIK3CA, PIK3R1, mTOR/AKT, EGFR, FGFR
- *Tumour suppressor genes:* TP53, RB, BCOR, PTEN, CDKN2A, PPM1D

Given the number of driver mutations at diagnosis, targeted monotherapies are unlikely to improve outcomes and combination treatment will generally be required

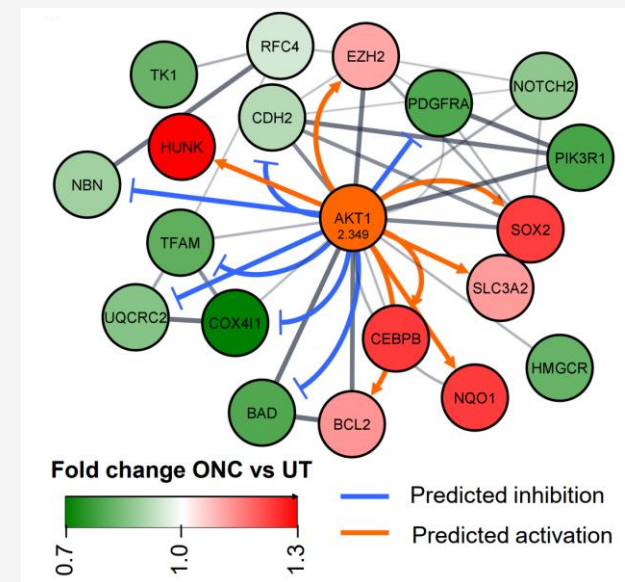
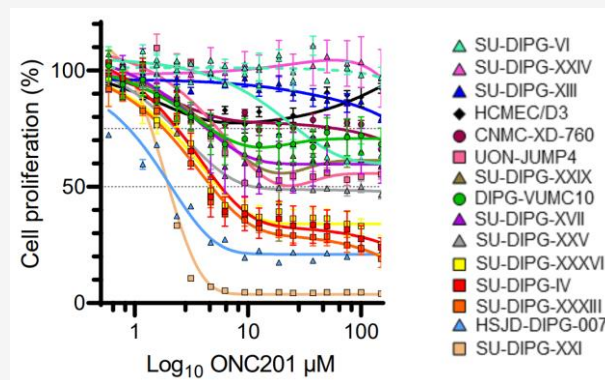
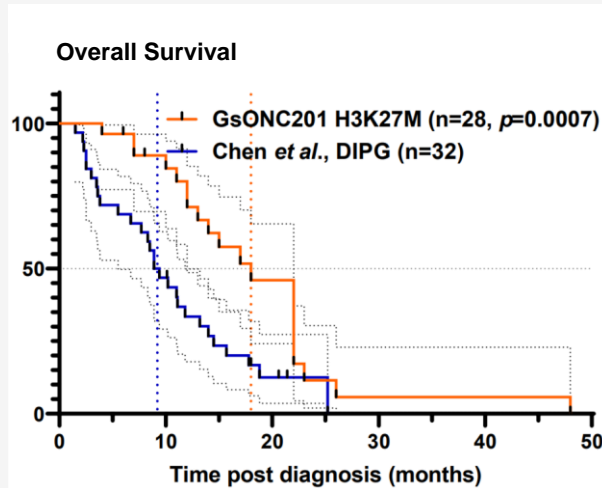


ONC201 has shown promise as a single agent in DIPG compassionate use experience

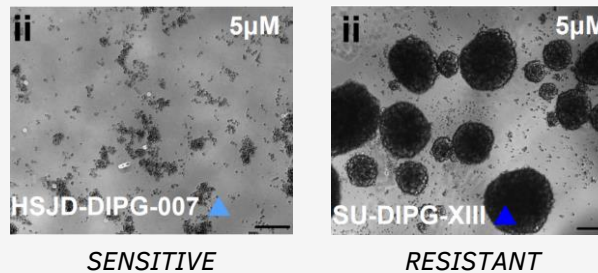
Apparent extension of overall survival in comparison to historical controls...

