Galmed Pharmaceuticals

Galmed Pharmaceuticals Announces Acceleration of its New Clinical Amilo-5MER program

- Phase 1a Clinical Trial to Begin in Q4 2020

TEL AVIV, Israel, Aug. 6, 2020 /PRNewswire/ -- Galmed Pharmaceuticals Ltd. (Nasdaq: GLMD) ("Galmed" or the "Company"), a clinical-stage biopharmaceutical company for liver, metabolic and inflammatory diseases provides today updated information on the Company's pipeline program.

Galmed is happy to announce significant progress in the development of Amilo-5MER, a 5 amino acid synthetic peptide MTADV (Methionine, Threonine, Alanine, Aspartic acid, Valine). The 5 amino acids sequence of Amilo-5MER is homologue to a specific MTADV sequence in the human CD44 variant found in synovial fluid cells from joints of rheumatoid arthritis (RA) patients.

Amilo-5MER is being developed through a research collaboration between Galmed and the Hebrew University of Jerusalem. The molecule originated in the laboratory of Prof. David Naor, from the Lautenberg Center for Immunology and Cancer Research, Faculty of Medicine, The Hebrew University. Prof. Naor and his team were the first to publish this specific sequence in the prestigious scientific communication Journal of Clinical Investigation [1].

Amilo-5MER binds to three pro-inflammatory amyloid proteins, Serum Amyloid A (SAA), Transthyretin and Apolipoprotein B with high affinity. The first two are known to be active only in their aggregated forms. By binding to SAA, Amilo-5MER interferes with SAA aggregation and therefor inhibits the destructive autocrine, self-amplifying cytokine loop that causes additional inflammatory reaction.

We are presenting today mechanistic and pre-clinical data which supports an IND submission and the initiation of first in human studies expected to begin later this year.

SAA constitutes acute phase reactants, whose concentration in serum rise rapidly in response to acute stimuli such as infection and trauma. An elevated concentration of SAA was identified in sera of patients with multiple autoimmune diseases and more recently, an outstanding increase of SAA was also detected in COVID-19 infected patients[2-3]. SAA in its aggregated form, is a potent and rapid inducer of cytokine secretion (particularly Interleukin 6 (IL-6). IL-6 plays an important role in chronic inflammation and is implicated in the pathogenesis of many autoimmune diseases, such as Multiple Sclerosis (MS),

Rheumatoid Arthritis (RA), Inflammatory Bowel Disease (IBD) and acute COVID 19. Interference with SAA polymerization and aggregation is a valid target to prevent chronic inflammatory conditions.

Amilo-5MER has been shown to significantly reduce chronic inflammation in animal models of RA, IBD and MS (research work supported by a grant to Prof. Naor from the National Multiple Sclerosis Society (NMSS) of the USA). Amilo-5MER provides a unique mechanism of action to interfere with this vicious cycle, enabling a specific treatment for chronic inflammatory diseases. Data generated from multiple in-vitro, in-vivo and human ex-vivo models have shown that Amilo-5MER significantly improves clinical symptoms. Histological improvements and reduction of pro-inflammatory cytokine secretion were also observed.

An ex-vivo study to investigate the effect of Amilo-5MER on peripheral blood mononuclear cells (PBMCs) from healthy subjects stimulated by SAA, demonstrated significant reduction of IL-6 secretion. This data suggests that Amilo-5MER may also have a role in the treatment of patients with severe COVID-19 acute respiratory distress syndrome (ARDS), characterized by significantly high levels of SAA and IL-6 secretion which is the main cause for the cytokine storm in these patients. An ex–vivo study on PBMCs of patients infected with Covid-19 is ongoing. An alternative mechanism to reduce IL-6 levels (via humanized monoclonal antibody IL-6 receptor antagonist) is currently being evaluated in a Phase 3 Study sponsored by Hoffman La Roche (COVACTA) in Patients with Severe COVID-19 Pneumonia (ClinicalTrials.gov Identifier: NCT04320615).

Amilo-5MER is considered a New Chemical Entity. As such, it is eligible for NCE patent protection until July 2034. Patents have been granted and maintained in the US (US 1061181937),Europe (EP 3169343) and Australia (AU 2015291151) and have been allowed in Japan (JP 6671363).

"Specifically targeting SAA, the key player in this destructive, autocrine, self-amplifying vicious cycle of inflammation, without suppressing the patient's ability to mount sufficient immune response, has been an unresolved aim in clinical research. Amilo-5MER provides a unique mechanism of action to interfere with this vicious cycle, enabling a specific treatment of chronic inflammatory diseases and hopefully also acute COVID 19. Amilo-5MER has an excellent safety profile and provides a promising selective immune modulation without affecting the patient's immune surveillance," said Dr. Liat Hayardeny, Chief Scientific Officer of Galmed.

