Aramchol Phase II b Results & Phase III Outlook

• Scientific Rationale surrounding Aramchol
• Clinical Development Plan for Phase III

Liat Hayardeny – Brück (PhD, MBA)
Chief Scientific Officer
Safe Harbor and Disclaimer Statement

This presentation contains forward-looking statements about our expectations, beliefs or intentions regarding, among other things, our product development efforts, business, financial condition, results of operations, strategies or prospects. In addition, from time to time, we or our representatives have made or may make forward-looking statements, orally or in writing. Forward-looking statements can be identified by the use of forward-looking words such as “believe,” “expect,” “intend,” “plan,” “may,” “should” or “anticipate” or their negatives or other variations of these words or other comparable words or by the fact that these statements do not relate strictly to historical or current matters. These forward-looking statements may be included in, but are not limited to, this presentation, various filings made by us with the SEC, press releases or oral statements made by or with the approval of one of our authorized executive officers. 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 factors summarized below.

These factors include, but are not limited to, the following: the timing and cost of Galmed’s planned Phase III ARMOR trial for Aramchol™, or whether a Phase III ARMOR trial will be conducted at all; completion and receiving favorable results of a planned Phase III ARMOR trial for Aramchol™; regulatory action with respect to Aramchol™ by the FDA or the EMA; the commercial launch and future sales of Aramchol™ or any 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; 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.

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. 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 included in, but not limited to, this presentation speak only as of the date hereof and are expressly qualified in their entirety by the foregoing. 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.

This presentation shall not constitute an offer to sell or the solicitation of an offer to buy, nor shall there be any sale of these securities in any state or other jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or other jurisdiction.
Aramchol – Liver Targeted SCD 1 Modulator

- **FABAC- fatty acid Bile acid conjugate**
  - MW = 702.12
  - BCS Class IV
  - T1/2 ss = 72.4 hrs

- **Aramchol in pre clinical models:**
  - Down regulation of liver FA in multiple dietary models
  - Down regulation of collagen in TAA animal models for liver fibrosis
  - Target directly HSC to down regulate collagen and α SMA production
    *(Friedman S et al. Poster 2060 AASLD 2018)*

- **Aramchol in Phase 2a showed significant reduction in liver fat: relative change in MRS**

---

1. Aramchol Reduces Established Fibrosis in MCD Diet Animal Model, EASL 2017 poster
2. Role of Aramchol in steatohepatitis and fibrosis in mice. Mato et al. Accepted to Hepatology Communications. 2017
3. R. Golan-Gerstl1, M. Valitsky1, R. Oren1, E. Brazovski2, L. Hayardeny1, S. Shimon Reif. "The anti-fibrotic effect of Aramchol on liver fibrosis in TAA animal model" (2017); The international liver congress (EASL), Amsterdam, the Netherlands.
Scientific Rationale for SCD1 Down Regulation in NASH

NAFLD (Steatosis)  NASH (Steatohepatitis)  NASH + Fibrosis

Pathophysiology of NASH

De-compensated Cirrhosis/ HCC
Down Regulation of SCD1 in Hepatocytes Leads to Reduction in Liver Fat

1. Aramchol Reduces Established Fibrosis in MCD Diet Animal Model, EASL 2017 poster
Down Regulation of SCD1 in Hepatocytes Leads to Reduction in Liver Fat

1. Aramchol Reduces Established Fibrosis in MCD Diet Animal Model, EASL 2017 poster

Food Consumption

ACC

Serum FA

SCD1

Fatty Acid

Fibrosis & Liver Damage

↓ Malonyl-Co A

↑ SPT₁

↓ FA Oxidation

Galmed Pharmaceuticals

Lipid Droplets

VLDL

MUFA

DG

TG

GSH/GSSG

P

AMPK

P

62%

56%
Scientific Rationale for SCD1 Down Regulation in NASH

NAFLD (Steatosis) → NASH (Steatohepatitis) → NASH + Fibrosis → De-compensated Cirrhosis/ HCC

Pathophysiology of NASH
Direct Effect on Fibrosis via Down Regulation of SCD 1 in HSC’s

1. Aramchol Reduces Established Fibrosis in MCD Diet Animal Model, EASL 2017 poster
3. R. Golan-Gerstl1, M. Valitsky1, R. Oren1, E. Brazovski2, L. Hayardeny1, S. Shimon Reif. "The anti-fibrotic effect of Aramchol on liver fibrosis in TAA animal model" (2017); The international liver congress (EASL), Amsterdam, the Netherlands.
Direct Effect on Fibrosis via Down Regulation of SCD 1 in HSC’s

1. Aramchol Reduces Established Fibrosis in MCD Diet Animal Model, EASL 2017 poster
3. R. Golan-Gerstl1, M. Valitsky1, R. Oren1, E. Brazovski2, L. Hayardeny1, S. Shimon Reif. "The anti-fibrotic effect of Aramchol on liver fibrosis in TAA animal model" (2017); The international liver congress (EASL), Amsterdam, the Netherlands.
ARMOR – ARaMchol for NASH Resolution & Fibrosis Improvement

**Visits Schedule**

- Phase 3 - Histology based (52w)
- Phase 4 - Clinically based (~5 years)

**Placebo**

**Aramchol 300mg BID**

**2000 patients 2:1 randomization**

**NASH resolution w/o worsening of fibrosis**

**Fibrosis improvement w/o NASH worsening**

**Composite of clinical events related to disease progression**

**Screening biopsy**

**Week 52 biopsy**

**5 years biopsy**

**EOS**

*EOS will occur at the time when a pre-specified number of clinical events have been observed or when the last randomized subject completes 5 years of treatment, whichever comes first.*
## Patient Population - Key Inclusion Criteria

