**ASX & Media Release**

# Final Data Confirms Successful Phase I/IIa Clinical Trial for PAT-SM6

- **4/12 patients (33%) showed evidence of stable disease; 2 patients for more than 130 days**
- **A clinically-relevant mean time to next therapy of 51 days**
- **PAT-SM6 specifically targets myeloma tumour cells in vivo and stimulates signifcant immune responses**
- **All dose levels administered were safe with no adverse events observed**
- **No evidence of immunogenicity; PK analysis showed PAT-SM6 to have a half-life of 7 hrs**

**Melbourne, Australia; 27 March, 2014:** Patrys Limited (ASX: PAB; "the Company"), a clinical stage biotechnology company, is pleased to announce the final results from its Phase I/IIa, open-label study in patients with refractory or relapsed multiple myeloma (MM).

This trial was conducted in 12 patients (10 male and 2 female, median age 71 years) with refractory or relapsed MM. On average each patient had received five prior lines of therapy, including proteasome inhibitors, immunomodulatory (IMID) drugs or stem cell transplantation.

Twelve patients (3 in each cohort) received 4 intravenous infusions of PAT-SM6 at 0.3mg/kg, 1mg/kg, 3mg/kg or 6mg/kg per dose. All patients were then assessed for a response at 36 days post final treatment.

The primary endpoint of the study was safety and tolerability. At all dose levels tested, PAT-SM6 was well tolerated with no serious adverse events (SAEs) or dose limiting toxicities being reported. A maximal tolerated dose (MTD) was not reached.

Secondary endpoints were designed to measure efficacy as determined by a series of well-established laboratory assays. Overall, 4/12 patients (33%) treated with PAT-SM6 showed evidence of stable disease (SD) according to the International Myeloma Working Group (IMWG) criteria. One patient who received 3mg/kg of PAT-SM6 was stable for 138 days before additional therapy was needed whilst another patient, who received 6mg/kg of PAT-SM6, has been stable for 154 days and is currently therapy free.

These data compare favorably with another antibody (Elotuzumab) currently in Phase 3 combination trials for MM. When tested in a Phase I trial, 26.5% (9/35) patients treated with increasing doses of Elotuzumab (0.5– 20mg/kg) responded with SD. Like PAT-SM6, this antibody was used as a single agent. The information on the clinical efficacy of Elotuzumab is publicly available.

Importantly, patients treated with PAT-SM6 had a mean time to next therapy of 51 days which is considered clinically significant.

Patients who had received prior treatment with proteasome inhibitors responded much better to PAT-SM6 treatment than patients who had been previously treated with IMIDs or other chemotherapeutics. This observation is very exciting as it indicates that PAT-SM6 may act synergistically with proteasome inhibitors (such as Carfilzomib) to induce better clinical responses. Such a hypothesis will be tested in Patrys' next clinical trial in which PAT-SM6 will be used in combination with Amgen's Carfilzomib.

11/ 12 patients went on to receive additional salvage therapy after completing the PAT-SM6 clinical trial. Remarkably, 7/ 11 patients responded very positively with a partial response (PR) while 3 others responded with SD indicating that PAT-SM6 treatment may make cancer cells more sensitive to killing by other chemotherapeutics.

Analysis of blood samples collected during the trial confirmed that no patient generated a significant adverse immune response to PAT-SM6 (immunogenicity). This is an important finding as adverse immune reactions to existing marketed antibodies is known to limit the effectiveness of these treatments.

Pharmacokinetic analysis demonstrated linear dose proportional increases in maximum serum concentration (Cmax) of PAT-SM6. Systemic exposure to the drug, demonstrated by area under the curve (AUCt) was in line with Cmax and showed similar linear behavior. Patients displayed apparent linear pharmacokinetics with a rapid distribution phase followed by a slower disposition phase and a half-life of about 7 hours. The parameters of half-life, volume of distribution and clearance were consistent across the dose levels and between cycles, indicating that higher doses do not affect the general pharmacokinetic properties of PAT-SM6.

Post treatment with PAT-SM6, malignant cells were isolated from the patient's blood or bone marrow and analysed for the presence of the infused antibody. It was shown conclusively that PAT-SM6 specifically targeted and bound to the myeloma cells. Furthermore analysis of patient's immune systems indicated that PAT-SM6 is capable of inducing an immune response by both stimulating and increasing the absolute number of CD8+, NK and regulatory T-cells. These cells are specifically capable of regulating the growth and dissemination of tumours. Such changes were more significant in patients who had experienced stable disease post treatment with PAT-SM6. These data may indicate specific crosstalk between PAT-SM6 and immune cells, a previously unreported finding that warrants further investigation.

Dr. Marie Roskrow, Patrys' CEO said: "The trial results are especially exciting because they reflect single-agent activity in a difficult-to-treat population. Due to very high rates of relapse, the combination of multiple agents is increasingly becoming a therapy of choice for patients with MM. Therefore, the results obtained in this trial strongly support further evaluation of PAT-SM6 in combination with Carfilzomib which is the basis of our planned Amgen sponsored clinical trial."

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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:**
PAT-SM6 is a natural human IgM antibody which has been shown to have potent anti-cancer properties in a large number of laboratory and animal studies. More specifically, Patrys has 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. Patrys has filed patent applications to cover the PAT-SM6 antibody molecule, disease target, and the mechanism of action. Patrys' PAT-SM6 has shown convincing evidence of potential therapeutic benefit in the recently completed Phase I/IIa clinical trial in patients with relapsed and refractory multiple myeloma. PAT-SM6 has been granted orphan drug status in Europe and the USA for multiple myeloma. Patrys has also successfully completed a Phase I clinical trial to evaluate PAT-SM6 as a therapy for melanoma. Patrys is now preparing for the next clinical trial (a combination study of PAT-SM6 and Carfilzomib) which is to be sponsored by Onyx Pharmaceuticals, a subsidiary of Amgen.

**About GRP78:**
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. Once bound, the PAT-SM6/GRP78 complex is then internalised into cancer cells inducing apoptosis and cell death. 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.