Galmed Pharmaceuticals

Galmed's 600 mg Aramchol™ Achieved a Regulatory Approvable Endpoint Showing NASH Resolution Without Worsening of Fibrosis, in NASH Patients, in the Global Phase 2b ARREST 52-Week Study

Data Strongly Support Advancement of Aramchol™ 600mg to Phase 3

TEL AVIV, Israel, June 12, 2018 /PRNewswire/ --

- S*tatistically significant reduction in liver fat was demonstrated by Magnetic Resonance Spectroscopy (MRS) in patients completing 52 weeks of treatment with Aramchol 400mg vs. placebo. Post hoc analysis of MRS responders, defined by a reduction of ≥5% absolute change from baseline, demonstrated a clinically and statistically significant effect of Aramchol 600mg vs. placebo.*
- *Significantly more patients treated with Aramchol 600mg vs. placebo showed NASH resolution without worsening of fibrosis in the 52-week biopsy, a regulatory approvable endpoint.*
- *A higher proportion of patients with at least one-point improvement in fibrosis score without worsening of NASH was demonstrated in Aramchol 600mg vs. placebo, in the 52-week biopsy, a regulatory approvable endpoint.*
- *Statistically significant reductions in ALT and AST were demonstrated in Aramchol 400mg and 600mg vs. placebo.*
- *Aramchol continues to show favorable safety and tolerability profile.*

Conference call scheduled for 8:00 AM Eastern Time Tuesday June 12

Galmed Pharmaceuticals Ltd. (Nasdaq: GLMD) ("Galmed" or the "Company"), a clinical-stage biopharmaceutical company focused on the development of Aramchol™, an oral, once-daily, liver-targeted SCD1 modulator, for the treatment of non-alcoholic steatohepatitis (NASH), announced top-line, 52-week results from the global Phase 2b ARREST study. In the ARREST study, patients underwent MRS and biopsy at baseline and week 52, which were centrally read, blinded to treatment allocation. The primary endpoint of the study was the change from baseline to end of study in liver triglycerides ratio as measured by MRS (Aramchol 600mg vs. placebo). Secondary endpoints, demonstrated through biopsy, included fibrosis improvement by at least one stage or more without worsening of NASH (defined by an increase of inflammation and or ballooning) and NASH resolution (defined by ballooning score 0 and inflammation score 0-1 at termination) without worsening of fibrosis. Other secondary endpoints included improvement (2 points or more) in NASH activity index, as measured by NAS or SAF, without worsening fibrosis and change in baseline to week 52/termination in ALT (U/L).

247 patients with biopsy-proven NASH who were overweight or obese and had pre-diabetes or type II

diabetes mellitus were randomized in a ratio of 2:2:1 (600mg, 400mg and placebo). Baseline histology of enrolled patients demonstrated a population with advanced disease, with 60% having stage 2 and 3 fibrosis and 70% having NAS≥5 at baseline.

Results from the study showed a statistically significant reduction in liver fat by MRS with Aramchol 400mg vs. placebo (p=0.0450) and not with 600mg (p=0.0655). Further, analysis of MRS responders defined by a reduction of ≥5% absolute change from baseline demonstrated a clinically and statistically significant effect of Aramchol 600mg vs placebo (47.0% vs. 24.4%; p=0.0279).

Results for the two biopsy endpoints, which may currently constitute a primary endpoint for a Phase 3 trial to support an FDA marketing application, demonstrated the following: (i) significantly more patients treated with Aramchol 600mg vs. placebo achieved NASH resolution without worsening of fibrosis (16.7% vs. 5.0%; p=0.0514) and NASH resolution (19.2% vs. 7.5%; p=0.0462); and (ii) a higher proportion of patients showed at least one-point improvement in fibrosis score without worsening of NASH in Aramchol 600mg vs. placebo (29.5% vs. 17.5%; p=0.2110).

Statistically significant reductions in live enzymes alanine transaminase (ALT) and aspartate transaminase (AST) were demonstrated in both Aramchol arms vs. placebo (p≤0.0002) and (p≤0.001), respectively.

Secondary endpoints based on NAS and SAF activity score, ≥2 points improvement, show a higher proportion of patients with improvement in the Aramchol arms (600mg>400mg>placebo; P>0.05).

