Beacon DDR
Targeted Therapies

MAKE FASTER AND BETTER INFORMED DRUG DEVELOPMENT DECISIONS

In partnership with the world's leading drug development experts to help you keep up with the pace of preclinical and clinical research developments.

INTERVIEW WITH **JAMES CAMPBELL – PATRYS CEO**

Dr. Campbell has over 20 years experience in the biotech industry, here we discuss Patrys' novel DDR therapeutic technology, and how Beacon has aided their development approach. Based in Melbourne, Australia, and listed on the Australian Securities Exchange (ASX: PAB), Patrys is a drug development company focused on commercialising antibody therapies for oncology. In 2016, Patrys secured an exclusive, worldwide license from Yale University for the use of nucleus-penetrating, "deoxymab" antibodies as human therapeutic agents for treatment and management of cancer.

Find out more about this data and how we can help you leverage this insight by visiting **www.beacon-intelligence.com/solutions/ddr** to request a demo or download our brochure.

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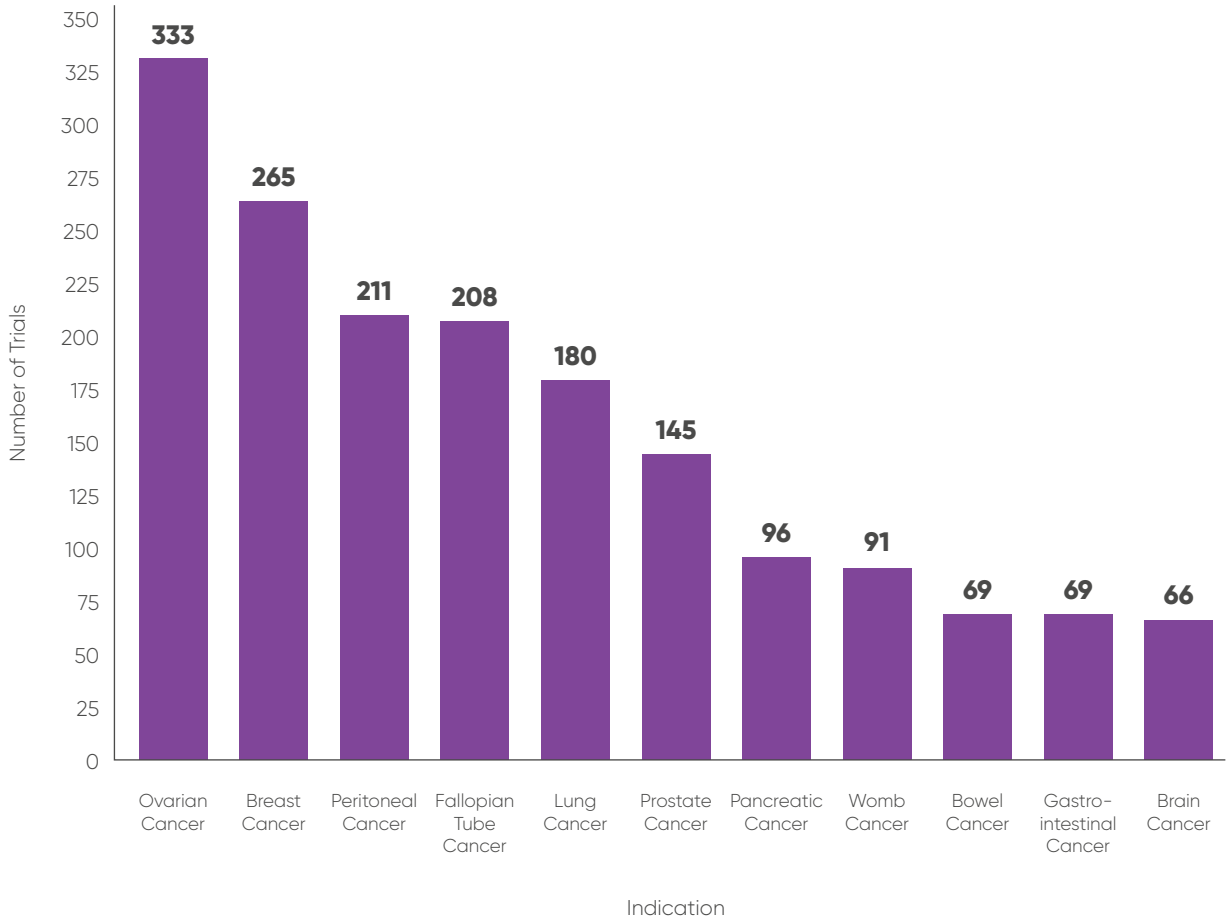
Q **Most of the molecules that are targeting DDR deficient cancers are small molecules, how did Patrys end up developing your antibodies and what are the advantages of this approach versus other antibodies but more specifically, therapies in this space? How does having a differentiated approach affect the way that you view the space?**