...but different tumours have widely varying sensitivity to ONC201...

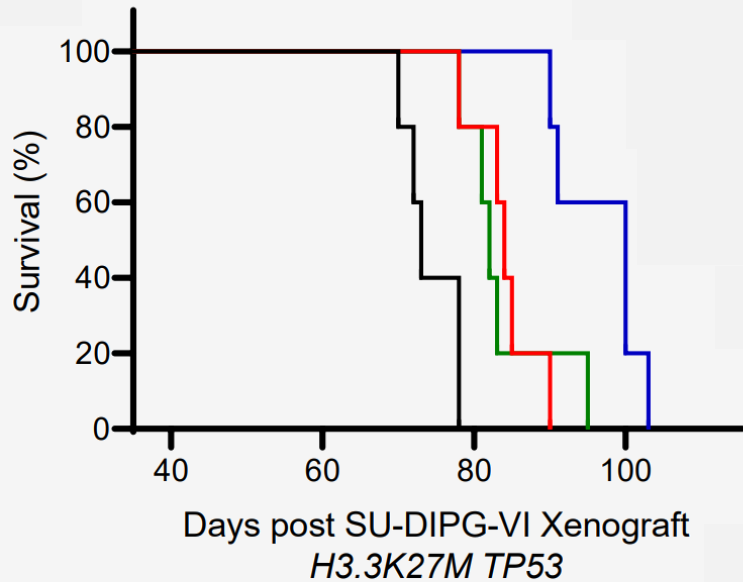
...and PI3K / AKT signalling seems to be a primary resistance mechanism



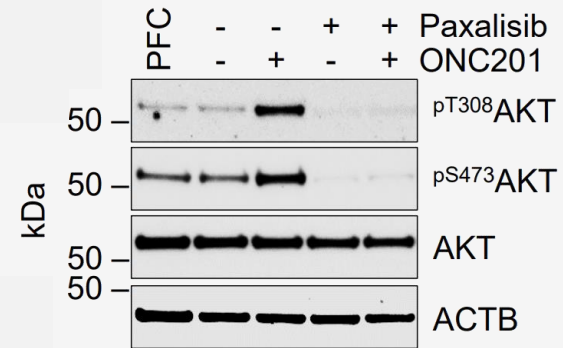
- 20.2 months OS versus 10.8 for historical controls
- However, variable response and all patients eventually progress



Combination of ONC201 and paxalisib appears synergistic



- Vehicle (n=6)
 - ONC201 125 mg/kg QW (n=6)
 - Paxalisib 10 mg/kg TIW (n=6)
 - ONC201 QW + Paxalisib TIW (n=6)
- Statistical significance markers: ** indicates p < 0.01, * indicates p < 0.05.

