Galmed Pharmaceuticals

Galmed reports results from the Open-Label part of the ARMOR study showing improvements in histology, imaging, and biomarkers with Aramchol

- Histological improvement in fibrosis (≥1 stage) was demonstrated in 39% of subjects according to NASH CRN, in 61% of subjects by ranked assessment with a highly statistically significant ($p<0.0001$) reduction in fibrosis score demonstrated using AI-assisted, digital pathology reading
- Highly statistically significant ($p<0.0001$) reduction in liver stiffness by Fibroscan
- Highly statistically significant ($p<0.0001$) reduction in biochemical markers of liver injury ALT and AST
- Highly statistically significant reductions in major fibrosis biomarkers: FIB-4 ($p<0.0001$), Pro-C3 ($p<0.0001$) and ELF ($p= 0.0038$) at week 24
- Galmed is submitting all data to the FDA to initiate discussions on incorporating more sensitive histology reading methodologies as primary endpoints in NASH clinical studies and is actively looking for partnering opportunities to continue Aramchol's clinical development.

TEL AVIV, Israel, Jan. 4, 2023 /PRNewswire/ -- Galmed Pharmaceuticals Ltd. (NASDAQ: GLMD) ("Galmed" or the "Company"), a clinical-stage biopharmaceutical company for liver, metabolic and inflammatory diseases reported today full results from the Open-Label Part of the ARMOR study corroborating effects of Aramchol across all efficacy parameters.

The study enrolled 157 subjects with biopsy-proven NASH randomized 1:1:1 into three groups differing in the timing of the post-baseline liver biopsy (Week 24, Week 48, and Week 72). Fifty-one (51) subjects underwent post-baseline biopsies prior to study discontinuation (28 subjects at <48 weeks and 23 subjects at ≥48 weeks). The study was designed to assess the safety, pharmacokinetics (PK) and efficacy kinetics as a function of treatment duration. Three independent pathologists and three different histopathology reading methodologies were used to assess the antifibrotic effect of Aramchol: fibrosis stage based on NASH CRN; ranked assessment (improvement/worsening/stable) of paired (pre- and post-baseline) biopsies, blinded to sequence; and an automated and continuous score of Fibrosis Composite Severity (FCS), using FibroNest™, a quantitative AI digital pathology image analysis method. Noninvasive tests (NITs) included imaging (fibroscan) and biomarkers (liver enzymes, FIB-4, Pro-C3 and ELF).

Aramchol treatment resulted in a high proportion of subjects showing fibrosis improvement based on all three biopsy reading methodologies, with a larger treatment effect with longer duration of therapy. Following a treatment duration of 48 weeks or more, improvement in fibrosis was demonstrated in 39% of subjects according to NASH CRN and 61% of subjects according to ranked assessment. At Week 48 AI demonstrated fibrosis improvement in 100% of subjects when responders were defined by an absolute reduction of the FCS score >0.3, 65% when responders were defined by a relative reduction of >25%, and a statistically significant reduction from baseline in mean FCS score ($p<0.0001$). NASH resolution without worsening of fibrosis was demonstrated in 26.5% of subjects.

Fibroscan, ALT, AST, and FIB4 were analyzed using MMRM, based on all subjects (N=154). Fibroscan results were consistent, with an improvement in fibrosis showing a mean absolute reduction from baseline to week 72 of 2.5 kPa ($p<0.0001$). At Week 72, ALT was reduced by 22 U/L ($p<0.0001$), AST was reduced by 18 U/L ($p<0.0001$), and FIB-4 was reduced by 0.30 ($p<0.0001$).

Pro-C3 and ELF were analyzed for 43 subjects at week 24 showing reduction in both Pro-C3 levels ($p<0.0001$) and ELF ($p=0.0038$).

The Open Label part demonstrated the good safety profile of Aramchol 300mg BID including long-term follow up. The incidence of serious adverse events (SAEs) was consistent with the population (10.4%) and early discontinuation rates due to adverse events (AEs) were low (4.5%).

Prof. Vlad Ratziu, ARMOR study co-Principal investigator commented: "The strength of the data we present today is in its internal consistency and coherence. Effects of Aramchol are demonstrated across all efficacy parameters with improvement over time. We used an extremely rigorous pathology reading methodology with three independent readers and three different morphological assessments of fibrosis, including digital pathology, all corroborating the antifibrotic activity of Aramchol".

Prof. Ratziu concluded that "The type and magnitude of effects we see with Aramchol compared to other NASH candidates, together with its unique mechanism of action and safety, potentially position Aramchol as a leading treatment for patients with NASH".

Allen Baharaff, Co-founder, President and CEO of Galmed added "the study answered the key questions it set up to answer: Aramchol's anti-fibrotic effects are seen across measures, a longer treatment duration improves outcomes and the safety profile of the 300mg BID dose regimen remains good. Importantly, we clearly demonstrated the challenges and opportunities of different pathology reading methodologies and are prepared to discuss with the FDA incorporating more sensitive methodologies as primary endpoints in NASH clinical studies. This can have a critical impact on the expected variability and sample size of future NASH studies. As we continue to evaluate our strategic alternatives, the advancement of Aramchol into the Double-Blind part of the ARMOR study depends on the outcome of this process and at present we do not have plans to initiate the Double-Blind part of the study".

