ASX & Media Release

New Data Strengthens PAT-SM6 Profile as an Anti-cancer Treatment

- **PAT-SM6 binds to two cancer targets GRP78 and LDL**
- **GRP78 and LDL compete for binding to PAT-SM6 despite having very different structures**
- **Strong and specific binding of GRP78 and LDL is driven by multipoint attachment due to pentameric nature of PAT-SM6**

Melbourne, Australia; 22 April, 2013: Patrys Limited **(ASX: PAB),** a clinical stage biopharmaceutical company is pleased to announce the publication of a new scientific article in the current edition of the Public Library of Science (PLOS ONE) journal regarding its lead candidate PAT-SM6.

Recent studies show that PAT-SM6, a monoclonal IgM antibody, has the ability to bind to two structurally different targets. These targets are an isoform of the glucose-regulated protein 78 (GRP78) which is present on the surface of tumour cells, but absent on normal tissues, and low density lipoprotein (LDL). It appears that the anti-cancer activity of PAT-SM6 is enhanced in the presence of LDL.

Previous studies have shown that PAT-SM6 interacts with its target GRP78 and induces killing of tumour cells through its multivalent nature and its ability to form many bond interactions with multiple target molecules clustered on the surface of tumour cells. The combined strength of these multiple interactions is called “avidity”.

The results presented in this latest study suggest a similar avidity-based mechanism operates for the binding of PAT-SM6 to LDL and it is believed that this is responsible for more effective cell death.

Laboratory experiments designed to mimic the natural clustering of targets on the surface of cancer cells, show strong and specific avidity based interaction of PAT-SM6 to both targets. Furthermore, GRP78 and LDL were found to compete for binding sites on the PAT-SM6 antibody despite having quite different structures. These results support the hypothesis that the biological action of PAT-SM6 in killing tumour cells depends on the multipoint attachment of targets to PAT-SM6 and the ability to interact simultaneously with LDL and multiple GRP78 molecules. This process triggers cell death in a more dramatic manner than the cell death caused by PAT-SM6’s binding to GRP78 alone. This unique pathway offers a promising mechanism for fighting cancer not offered by any other known therapies.

This work is the result of a collaboration between University of Melbourne’s Associate Professor Geoff Howlett, Dr Terry Mulhern and Dr Danny Hatters from the Bio21 Institute at Parkville and Patrys. A Federal Government’s Australian Research Council (“ARC”) grant was awarded to Patrys in November 2009 to support this collaboration and further evaluate the mechanisms by which PAT-SM6 kills cancer cells.

University of Melbourne Associate Professor Geoff Howlett said: "This is an exciting project that is utilizing state-of-the-art modern technology to investigate the potential of a novel IgM antibody to specifically cause tumour cell death. The study demonstrates the importance of avidity binding and multipoint attachment of LDL and GRP78 to PAT-SM6 in killing tumour cells".

Patrys CEO Dr. Marie Roskrow, added: "These studies highlight the potential of natural human IgM antibodies in anti-cancer therapy and this unique mechanism of action, not used by any other known cancer therapy, further strengthens PAT-SM6's profile as an effective anticancer agent. This is very encouraging as we move forward with our multi dose clinical trial of PAT-SM6 in patients with multiple myeloma".

A summary of the full article is available for download at: http://dx.plos.org/10.1371/journal.pone.0061239.

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About Patrys Limited:
Based in Melbourne, Australia, Patrys (ASX: PAB) is focused on the development of natural human antibodies as therapies for cancer and other major diseases. Patrys has a deep pipeline of anti-cancer natural human antibodies that enable both internal development and partnering opportunities. More information can be found at www.patrys.com.

About PAT-SM6:
The natural human antibody PAT-SM6 has been shown to have potent anti-cancer properties in a large number of laboratory and animal studies. More specifically, Patrys has now screened PAT-SM6 against more than 200 tumours from individual patients with various cancers, and the product binds to over 90% of the tumours screened regardless of cancer type or patient age, gender or disease stage. With respect to multiple myeloma PAT-SM6 has shown particularly strong promise. Patrys has filed patent applications to cover the PAT-SM6 antibody molecule, disease target, and the mechanism of action. Patrys has successfully completed a Phase I clinical trial to evaluate PAT-SM6 as a therapy for melanoma. In November 2012, Patrys commenced a PAT-SM6 clinical trial in patients with multiple myeloma. Multiple myeloma is a type of bone marrow cancer that affects approximately 1,200 Australians each year with 39% five-year survival rate.

About GRP78 and LDL:
Patrys clinical candidate PAT-SM6 binds to a form of Glucose-regulated protein 78 (GRP78), which is expressed on the surface of cancer cells but not detected on the surface of healthy cells. The second target for PAT-SM6 is oxidised low density lipoprotein (oxLDL) and very low-density lipoprotein (VLDL). More specifically, experiments have shown that PAT-SM6 binds to oxLDL, then binds to GRP78 expressed on surface of cancer cells, and "imports" the oxLDL into the cancer cell, causing intracellular deposition of lipids. Once bound, the PAT-SM6/LDL/GRP78 complex is then internalized into cancer cells inducing apoptosis and cell death. The anti-cancer activity of PAT-SM6 is enhanced in the presence of oxLDL. The potential of GRP78 as a target for cancer therapy is supported by extensive third party literature that has reported several roles played by GRP78 with respect to promoting tumour proliferation, tumour survival, metastases and resistance to a wide variety of existing anti-cancer therapies. As a result, GRP78 expression has been correlated with an adverse prognosis in melanoma, breast, lung, gastric, hepatocellular and prostate cancer, and drug resistance in breast cancer. Given GRP78's reported roles with respect to several cancers, a molecule such as PAT-SM6 presents a promising anti-cancer treatment to the extent it interferes with the function of GRP78 in cancer.