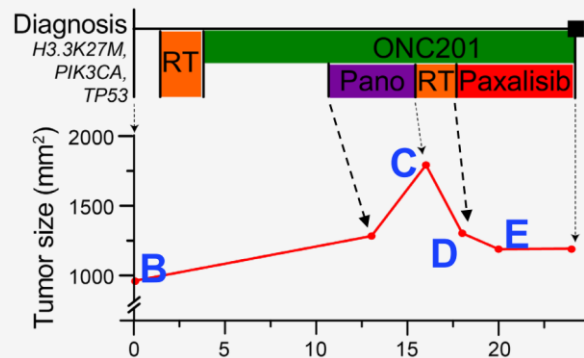


Addition of paxalisib rescues ONC201 from pAKT activation

Clinical cases from compassionate use experience corroborate laboratory data

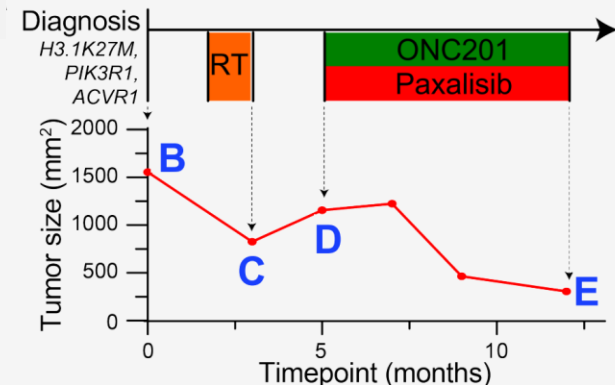
Patient 1

- Commenced ON201 + paxalisib immediately following re-irradiation
- At 5 months, MRI showed continued regression of primary tumour and clinical improvement
- Patient succumbed unexpectedly of pneumonia, with autopsy showing no evidence of new tumour growth or tumour-related mortality



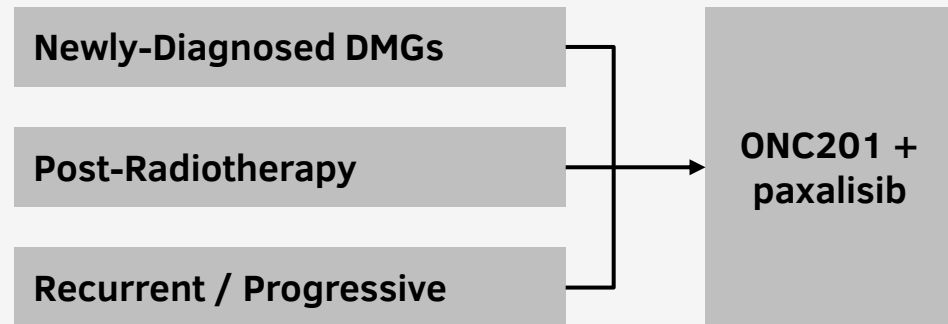
Patient 2

- Commenced ONC201 + paxalisib following radiotherapy after diagnosis
- Tumour size has decreased by 80% (versus diagnosis) or 68% (versus post-RT)
- Patient has returned to school with marked reduction of DIPG-associated symptoms, and dramatic and continued tumour regression



A phase II clinical trial is underway to formally evaluate the combination of ONC201 and paxalisib

- Phase II interventional study, sponsored by the Pacific Pediatric Neuro-Oncology Consortium (PNOC)
- Up to 216 participants in multi-arm adaptive design
- Patients with H3K27M-mutant diffuse midline glioma
- Age 2 – 39 years



Pacific Pediatric
Neuro-Oncology
Consortium

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Atypical Teratoid / Rhabdoid Tumor (AT/RT)

