# News Release

**Kamada Announces Positive Interim Results from Phase I/II Clinical Study of its human Alpha-1 Antitrypsin to Treat Graft-versus-Host Disease Presented at the American Society of Hematology Annual Meeting**

Results support publication of pre-clinical data in *Blood* in September

**NESS ZIONA, Israel (December 11, 2014) – Kamada Ltd. (NASDAQ and TASE: KMDA),** a plasma-derived protein therapeutics company focused on orphan indications, reports that interim data from a Phase I/II clinical study of the Company's proprietary human Alpha-1 Antitrypsin (AAT) conducted by the Fred Hutchinson Cancer Research Center in Seattle, Washington, for the treatment of graft-versus-host-disease (GvHD) were highlighted in a poster presentation at the 56th American Society of Hematology Annual Meeting and Exposition being held from December 5-9, 2014 in San Francisco.

Interim results from the Phase I/II study were presented in a poster entitled "Alpha 1 Anti-Trypsin (AAT) offers potent therapy for Steroid Resistant Gut GvHD: Interim Results of a Phase I/II Clinical Study," on Monday December 8, 2014 by A. Mario Marcondes M.D. Ph.D, Clinical Research Associate at the Fred Hutchinson Cancer Research Center, Research Assistant Professor at the University of Washington and an investigator of the clinical study.

GvHD is a major complication of allogeneic hematopoietic cell transplantation (HCT). Severe acute GvHD can be life threatening and it is associated with a loss of proteins including AAT.

The Phase I/II study is being conducted by the Fred Hutchinson Cancer Research Center in Seattle, Washington in cooperation with Baxter International Inc. and Kamada using Kamada's AAT. The study (ClinicalTrials.gov identifier: NCT01523821) is an open label, dose escalation, safety and efficacy study. The study is evaluating 24 GvHD patients who suffer from inadequate response to steroid treatment following HCT. The patients are enrolled into 4 dose cohorts. The primary outcome of the study is to evaluate the efficacy of AAT in ameliorating the severe intestinal inflammation associated with GvHD.

To date, 7 patients with hematologic malignancies were enrolled, 6 of which were enrolled in the first cohort. Patients showing no clinically satisfactory responses to steriods were given AAT at 90 mg/kg IV on day 1, followed by 30 mg/kg (first cohort) every other day for a total of 8 doses (15 days).

Preliminary results indicated that continuous administration of AAT as therapy for steroid resistant gut GvHD is feasible in the subject population. Indication of healing of the bowel mucosa was seen to decrease in diarrhea, in intestinal protein loss, including AAT, and in endoscopic evaluation. Additionally, following examination of pro-inflammatory cytokines, in the preliminary results AAT administration suppressed serum levels of pro-inflammatory cytokines and interfered with GvHD biomarkers.

Separately, investigators at the Fred Hutchinson Cancer Research Center published additional non-clinical and clinical observational data in the September edition of *Blood*, in an article entitled “α-1-antitrypsin (AAT)-modified donor cells suppress GvHD but enhance the GVL effect - a role for mitochondrial bioenergetics.”

The researchers showed an inverse correlation between plasma AAT levels in human donors and the development of acute GvHD in the recipients (n=111; p=0.0006). The higher the level of AAT in the donor blood, the less likely the recipient develops GvHD (n=111; p=0.0006). Furthermore, in murine models, mice given cells from AAT-treated donors experienced less weight loss, had lower GvHD incidence and severity, and reduced mortality compared with albumin controls. The benefit was further enhanced when donor *and* recipient were treated. The study results showed that AAT treatment of healthy murine donors promotes the expansion of dendritic cells, T-regulatory (T-regs) and natural killer cells, decreases pro-inflammatory and enhances anti-inflammatory cytokines, such as IL-10 and IL-1Ra. Importantly, AAT does not suppress the activity of IL-2, an essential cytokine for the generation of T-regs, which are important in the development of graft tolerance. Moreover, suppression of GvHD did not interfere with Graft-versus-leukemia (GVL) but, in fact, enhanced the GVL effect.

According to the article, “these experiments show that AAT exerts potent GvHD protection while maintaining or enhancing GVL activity.”

“These positive interim results are very promising and encouraging, supporting our decision to continue to pursue our global clinical development plans for AAT in treating and preventing GvHD,” stated David Tsur, co-Founder and Chief Executive Officer of Kamada. “Importantly, the preclinical data support the positive interim results from the Phase I/II clinical study of AAT, which is aimed at treating the gut involvement in steroid-resistant GvHD.”

“Given the favorable safety profile of Glassia, there is a strong rationale to support the development of this new indication and an increased likelihood of our AAT becoming an effective therapy for this potentially life-threatening disease,” concluded Mr. Tsur.