A Patrys' deoxymab antibodies are the only antibodies that show single agent synthetic lethality. In multiple models we've shown reduction of cancer load in DDR deficient cancer cell lines, but this is lost in the matching DDR proficient comparator lines. This positions deoxymabs well for cancers such as Triple-Negative Breast Cancer (TNBC), and other cancers on both sides of the blood brain barrier with significant rates of DDR mutations. Comparing to small molecule therapeutics, we'd expect more benign side effect profiles, and the fact that deoxymabs can transit across the blood-brain barrier (BBB) offers significant advantages over existing agents. We think the unique differentiators of our deoxymabs position us well for clinical development, and we look forward to providing additional options for treating physicians.

TOP DDR DISEASE INDICATIONS BY NUMBER OF TRIALS



Source: Beacon DDR November 2021

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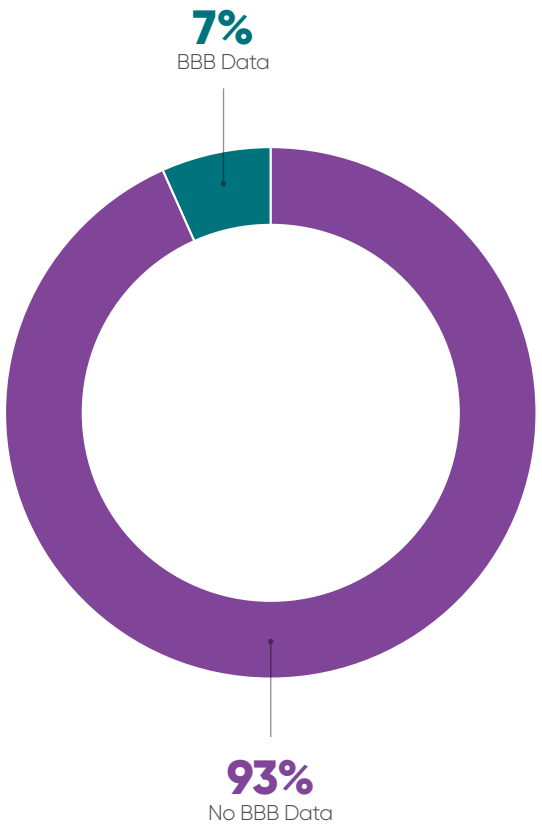
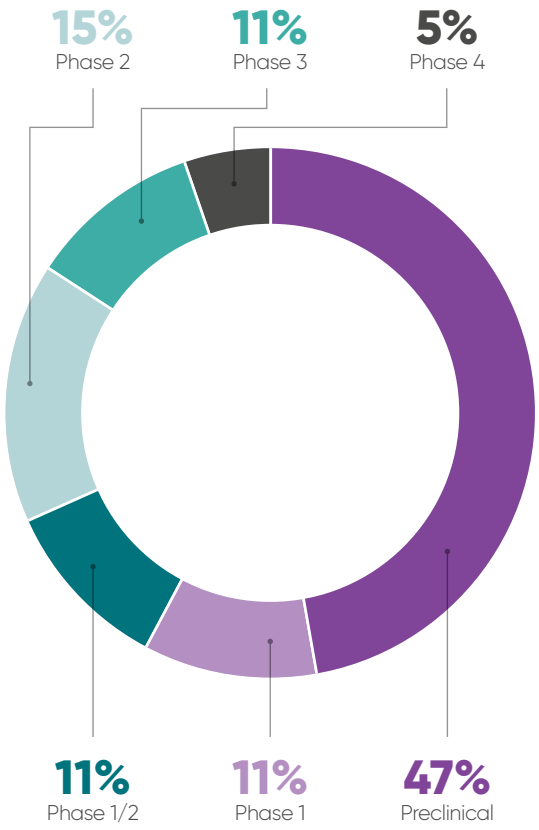
DDR ASSETS BY BBB DATA DISCLOSURE STATUS