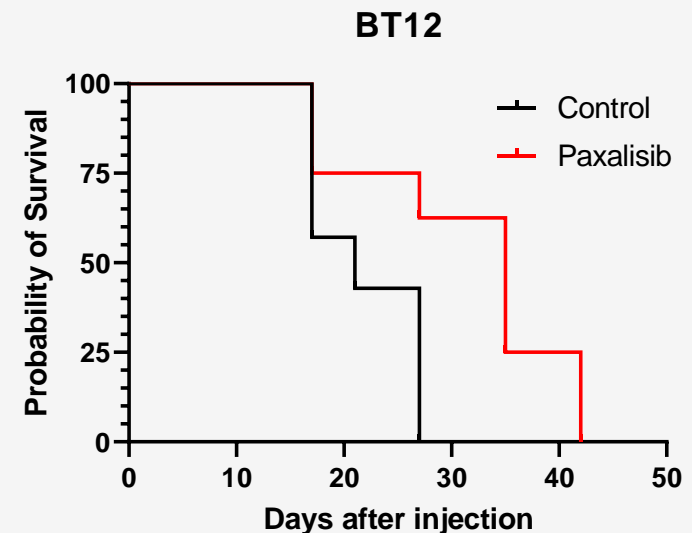
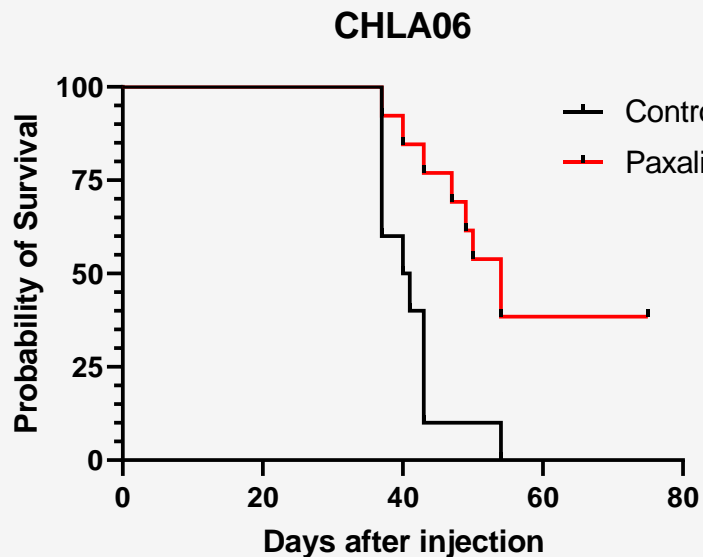
- Atypical Teratoid Rhabdoid Tumors are the most common malignant brain tumors of infancy
 - Occurs in the cerebellum or brainstem
 - Usually develops by age three but can occur in older children
 - Presenting symptoms include
 - Issues with balance/coordination/walking
 - Twitches, unusual facial expressions
 - Nausea/Vomiting/Headaches
 - Activation of the PI3k-Akt-mTOR pathway is commonly observed in patients with AT/RT
 - No FDA approved therapies exist
 - Surgery, chemotherapy and radiation are the current mainstay of treatment

Kazia Therapeutics Announces Collaboration with Johns Hopkins University For Pediatric Brain Cancers

- Lead researcher
 - Jeffrey Rubens, MD
 - Assistant Professor of Pediatrics & Oncology
 - Sidney Kimmel Cancer Center, Johns Hopkins University
- Objective
 - Establish efficacy of Paxalisib in AT/RT and other aggressive pediatric brain tumors via *in vitro* and proprietary *in vivo* models
 - Evaluate the synergistic effect of Paxalisib and other brain penetrant drugs on the slowing of tumour growth and extending overall survival in various preclinical models
 - Develop rationale and preclinical package to rapidly translate into the clinical setting

Kazia Therapeutics Announces Preclinical Data Presented at 2022 AACR and ISPNO Meetings

Paxalisib monotherapy slows tumor growth and extends survival in mice bearing AT/RT orthotopic xenograft tumors



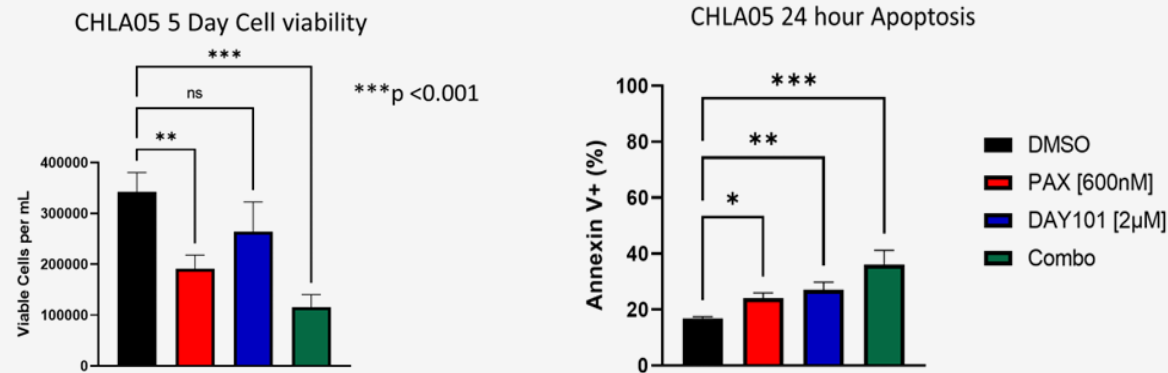
Source: AACR 2022 & ISPNO 2022 Poster Presentations:

The PI3k inhibitor Paxalisib combined with the novel HDAC1/3 inhibitor RG2833 may improve survival in mice bearing orthotopic xenografts of AT/RT.