About ARMOR Study

ARMOR is a Phase 3 study comprised of two-parts, an open-label part and a randomized, double-controlled, placebo part, designed to evaluate the safety and efficacy of Aramchol in approximately 200 sites in the U.S., Europe and Latin America.

The first part, an open-label study, was designed to evaluate treatment response kinetics, pharmacokinetics and safety of twice daily administration of Aramchol 300mg (new dosing regimen with higher exposure) in approximately 150 subjects with NASH and liver fibrosis stage 1-3 (F1 capped at 30 subjects). Patients were randomized (1:1:1) into three groups with post-baseline liver biopsy being performed at 24 weeks, 48 weeks, or 72 weeks, respectively. In May 2022, the Company concluded that the Open-Label part of the study met its objective and discontinued the Open-Label part.

The second part, a randomized, double-blind, placebo-controlled study, is designed to evaluate the safety and efficacy of Aramchol Meglumine to support regulatory approval, with both a histology-based phase and a clinically based phase. As currently designed, a total of 2000 subjects with NASH and liver fibrosis stage 2 and 3 who are overweight and are either pre-diabetic or have type 2 diabetes are expected to be randomized 2:1 to receive Aramchol Meglumine or matching placebo. In the histology-based phase, we intend to treat 1000 subjects with Aramchol or matching placebo for 72 weeks until the second biopsy. The histology-based data is intended to serve as the basis for the submission of a Sub-part H marketing authorization application under regulatory provisions of accelerated/conditional approval.

Following the discontinuation of the Open-Label Part of the ARMOR Study, the Company has no current plans to initiate the Double-Blind part of the ARMOR Study, the commencement of which depends on the outcome of its evaluation of strategic alternatives.

About Galmed Pharmaceuticals Ltd.

Galmed Pharmaceuticals Ltd. is a clinical stage drug development biopharmaceutical company for liver, metabolic and inflammatory diseases. Their lead compound, Aramchol™, a backbone drug candidate for the treatment of NASH and fibrosis is currently in a Phase 3 registrational study. Galmed is also collaborating with the Hebrew University in the development of Amilo-5MER, a 5 amino acid synthetic peptide.

Forward-Looking Statements:

Forward-looking statements relate to anticipated or expected events, activities, trends or results as of the date they are made. Because forward-looking statements relate to matters that have not yet occurred, these statements are inherently subject to risks and uncertainties that could cause our actual results to differ materially from any future results expressed or implied by the forward-looking statements. Many factors could cause our actual activities or results to differ materially from the activities and results anticipated in forward-looking statements, including, but not limited to, the timing and cost of our any pre-clinical or clinical trial, for our product candidates;completion and receiving favorable results of any pre-clinical or clinical trial;the impact of the COVID-19 pandemic on our operations;regulatory action with respect to Aramchol or any other product candidate by the U.S. Food and Drug Administration, or the

FDA, or the European Medicines Authority, or EMA, including but not limited to acceptance of an application for marketing authorization, review and approval of such application, and, if approved, the scope of the approved indication and labeling;the commercial launch and future sales of Aramchol and any future product candidates;our ability to comply with all applicable post-market regulatory requirements for Aramchol or any other product candidate in the countries in which we seek to market the product;our ability to achieve favorable pricing for Aramchol or any other product candidate;our expectations regarding the commercial market for non-alcoholic steato-hepatitis, or NASH, in patients or any other targeted indication;third-party payor reimbursement for Aramchol or any other product candidate;our estimates regarding anticipated capital requirements and our needs for additional financing;market adoption of Aramchol or any other product candidate by physicians and patients;the timing, cost or other aspects of the commercial launch of Aramchol or any other product candidate;our ability to obtain and maintain adequate protection of our intellectual property;the possibility that we may face third-party claims of intellectual property infringement;our ability to manufacture our product candidates in commercial quantities, at an adequate quality or at an acceptable cost;our ability to establish adequate sales, marketing and distribution channels;intense competition in our industry, with competitors having substantially greater financial, technological, research and development, regulatory and clinical, manufacturing, marketing and sales, distribution and personnel resources than we do;the development and approval of the use of Aramchol or any other product candidate for additional indications or in combination therapy;our ability to maintain the listing of our ordinary share on The Nasdaq Capital Market; andour expectations regarding licensing, acquisitions and strategic operations. We believe these forward-looking statements are reasonable; however, these statements are only current predictions and are subject to known and unknown risks, uncertainties and other factors that may cause our or our industry's actual results, levels of activity, performance or achievements to be materially different from those anticipated by the forward-looking statements. We discuss many of these risks in our Annual Report on Form 20-F for the year ended December 31, 2021 filed with the SEC on May 2, 2022 in greater detail under the heading "Risk Factors" and elsewhere in the Annual Report, in our Reports on Form 6-K filed with the SEC on August 4, 2022 and November 16, 2022 and this press release. Given these uncertainties, you should not rely upon forward-looking statements as predictions of future events. All forward-looking statements attributable to us or persons acting on our behalf speak only as of the date hereof and are expressly qualified in their entirety by the cautionary statements included in this report. We undertake no obligations to update or revise forward-looking statements to reflect events or circumstances that arise after the date made or to reflect the occurrence of unanticipated events. In evaluating forward-looking statements, you should consider these risks and uncertainties.

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https://galmedpharma.investorroom.com/2023-01-04-Galmed-reports-results-from-the-Open-Label-part-of-the-ARMOR-study-showing-improvements-in-histology,-imaging,-and-biomarkers-with-Aramchol