NOXOPHARM

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13-15 September 2021

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Veyonda® currently is not approved for use in Australia or any other country.

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cancer

Chronic inflammation

Autoimmunity

Neurodegenerative diseases

Human degenerative disease

Involves multiple mutations, multiple errors

Therapies targeting single errors are restricted in their benefit

Single drugs targeting multiple errors

OR

The choice is polypharma

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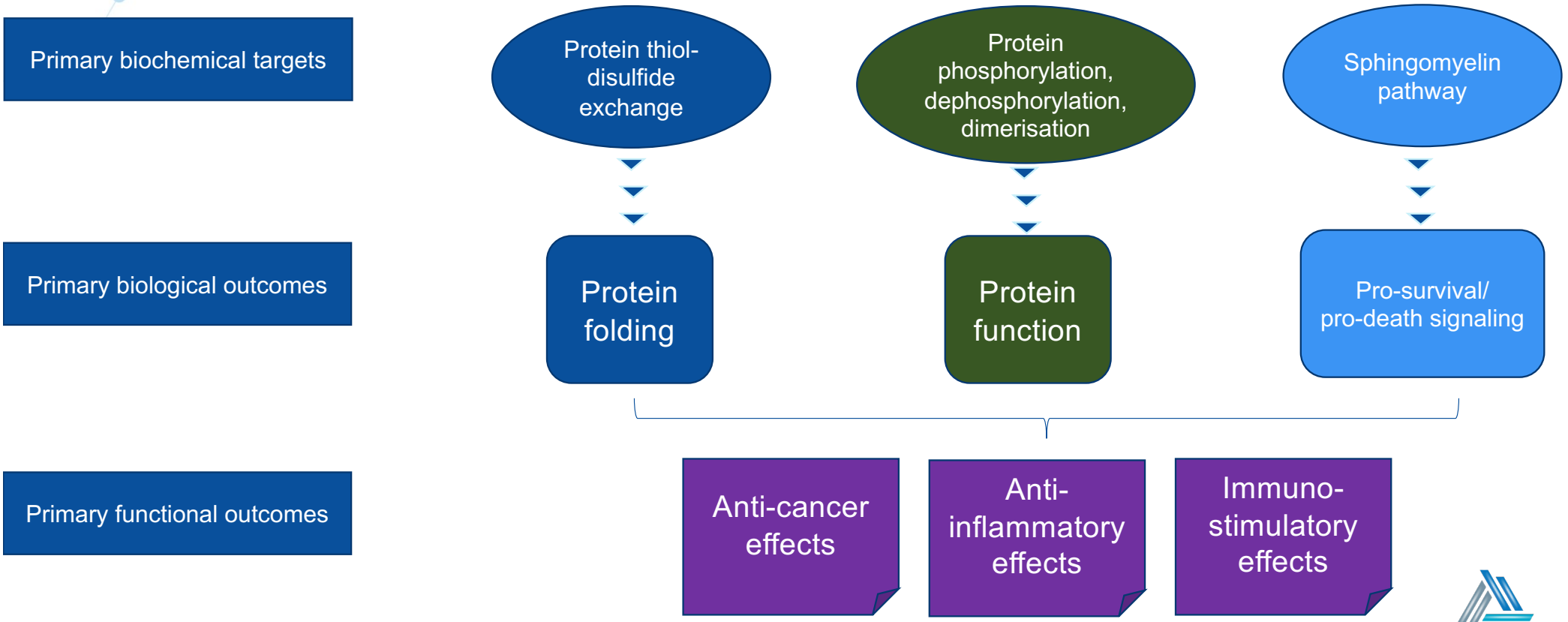
Introducing

idronoxil (Veyonda®)

A novel multi kinase and membrane NAD(P)H-oxidase inhibitor targeting aberrant protein behaviour



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Four R&D Businesses in One Company

Veyonda®

Cancer treatment enhancement

Cancer Research Pipeline

Cancer growth factor inhibitors

Veyonda®

Septic shock

pharmorage

Chronic inflammatory diseases/autoimmune diseases

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Veyonda®

Cancer treatment enhancement

A revolutionary concept in cancer therapy involving a drug (Veyonda®) with **multiple mechanisms of action** that aims to boost the effectiveness of other standard anti-cancer therapies