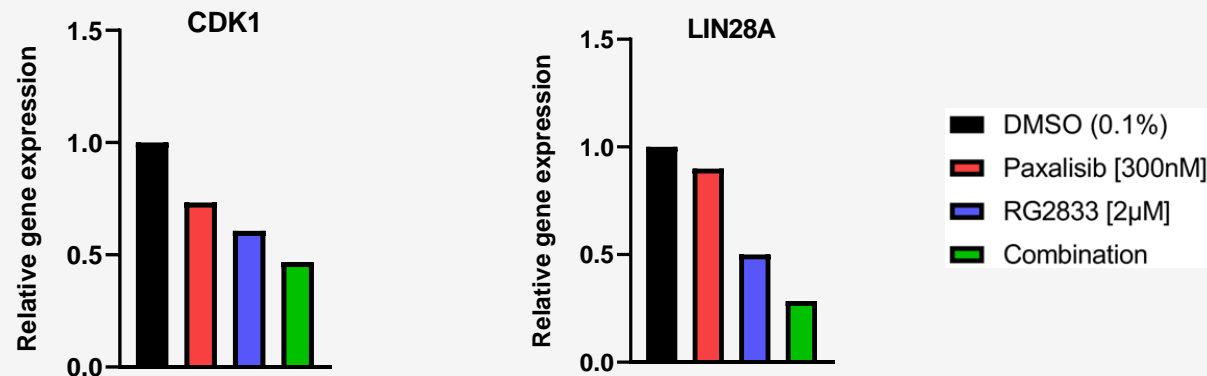
Dual Inhibition of mTOR and MAPK pathways act synergistically to disrupt metabolic pathways and extend survival in orthotopic xenograft models of AT/RT

Kazia Therapeutics Announces Preclinical Data Presented at 2022 AACR and ISPNO Meetings (continued)

Combination of Paxalisib with DAY101 synergizes to slow AT/RT cell growth



Paxalisib combines with RG2833 to disrupt cell cycle regulation and expression of stem cell factors



Source: AACR 2022 & ISPNO 2022 Poster Presentations:

The PI3k inhibitor Paxalisib combined with the novel HDAC1/3 inhibitor RG2833 may improve survival in mice bearing orthotopic xenografts of AT/RT.

Dual Inhibition of mTOR and MAPK pathways act synergistically to disrupt metabolic pathways and extend survival in orthotopic xenograft models of AT/RT

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Kazia has interest in at least three forms of childhood brain cancer

| | Diffuse Midline Gliomas (DMG, DIPG) | Atypical Teratoid / Rhabdoid Tumors (AT/RT) | Others (Medulloblastoma & HGG) |
|-------------------------------|--|--|--|
| Preclinical Research | Positive preclinical data in combination with ONC201 presented at ISPNO conference in Jun 2022 | Positive preclinical data as monotherapy and in combination presented at AACR conference in Apr 2022 | <i>Research proposals under discussion</i> |
| Clinical Trials | Phase I monotherapy clinical trial nearing completion at St Jude Children's Research Hospital (presented at SNO; Nov 2019) | <i>Clinical trial opportunities under discussion</i> | <i>Clinical trial opportunities under discussion</i> |
| | Phase II clinical trial in combination with ONC201, led by PNOG, commenced recruitment in Nov 2021 | | |
| Regulatory Interaction | Orphan Drug Designation (ODD) and Rare Pediatric Disease Designation (RPDD) granted by FDA in Aug 2020 | Orphan Drug Designation (ODD) granted by FDA in June 2022 | <i>Regulatory strategy under discussion</i> |

HGG: High Grade Glioma

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