ASX & Media Release

PAT-DX1 novel mechanism for crossing the blood brain barrier confirmed

Melbourne, Australia; 16 March 2020: Patrys Limited (ASX: PAB, "Patrys" or the "Company), a therapeutic antibody development company, is pleased to announce new pre-clinical data for its lead candidate, PAT-DX1. The studies provide critical mechanistic data which explains PAT-DX1's ability to cross the blood-brain barrier (BBB), via the equilibrative nucleoside transporter 2 (ENT2) pathway. This data will support Patrys' planned Investigational New Drug (IND) filing to clinically test PAT-DX1 against brain tumours and metastases as well as other cancers.

Key highlights

- **Dr. James Hansen and Dr. Jiangbing Zhou at Yale School of Medicine designed and completed new studies that establish the mechanism by which PAT-DX1 crosses the BBB**
- **Analysis from *in vitro* and *in vivo* (animal) studies confirm that PAT-DX1 crosses the BBB via the ENT2 pathway, a novel mechanism for drug delivery**
- **These findings support previous pre-clinical studies where PAT-DX1 increased tumour suppression in brain cancers and metastases, further strengthening the biologic rationale to enter the clinic**
- **The data will support the upcoming IND filing and forms part of the data package that will underpin future strategic discussions**

Patrys Chief Executive Officer and Managing Director, Dr. James Campbell said: *"It is well known that the human BBB prevents antibodies and the majority of small molecule therapeutics from entering the central nervous system. However, PAT-DX1 has proven to be an exception to this rule and has shown activity against brain tumours in mouse models of glioblastoma and triple negative breast cancer brain metastases. The study data clearly illustrates how PAT-DX1 is able to achieve these outcomes, and provides compelling evidence of an ENT2-mediated method of BBB penetration by PAT-DX1. The ability to explain PAT-DX1's entirely new and highly effective mechanism of action supports our plans to advance to IND filing and commence clinical studies, together with enhancing partnering discussions."*

The investigation was conceived, designed, and led by Dr. James Hansen and Dr. Jiangbing Zhou of the Yale School of Medicine. They initially completed an *in vitro* study that highlighted ENT2's role in transporting PAT-DX1 across a model of the human BBB, and showed that co-treatment with a small molecule inhibitor of ENT2 blocks this transport.

A transwell membrane model (composed of human brain endothelial cells and normal human astrocytes adhered to a membrane) tested the ability of PAT-DX1 to cross the BBB in the presence or absence of an ENT2 inhibitor. In absence of the ENT2 inhibitor, PAT-DX1 crossed the BBB efficiently, while other molecules of similar molecular weight were blocked. The addition of the ENT2 inhibitor significantly impaired PAT-DX1 transport across the BBB, demonstrating that PAT-DX1 crosses the BBB via the ENT2 pathway.

Following this finding, Dr. Hansen and Dr. Zhou completed a new animal study that confirmed that PAT-DX1 crosses the BBB and localises to orthotopic brain tumours in mice, and that co-treatment of mice with a small molecule inhibitor of ENT2 blocks this activity.

The new animal study was conducted with a highly aggressive human glioblastoma (GBM) tumour explant to generate brain tumours in mice. Mice (4 per group) were randomised to tail vein treatment with either (1) Control vehicle; (2) Fluorescently-labelled PAT-DX1; or (3) Fluorescently-labelled PAT-DX1 + small molecule ENT2 inhibitor. Twenty-four hours after treatment the localisation of PAT-DX1 to brain tumours was visualised by the fluorescence signal. Strong fluorescence signal was detected in the brain tumours in mice treated with PAT-DX1 alone, and this signal was reduced by >50% in mice co-treated with ENT2 inhibitor. These findings confirm the results from the transwell model.

The new study contributes to efforts to identify and optimise mechanisms of action for PAT-DX1, which supports the clinical development of Patrys' broader portfolio. The study data strengthens the planned IND filing, provides biologic rationale to advance PAT-DX1 to commence clinical testing, particularly against brain tumours and metastases, and forms part of the data package that underpins future strategic discussions.

-Ends-

This announcement is authorised for release by the Board of Directors of Patrys Limited.

For further information, please contact:

General enquiries
James Campbell
Chief Executive Officer
P: +61 3 96703273
info@patrys.com

Media enquiries:
Haley Chartres
H^CK
P: +61 423 139 163
haley@hck.digital

Registered Office Address
Level 4, 100 Albert Road
South Melbourne VIC 3205

About Patrys Limited
Based in Melbourne, Australia, Patrys (ASX:PAB) is focused on the development of its Deoxymab platform of cell-penetrating antibodies as therapies for a range of different cancers. More information can be found at www.patrys.com.

About Patrys' Deoxymab 3E10 platform – lead candidates PAT-DX1 and PAT-DX1-NP:
Deoxymab 3E10 is a DNA damage-repair (DDR) antibody that was first identified in lupus as an autoantibody that bound to normal cells. Of particular interest is that whilst most antibodies bind to cell surface markers, Deoxymab 3E10 penetrates into the cell nuclei and binds directly to DNA where it inhibits DNA repair processes and kills cells that have mutations or deficiencies in DNA repair mechanisms as found in various cancer cells. Deoxymab 3E10 has single agent therapeutic potential and has been shown to significantly enhance the efficacy

of both chemo- and radiotherapies. Further, Deoxymab 3E10 can be conjugated to nanoparticles to target delivery of chemotherapeutics and imaging agents to tumors.

Patrys has developed a humanised form of Deoxymab 3E10, PAT-DX1 with improved activity over the original version of 3E10, and is progressing this, and a nanoparticle-conjugated form (PAT-DX1-NP) towards the clinic. In a range of pre-clinical cancer models PAT-DX1 has shown significant ability to kill cancer cells in cell models, human tumor explants, xenograft and orthotopic models. Treatment with PAT-DX1 has been shown to significantly improve survival in orthotopic models of both triple negative breast cancer brain metastases and glioblastoma. PAT-DX1 has also been shown to enhance the therapeutic effect of low dose radiation and work synergistically with the approved PARP inhibitor, olaparib. Patrys believes that PAT-DX1 may have application across a wide range of malignancies such as gliomas, melanomas, prostate, breast, pancreatic and ovarian cancers. Patrys' rights to Deoxymab 3E10 are part of a worldwide license to develop and commercialise as anti-cancer and diagnostic agents a portfolio of novel anti-DNA antibodies and antibody fragments, variants and conjugates discovered at Yale University.

About Glioblastoma (GBM)

Glioblastoma is a particularly aggressive, highly malignant form of brain cancer characterised by very fast cellular reproduction. Glioblastomas constitute approximately 17% of all primary brain cancers, with almost 12,000 new cases diagnosed in the U.S. each year[1]. The current standard of care for glioblastoma is surgical resection followed by radiation and chemotherapy (temozolomide, trade name TEMODAR®), with a median survival period of 15 months[2], depending on disease severity.

[1] American Association of Neurological Surgeons (AANS), Glioblastoma Multiforme

[2] Davis ME. Glioblastoma: Overview of Disease and Treatment. Clin J Oncol Nurs. 2016;20(5 Suppl):S2–S8. doi:10.1188/16.CJON.S1.2-8