HIGHEST PHASE OF DEVELOPMENT IN ASSETS WITH BBB DATA



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Q **Your antibodies have a fantastically unique feature in that they are able to cross the blood-brain barrier (BBB), although as small molecules, other DDR therapies are able to do this too. We all know how challenging it is to treat brain cancers, leaving a desperate unmet need for patients. How are you planning on making the most out of this exciting property?**

A Experience to date with PARP inhibitors suggests that the clinical development of DDR inhibitors for brain cancers such as glioblastoma will be challenging due to several factors, most notably limited penetration of the BBB and the overlap of toxicities of DDR inhibitors with existing standards of care. Our preclinical experience has not shown either of these issues, in fact we've shown that deoxymabs increase the efficacy of low dose radiation in glioblastoma. Further, we believe that the differentiated mechanism of action of our deoxymabs, where the antibody directly blocks repair mechanisms rather than antagonizes a specific protein, facilitates combinatorial efficacy for a range of different DDR mutations. This creates a niche that will offer new opportunities for treatment. We envisage that a range of brain cancers, particularly glioblastoma and metastatic TNBC will be the focus of phase 2 clinical studies which will come after our planned phase 1 first-in-human study in late 2022.

Source: Beacon DDR November 2021

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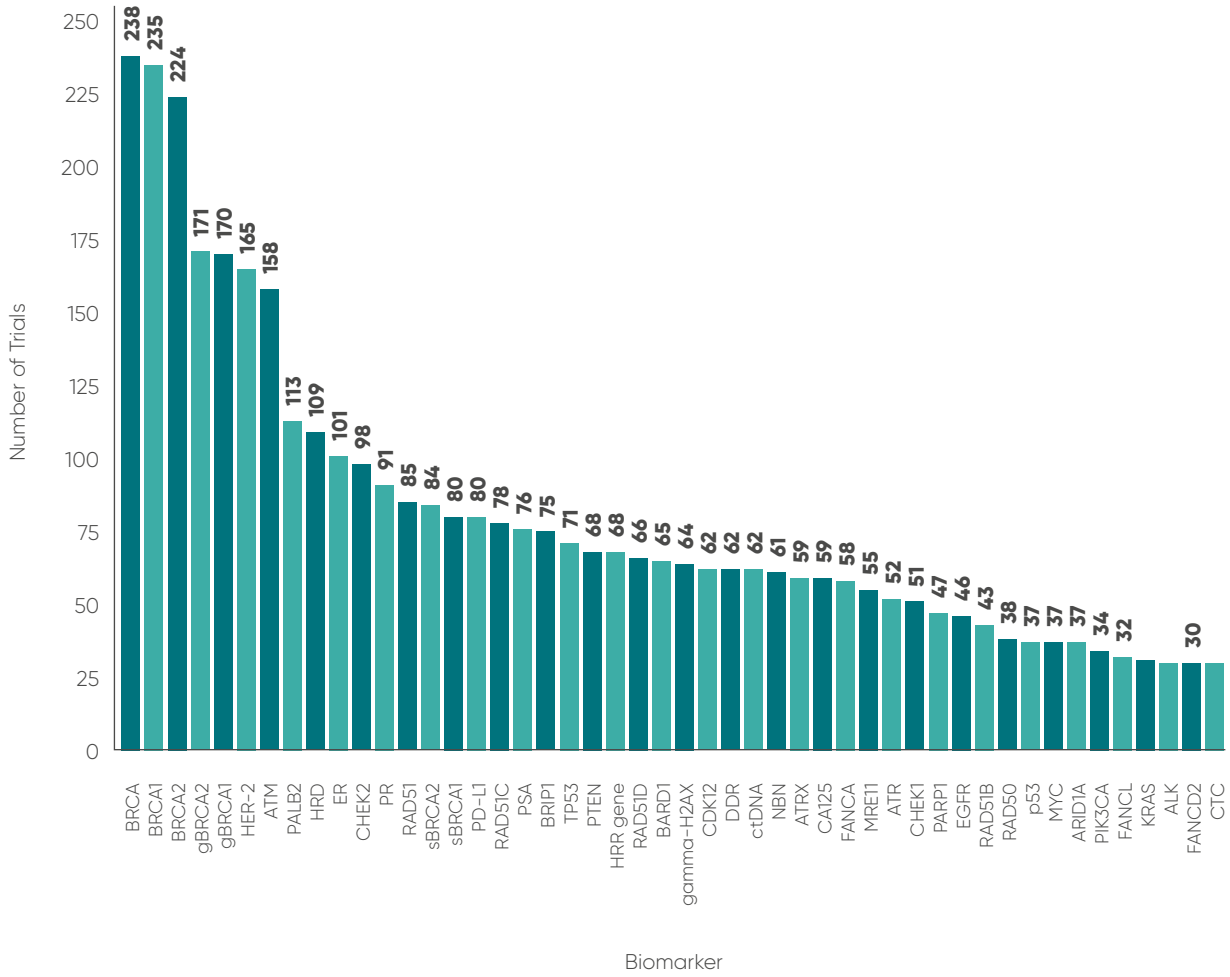
Q **As targeting the DDR was pioneered by the development of PARPi to treat BRCA-mutant tumours perhaps you view your competition as focusing more on a particular biomarker than a particular tumour or technology? Are you planning on following in the footsteps of established biomarkers or do you prefer to carve your own niche?**