Allen Baharaff, Galmed's CEO noted: "Amilo-5MER is an exciting and complimentary addition to Galmed's pipeline which focus on liver, metabolic and immune diseases. The accelerated development of Amilo-5MER from proof of concept to a Phase 1-ready compound demonstrates our core competence in identifying and efficiently advancing scientific innovation molecules from Israeli academia to clinical studies. Galmed's senior research and development team has years of CMC, toxicology, regulatory and clinical experience in successfully developing peptides for chronic inflammatory diseases from bench to bedside. We are looking forward to the rapid clinical development of Amilo-5MER for the benefit of the

many patients in need."

Recent research and development of Amilo-5MER is being conducted under a research and option agreement between Galmed and Yissum, the tech transfer company of the Hebrew University. Galmed has completed all IND-enabling studies for Amilo-5MER, including API manufacturing, toxicology, and other supporting data. Galmed is planning to submit an IND in Q4 2020 and initiate a first in human Phase 1 study in the UK in Q4 2020. If the Phase 1 study is successful, Galmed plans to exercise its option to receive an exclusive license to the Amilo-5MER technology and enter into a definitive license agreement with Yissum. Initiation of a Phase 1b/2a study for biomarkers (SAA in serum) for IBD is planned in H2 21 as well as potentially for the treatment of COVID-19.

An accompanying powerpoint presentation has been made available under "Events & Presentations" of the investor relations section of Galmed's website at http://galmedpharma.investorroom.com/download/AmiloMERFINAL.pdf

1. Shlomo Nedvetzki et al., A mutation in a CD44 variant of inflammatory cells enhances the mitogenic interaction of FGF with its receptor, J. Clin. Invest. 111:1211–1220 (2003).
2. Huan Li et al., SAA is a biomarker to distinguish severity and Prognosis of Coronavirus Disease 19 (COVID 19) Journal of Infection. 80, 646-655, 2020
3. Xiao-Neng Mo et al., Serum Amyloid A is a predictor for prognosis of COVID-19. Respirology 25, 764-765, 2020

About Galmed Pharmaceuticals Ltd.

Galmed Pharmaceuticals Ltd. is a clinical stage drug development biopharmaceutical company for liver, metabolic and inflammatory diseases. Our lead compound, Aramchol™, a backbone drug candidate for the treatment of NASH and fibrosis is currently in a Phase 3 registrational study. We are also collaborating with the Hebrew University in the development of Amilo-5MER, a 5 amino acid synthetic peptide and plan to initiate a first in human study by the fourth quarter of 2020.

Forward-Looking Statements:

This press release may include forward-looking statements. Forward-looking statements may include, but are not limited to, statements relating to Galmed's objectives, plans and strategies, as well as statements, other than historical facts, that address activities, events or developments that Galmed intends, expects, projects, believes or anticipates will or may occur in the future. These statements are often characterized by terminology such as "believes," "hopes," "may," "anticipates," "should," "intends," "plans," "will," "expects," "estimates," "projects," "positioned," "strategy" and similar expressions and are based on assumptions and assessments made in light of management's experience and perception of historical trends, current conditions, expected future developments and other factors believed to be appropriate. Forward-looking statements are not guarantees of future performance and are subject to

risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statements. Many factors could cause Galmed's actual activities or results to differ materially from the activities and results anticipated in forward-looking statements, including, but not limited to, the following: the timing and cost of Galmed's pivotal Phase 3 ARMOR trial, or the ARMOR Study; completion and receiving favorable results of the ARMOR Study for Aramchol or any other pre-clinical or clinical trial; the impact of the coronavirus outbreak; regulatory action with respect to Aramchol by the FDA or the EMA; the commercial launch and future sales of Aramchol or any other future products or product candidates; Galmed's ability to comply with all applicable post-market regulatory requirements for Aramchol in the countries in which it seeks to market the product; Galmed's ability to achieve favorable pricing for Aramchol; Galmed's expectations regarding the commercial market for NASH patients; third-party payor reimbursement for Aramchol; Galmed's estimates regarding anticipated capital requirements and Galmed's needs for additional financing; market adoption of Aramchol by physicians and patients; the timing, cost or other aspects of the commercial launch of Aramchol; the development and approval of the use of Aramchol for additional indications or in combination therapy; and Galmed's expectations regarding licensing, acquisitions and strategic operations. More detailed information about the risks and uncertainties affecting Galmed is contained under the heading "Risk Factors" included in Galmed's most recent Annual Report on Form 20-F filed with the SEC on March 12, 2020, and in other filings that Galmed has made and may make with the SEC in the future. The forward-looking statements contained in this press release are made as of the date of this press release and reflect Galmed's current views with respect to future events, and Galmed does not undertake and specifically disclaims any obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

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