Programs

- **IONIC - checkpoint inhibitor therapy**
- **DARRT - radiotherapy**
- **CEP - chemotherapy**
- **LuPIN - radioligand therapy**

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Veyonda®

Cancer treatment enhancement

IONIC

Checkpoint inhibitor therapy

Challenge

- PD-1 inhibitor therapy relies on the presence of effector T-cells to take advantage of drug action
- ~95% of human tumours appear to lack effective immune function ('COLD')

Rationale

- Sphingosine-1-phosphate (S1P) key regulator of immune cell trafficking
- Most tumours over-express S1P
- High to low S1P gradient between tumour and blood causes egress of T-cells

Idronoxil

- Inhibits sphingosine kinase 1, blocking S1P production
- → upregulation of CD4+ and CD8+ T-cells
- → restoration of immune function in tumours ('COLD' to 'HOT')

Phase Ib trial

Veyonda + nivolumab

Cohort 1: 15 patients refractory to PD-1 inhibitor therapy

Cohort 2: 15 patients PD-1 inhibitor therapy naive

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Cancer treatment enhancement

DARRT

External beam radiotherapy

Challenge

- Low-dose EBRT triggers an immune response within single irradiated tumours
- On very rare occasions, that immune response shifts from a local to a systemic level → **abscopal response**

Rationale

- Immune (interferon) response to low-dose EBRT stems from damage to mitochondrial DNA
- That damage is repaired by autophagy
- Blocking autophagy extends the interferon response → **augmented abscopal response**

Idronoxil

- Inhibits autophagy
- Activates immune function

Phase II DARRT trial

Multi-national (*U.S., Australia, France, Hungary)*

~100 patients; prostate, breast, lung cancers refractory to standard therapies

Primary end-points: incidence of abscopal responses (RECIST), PFS

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Cancer treatment enhancement

LuPIN

Radioligand therapy

Challenge

- Effectiveness of targeted radiotherapy by radioligands dependent on expression of antigen target on cancer cells
- ^{177}Lu-PSMA therapy limited by rate of expression of PSMA on prostate cancer cells

Rationale

- One strategy is to increase PSMA expression
- Another is to enhance the damage inflicted by the available radioactivity

Idronoxil

- Blocks cell division (G_2M) → greater DNA damage
- Blocks DNA repair (topoisomerases 1 and 2; PARP1) → greater cytotoxicity

LuPIN phase I/II study

- 56 mCRPC patients
- Post-enza/abir and 2x taxanes
- mOS = 19.7 months

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Veyonda®

Cancer treatment enhancement

CEP

Chemotherapy

Challenge

High rates of inherent and acquired resistance in most tumour types to cytotoxic chemotherapies due to over-expression of pro-survival mechanisms

Idronoxil

- **Blocks external membrane NADH oxidase function → interferes with protein folding**
- **Blocks S1P expression → reduction in major pro-survival signaling**
- **Enhanced ceramide expression → increased pro-death signaling**
- **Increases immune cell recruitment**

Rationale

- **Priming cytotoxic effects of chemo drugs by reducing pro-survival signaling**

Phase Ib CEP-2 trial

IND granted July 2021

Multiple U.S. sites planned

First-line therapy doxorubicin and Veyonda in patients with soft tissue sarcomas

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Cancer Research Pipeline

‘Helper’ growth factor inhibitors

Many cancers, particularly the highly aggressive cancers, co-opt supporting healthy cells to supply growth factors that drive cancer cell growth.