At 52 weeks of treatment, Aramchol continues to show a favorable safety and tolerability profile. Serious Adverse Events (SAEs) were reported in 12.5%, 8.9% and 9.2% of patients in placebo, Aramchol 400mg and 600mg arms, respectively. No clustering of event type or atypical events for the studied population were reported in either Aramchol arms. Early terminations due to adverse events (AEs) occurred in 4.2%, 3.0% and 4.1% in placebo, Aramchol 400mg and 600mg arms, respectively.

	Placebo	***Aramchol 400mg***	***Aramchol 600mg***
MRS-Absolute change from baseline in mean liver fat (1)	-0.09%	-3.41% P=0.0450	**-3.18%** **P=0.0655**
MRS responders- Reduction of ≥5% in absolute change from baseline (1)	24.4%	36.7% P=0.0878	**47.0%** **P=0.0279**
NASH resolution without worsening of fibrosis (2)	5%	7.5% P=0.4955	**16.7%** **P=0.0514**

NASH resolution (2)	7.5%	12.5% P=0.2237	**19.2%** **P=0.0462**
Fibrosis improvement without worsening of NASH (2)	17.5%	21.3% P=0.8425	**29.5%** **P=0.2110**
ALT (U/L) Change from baseline (3)	+11.82	-12.0 P=0.0002	**-17.3** **P< 0.0001**

1) *Placebo N=41; 400mg N=90, 600mg N=83; Mixed Effect Model Repeat Measurement (MMRM) adjusted mean changes from baseline; p-values for comparison of active treatment arm vs. placebo.*
(2) Placebo N=40, 400mg N=80, 600mg N=78; Baseline adjusted logistic regression; p-values for comparison of active treatment arm vs. placebo.
(3) Placebo N=47, 400mg N=100, 600mg N=98; MMRM adjusted mean changes from baseline; p-values for comparison of active treatment arm vs. placebo.

"Some studies have shown an effect on NASH and some on fibrosis, while this study has shown an effect on both. Concomitant ALT reduction strengthens the histological findings," said Prof. Vlad Ratziu, M.D., Principal Investigator of the ARREST study and Professor of Hepatology, Sorbonne Université and Hospital Pitié – Salpêtrière, Paris, France. "Aramchol 400mg is probably sufficient for fat reduction but, biologically, a higher dose is needed for achieving more stringent histological endpoints such as NASH resolution and fibrosis reversal. NASH is a chronic disease with complex comorbidities and Aramchol's favorable safety and tolerability profile support long-term treatment," concluded Prof. Ratziu.

"Results seen in the ARREST 52-week study are comparable to other one-year trials recently published or presented in the NASH space. Pre-clinical studies had demonstrated that Aramchol has a unique mechanism of action that addresses both the metabolic dysfunction and fibrosis directly, and these mechanisms have been validated by findings in the ARREST study," said Prof. Scott Friedman M.D., Dean for Therapeutic Discovery and Chief Division of Liver Diseases, Icahn School of Medicine at Mount Sinai, New York, NY. "Specifically, data from my laboratory submitted to an upcoming conference confirm by transcriptomic analysis a broad anti-fibrotic effect of Aramchol in fibrogenic hepatic stellate cells, which is complementary to the data seen in this Phase 2b, biopsy-based clinical study. In my view, these results, together with its safety and tolerability, place Aramchol among the leading frontline therapeutic candidates under investigation for NASH."

"These are exciting data which demonstrate that 600mg of Aramchol improves disease activity, fibrosis and progression to cirrhosis which in the long term may translate to meaningful clinical improvement," said Prof. Arun Sanyal, M.D., Department of Internal Medicine, Division of Gastroenterology, Hepatology and Nutrition Virginia Commonwealth University and Co-Chair of the Liver Forum at the Forum for Collaborative Research at the University of California, Berkeley, School of Public Health. "Furthermore,

the dose dependency of the effects and the fact it was a global study represents the clinical reality of the global NASH pandemic and provides indications that these results are likely to be reproduced in a pivotal phase 3 trial."

"We have previously shown that MRS and MRI have a strong correlation in assessing liver fat content. A 5% absolute reduction in liver fat on MRS is likely to be clinically significant as demonstrated here with higher rates of resolution of NASH and one-stage improvement in fibrosis and a consistently robust dose-dependent decline in serum ALT with Aramchol in the ARREST Trial," said Prof. Rohit Loomba, MD, MHSc, Director, NAFLD Research Center, Director of Hepatology, Professor of Medicine University of California at San Diego. "The ARREST trial was notable in that MRS was performed in four continents for the assessment of treatment response."