A The last few years has seen great advances in the development of small molecules that target specific participants of the DDR. Our deoxymabs are complementary to these advances, offering pan-target single agent efficacy for a range of different mutations. Therefore our biomarker strategy will be a broad one, considering and selecting for the mutation status of a range of relevant DDR components, and even considering the broader implication of parameters such as RNA microsatellites.

BIOMARKER DISTRIBUTION IN DDR TRIALS



Source: Beacon DDR November 2021

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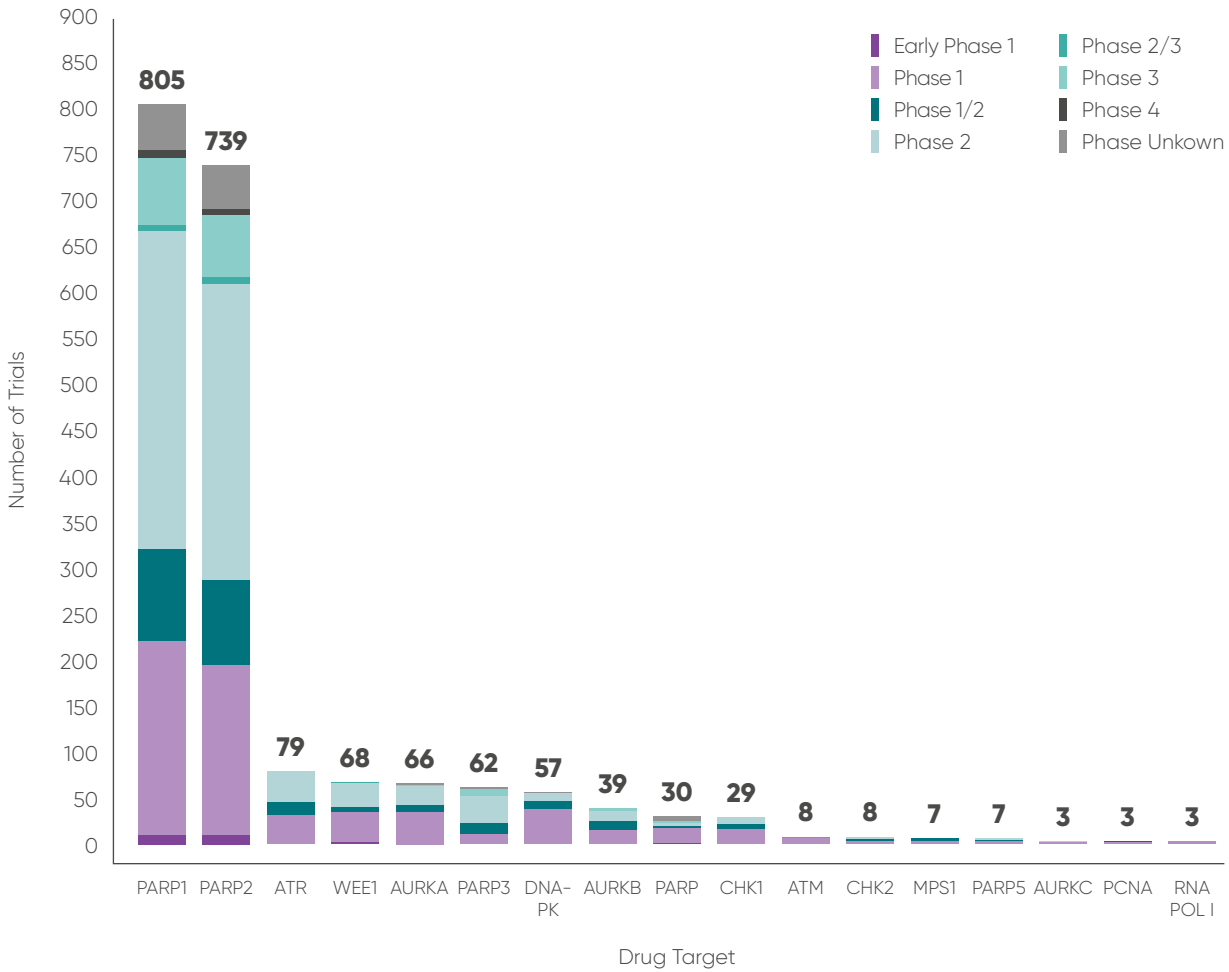
DDR TRIALS BY TARGET AND PHASE