**About Graph-versus-Host-Disease**

Graft-versus-host-disease is a common complication following an allogeneic tissue transplant. It is commonly associated with stem cell transplant, but the term also applies to other forms of tissue graft. Immune cells (white blood cells) in the tissue (the graft) recognize the recipient (the host) as "foreign." The transplanted immune cells then attack the host's body cells.

GvHD occurs in 30-70% of patients who undergo a medical procedure of allogeneic hematopoietic stem cell transplantation (HSCT), usually as a treatment to leukemia or other blood cancer or blood conditions. HSCT is a stem cell transplantation that is usually derived from an external (allogeneic) bone marrow donor. One of the most common and dangerous complications of HSCT is GvHD. GvHD is expressed in damage to the recipients’ tissues including damage to the liver, gastrointestinal system, skin and mucosal tissues, and is a major cause of morbidity and mortality in these patients.

Intravenously administered glucocorticoids, such as prednisone, are the standard of care in acute GvHD[1] and chronic GvHD.[2] The use of these glucocorticoids is designed to suppress the T-cell-mediated immune onslaught on the host tissues; however, in high doses, this immune-suppression raises the risk of infections and cancer relapse. In addition, more than 50% of patients do not respond well to steroids, and consequently have very low survival rates.

**About Glassia**

Glassia is the first available ready-to-infuse liquid alpha1-proteinase inhibitor (Alpha1-PI) and is indicated as a chronic augmentation and maintenance therapy in adults with clinically evident emphysema due to severe congenital AAT deficiency. Glassia is administered intravenously once a week to augment the levels of AAT in the blood. AAT is a protein derived from human plasma with known and newly discovered therapeutic roles given its immunomodulatory, anti-inflammatory, tissue protective and antimicrobial properties. Glassia is approved by the U.S. Food and Drug Administration and is marketed through a strategic partnership with Baxter International Inc. in the United States. **Please see the full prescribing information for Glassia at:** http://www.baxter.com/downloads/healthcare_professionals/products/Glassia_PI.pdf

**About Kamada**

Kamada Ltd. is focused on plasma-derived protein therapeutics for orphan indications, and has a commercial product portfolio and a robust late-stage product pipeline. The Company uses its proprietary platform technology and know-how for the extraction and purification of proteins from human plasma to produce Alpha-1 Antitrypsin (AAT) in a highly-purified, liquid form, as well as other plasma-derived proteins. AAT is a protein derived from human plasma with known and newly-discovered therapeutic roles given its immunomodulatory, anti-inflammatory, tissue-protective and antimicrobial properties. The Company's flagship product is Glassia®, the first and only liquid, ready-to-use, intravenous plasma-derived AAT product approved by the U.S. Food and Drug Administration. Kamada markets Glassia in the U.S. through a strategic partnership with Baxter International. In addition to Glassia, Kamada has a product line of nine other injectable pharmaceutical products that are marketed through distributors in more than 15 countries, including Israel, Russia, Brazil, India and other countries in Latin America, Eastern Europe and Asia. Kamada has five late-stage plasma-derived protein products in development, including an inhaled formulation of AAT for the treatment of AAT deficiency that completed pivotal Phase II/III clinical trials in Europe and entered Phase 2 clinical trials in the U.S. Kamada also leverages its expertise and presence in the plasma-derived protein therapeutics market by distributing 10 complementary products in Israel that are manufactured by third parties.

**Cautionary Note Regarding Forward-Looking Statements**

This release includes forward-looking statements within the meaning of Section 27A of the U.S. Securities Act of 1933, as amended, Section 21E of the U.S. Securities Exchange Act of 1934, as amended, and the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. Forward-looking statements are statements that are not historical facts, such as statements regarding assumptions and results related to financial results forecast, commercial results, timing and results of clinical trials and EMA and U.S. FDA authorizations. Forward-looking statements are based on

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[1] Goker, H; Haznedaroglu, IC; Chao, NJ (2001). "Acute graft-vs-host disease Pathobiology and management". *Experimental Hematology* **29** (3): 259–77. doi:10.1016/S0301-472X(00)00677-9. PMID

[2] Menillo, S A; Goldberg, S L; McKiernan, P; Pecora, A L (2001). "Intraoral psoralen ultraviolet a irradiation (PUVA) treatment of refractory oral chronic graft-versus-host disease following allogeneic stem cell transplantation". *Bone Marrow Transplantation* **28** (8): 807–8. doi:10.1038/sj.bmt.1703231. PMID 11781637.

Kamada's current knowledge and its present beliefs and expectations regarding possible future events and are subject to risks, uncertainties and assumptions. Actual results and the timing of events could differ materially from those anticipated in these forward-looking statements as a result of several factors including, but not limited to, unexpected results of clinical trials, delays or denial in the U.S. FDA or the EMA approval process, additional competition in the AATD market or further regulatory delays. The forward-looking statements made herein speak only as of the date of this announcement and Kamada undertakes no obligation to update publicly such forward-looking statements to reflect subsequent events or circumstances, except as otherwise required by law.

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