"We are excited with the ARREST results that will enable Galmed to meet with the regulators as soon as possible and discuss the pivotal study design," said Allen Baharaff President and Chief Executive Officer of Galmed. "It is extremely gratifying that Aramchol's scientific rationale for disease modification of NASH is being translated into clinical coherent results."

Conference Call and Webcast Information

Tuesday, June 12th @ 8:00am Eastern Time
Within the US: 1-800-239-9838
Outside the US: 1-323-794-2551
From Israel: 1809-212-883
Conference ID: 6065512

Webcast: http://public.viavid.com/index.php?id=130063.

Replays, Available through 06/26/18 at 11:59 pm Eastern Time:
Domestic: 1-844-512-2921
International: 1-412-317-6671
Replay PIN: 6065512

ARREST was a placebo-controlled, one-year global Phase 2b study in 247 biopsy-proven NASH patients to evaluate the safety and effectiveness of two different doses of Aramchol for the treatment of NASH in patients who are overweight or obese and have pre-diabetes or type II diabetes mellitus. In order to be eligible to participate, patients had to have NASH, as diagnosed by a biopsy centrally read (steatosis ≥1 + inflammation ≥1 + ballooning ≥1; total activity NAS score of 4 or more), be overweight or obese as measured by a Body Mass Index between 25 and 40 or waist circumference between 88cm to 200cm for

women, and between 102cm to 200cm for men. Patients were treated for 52 weeks before undergoing the second biopsy and MRS, with a 12 weeks post treatment follow up. Blinded to treatment assignment, all entry and week 52 liver biopsies and MRS were read by a single pathologist and a single reading center, respectively.

More information about the ARREST Study may be found onClinicalTrials.gov identifier: NCT02279524.

About Aramchol™ and Non-alcoholic Steatohepatitis (NASH)

Aramchol™ (arachidyl amido cholanoic acid) is a novel fatty acid bile acid conjugate, inducing beneficial modulation of intra-hepatic lipid metabolism. Aramchol™'s ability to modulate hepatic lipid metabolism was discovered and validated in animal models, demonstrating down regulation of the three key pathologies of NASH; steatosis, inflammation and fibrosis. The effect of Aramchol™ on fibrosis is mediated by down regulation of steatosis and directly on human collagen producing cells. Aramchol™ has been granted by the FDA Fast Track designation status for the treatment of NASH.

NASH is an emerging world crisis impacting an estimated 3% to 5% of the U.S. population and an estimated 2% to 4% globally. It is the fastest growing cause of liver cancer and liver transplant in the U.S. due to the rise in obesity. NASH is the progressive form of non-alcoholic fatty liver disease that can lead to cardiovascular disease, cirrhosis and liver-related mortality.

About Galmed Pharmaceuticals Ltd.:

Galmed is a clinical-stage biopharmaceutical company focused on the development of Aramchol™, a first-in-class, novel, once-daily, oral therapy for the treatment of NASH for variable populations, as well as other liver associated disorders.

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, including with respect to a Phase 3 trial, 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 ongoing Phase IIb ARREST Study, and planned Phase III trials for Aramchol™, or whether Phase III trials will be conducted at all; completion and receiving favorable results of these Phase IIb ARREST Study and Phase III trials for Aramchol™; regulatory action with respect to Aramchol™ by the FDA or the EMA; the commercial launch and future sales of Aramchol™ or any other future 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 in patients who are overweight or obese and have pre diabetes or type II diabetes mellitus; 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 13, 2018, 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.

SOURCE Galmed Pharmaceuticals Ltd.

For further information: Bob Yedid LifeSci Advisors, LLC 646-597-6979 Bob@LifeSciAdvisors.com Guy Nehemya VP Operations, Galmed Pharmaceuticals Ltd. guy@galmedpharma.com

---

Additional assets available online: Photos (1)

https://galmedpharma.investorroom.com/2018-06-12-Galmeds-600-mg-Aramchol-TM-Achieved-a-Regulatory-Approvable-Endpoint-Showing-NASH-Resolution-Without-Worsening-of-Fibrosis-in-NASH-Patients-in-the-Global-Phase-2b-ARREST-52-Week-Study