**Trials containing DDR therapies acting on more than one target are counted per target & cut-off is at > 3.*

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Q **Obviously the DDR therapeutics space is becoming increasingly complex. How has Beacon been supporting your efforts in dealing with this challenges?**

A Beacon is an invaluable part of our development and business development activities. As we evaluate the three waves of DDR therapeutics, from the incumbent PARPi molecules through to second generation targets such as ATR, DNA-PK and WEE1 then the novel targets such as Pol-theta, WRN, PARG, etc. We use Beacon to track pre-clinical targets and assets, then to help us model the therapeutic landscape into the next 10 years, which obviously informs business development efforts.

I think we can all be excited by what the future of DDR therapeutics offers, and the promise for patients with a range of difficult to treat tumours. Patrys, with its differentiated mechanism of action, is excited to be playing a role in this exciting field and looks forward to delivering on the promise of its deoxymabs for patients around the world.

Source: Beacon DDR November 2021

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WHAT'S NEXT?

Competition in general will heat up as companies exit stealth mode and disclose early-stage assets.

Will the development of PARP inhibitors continue to dominate the landscape? In 2021 we saw four times as many trials initiated studying PARPi as compared to DNA-PKi, ATRi, ATMi and WEE1i combined.

Potentially pivotal moments for "2nd generation" HRD targets mentioned above with the fascinating race between ATRi, ceralasertib and berzosertib as well as Zentalis touting a "potential registrational" phase 2 trial for WEE1i, Zn-c3. Further to ATR, PARP1 selective assets, including AstraZeneca's AZD5305, are likely to be critical in changing the DDR landscape.

After the first patients were dosed with a POLQ and USP1 drugs September, we look forward to seeing the first data readouts and more clinical entries for the much-touted POLQ inhibitors and other next-gen targets such as PARG and WRN.

WHAT WE COVER

Beacon DNA Damage Response (DDR) covers trial and drug records for clinical, preclinical, approved and discontinued therapeutics targeting key points in DNA damage response pathways

This module identifies drugs utilizing the concept of synthetic lethality, and covers DDR repair pathway components, including:

- Damage Sensors
- Signalling/ Mediator Proteins
- Cell Cycle Checkpoints
- Effector Proteins
- DNA Metabolism when in relation to repair and recombination

Several key therapeutic targets in the DDR landscape included in this module are:

- PARP
- ATM
- ATR
- CHK1/2
- WEE1
- DNA-PK
- POLQ
- WRN
- PARG

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