Noxopharm has identified a novel family of drugs with potential to block these signals

Programs

- Brain cancer (GBM)
- Pancreatic cancer

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Cancer Research Pipeline

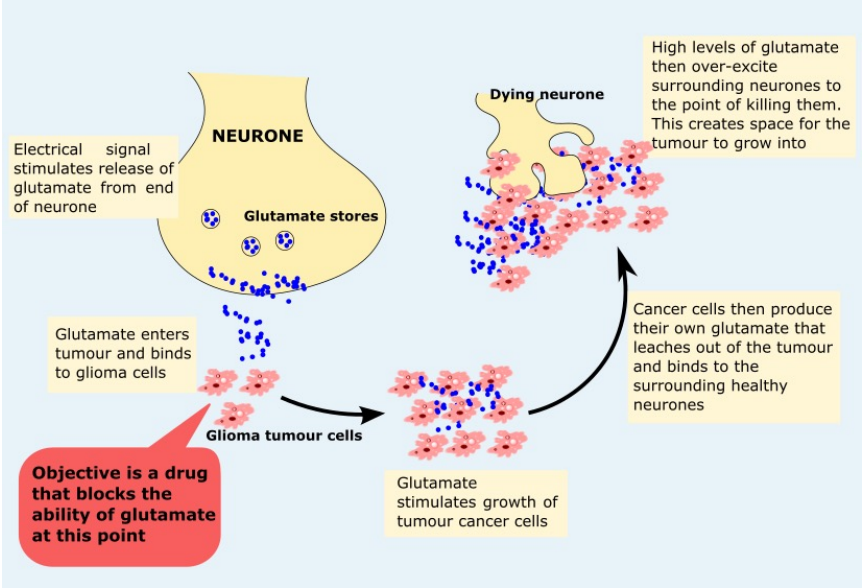
Brain cancer program

Noxopharm and U.S. National Cancer Institute to Collaborate on Promising New Approach to Treatment of Brain Cancer*

Major discovery by NOX scientists of new family of molecules

➡ Killing brain cancer cells directly

➡ Blocking 'helper' growth signals



*ASX Announcement 9 August 2021

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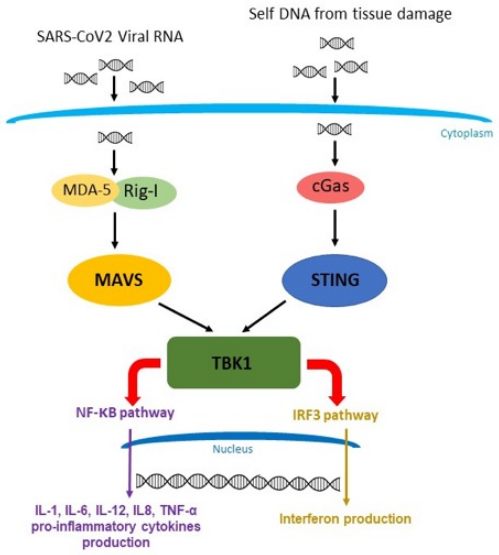
Septic shock

Challenge
To block the inappropriate hyper-inflammatory response to damage caused by the SARS-CoV-2 virus, without blocking a protective anti-viral immune response

Idronoxil

- **Potent inhibitor of cGAS-STING /TBK1 signaling pathway → blocking release of pro-inflammatpry cytokines**
- **Upregulates NK and T-cell function**



Phase I pilot trial completed

- **Hospitalised patients with moderate to severe ARDS requiring supplementary O_2**
- **Veyonda added to SOC**
- **Treatment well-tolerated**
- **37/38 patients recovered/1 death**
- **Pro-inflammatory cytokines all contained**

Phase 2 randomised controlled study proposed for Veyonda to be tested in hospitalized COVID-19 patients with mild hypoxia.

Anti-inflammatory drug offering broad-spectrum cytokine inhibition, but without immune-suppression

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Chronic inflammatory diseases/autoimmune diseases

pharmorage

Pharmorage, a collaboration between NOX and Hudson Institute of Medical Research.

Based on identification of a new family of drug compounds with highly selective activity against cGAS-STING/TBK1 signaling*

* ASX: 23 August 2021

Programs

Chronic inflammation

Autoimmunity

STING/TBK1 antagonists now centre of major industry interest as new drug class

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Key Metrics

(*at 8 September 2021*)

Market cap	**A$153m**
Share price	**A$0.53c**
Issued shares	**~288.3m**
Cash (at 30/6/21)	**A$26.8 m**

Anticipated News Flow (next 6 months)

- Progress in IONIC-1, DARRT-2 & CEP-2
- Phase 2 COVID-19 clinical trial update
- Oncology drug pipeline progress
- Pharmorage drug discovery progress

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