<table>
<thead>
<tr>
<th>ARREST</th>
<th>ARMOR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BMI:</strong> 25kg/m² - 40kg/m²</td>
<td><strong>BMI:</strong> 25kg/m² - 40kg/m²</td>
</tr>
<tr>
<td><strong>Known type II Diabetes Mellitus or Pre-diabetes</strong></td>
<td><strong>Known type II Diabetes Mellitus or Pre-diabetes</strong></td>
</tr>
<tr>
<td><strong>Histologically proven steatohepatitis with NAS ≥4:</strong></td>
<td><strong>Histologically proven steatohepatitis with NAS ≥4:</strong></td>
</tr>
<tr>
<td>Central reading performed by Prof. Carolin Lackner at the University of Graz Austria</td>
<td>Central reading performed by Prof. Carolin Lackner at the University of Graz Austria</td>
</tr>
<tr>
<td><strong>Fibrosis stage 0-3</strong></td>
<td><strong>Fibrosis stage 2-3</strong></td>
</tr>
<tr>
<td><strong>Normal synthetic liver function</strong></td>
<td><strong>Normal synthetic liver function</strong></td>
</tr>
<tr>
<td><strong>AST &gt; 20 IU/L</strong></td>
<td><strong>AST &gt; 20 IU/L</strong></td>
</tr>
</tbody>
</table>
### Patient Population - Key Exclusion Criteria

<table>
<thead>
<tr>
<th>ARREST</th>
<th>ARMOR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cirrhosis</strong></td>
<td><strong>Cirrhosis</strong></td>
</tr>
<tr>
<td>Patients with other active (acute or chronic) liver disease</td>
<td>Patients with other active (acute or chronic) liver disease</td>
</tr>
<tr>
<td>Weight loss of more than 5% within 6 months</td>
<td>Weight loss of more than 5% within 3 months</td>
</tr>
<tr>
<td>Bariatric surgery within 5 years</td>
<td>Bariatric surgery within 5 years</td>
</tr>
<tr>
<td>HIV</td>
<td>HIV</td>
</tr>
<tr>
<td>Diabetes mellitus other than type II</td>
<td>Diabetes mellitus other than type II</td>
</tr>
<tr>
<td>Treatment with other anti-diabetic medications, Unless started prior to biopsy (6/12 months depending on drug) and stable</td>
<td>Treatment with other anti-diabetic medications, Unless started prior to biopsy (6/12 months depending on drug) and stable</td>
</tr>
<tr>
<td>Uncontrolled arterial hypertension</td>
<td>Uncontrolled arterial hypertension</td>
</tr>
<tr>
<td>Uncontrolled hypothyroidism</td>
<td>Uncontrolled hypothyroidism</td>
</tr>
<tr>
<td>Renal dysfunction eGFR&lt; 40 ml/min</td>
<td>Renal dysfunction eGFR&lt; 40 ml/min</td>
</tr>
</tbody>
</table>
ARREST

NASH resolution without worsening of fibrosis

<table>
<thead>
<tr>
<th>Group</th>
<th>Proportion of Patients</th>
<th>Placebo (N=40)</th>
<th>Aramchol 400 (N=80)</th>
<th>Aramchol 600 (N=78)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aramchol 600 vs. Pbo</td>
<td>16.7%</td>
<td>7.5%</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>p</td>
<td>0.051</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>4.74 (0.99-22.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fibrosis improvement (≥1 stage) without worsening of NASH

<table>
<thead>
<tr>
<th>Group</th>
<th>Proportion of Patients</th>
<th>Placebo (N=40)</th>
<th>Aramchol 400 (N=80)</th>
<th>Aramchol 600 (N=78)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aramchol 600 vs. Pbo</td>
<td>29.5%</td>
<td>21.3%</td>
<td>17.5%</td>
<td></td>
</tr>
<tr>
<td>p</td>
<td>0.2110</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>1.88 (0.70-5.04)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ARMOR

ARMOR Endpoints:
NASH resolution without worsening of fibrosis OR
Fibrosis improvement (≥1 stage) without worsening of NASH

- Similar definitions used
- The study is powered for both endpoints
- One of these endpoints is required for study success
**ARMOR - Primary Clinically Based Endpoint**

**Progression to Cirrhosis**

<table>
<thead>
<tr>
<th>Group</th>
<th>Proportion of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (N=40)</td>
<td>3/40 (7.5%)</td>
</tr>
<tr>
<td>Aramchol 400 (N=80)</td>
<td>6/80 (7.5%)</td>
</tr>
<tr>
<td>Aramchol 600 (N=78)</td>
<td>1/78 (1.3%)</td>
</tr>
</tbody>
</table>

* Post hoc analysis; Although limited by sample size and duration, there was a smaller number of patients that progressed to cirrhosis in the 600 mg arm.

**Clinical Endpoint:**

- Composite of clinical events related to disease progression based on FDA guidelines
- Histological progression to cirrhosis included in this endpoint
Change From Baseline - ALT and AST

### Change from Baseline in ALT (U/L)

- **Aramchol 400 vs. Pbo**: p<0.001
- **Aramchol 600 vs. Pbo**: p<0.0001

<table>
<thead>
<tr>
<th>Week 24</th>
<th>Week 40</th>
<th>Week 52</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>Aramchol 400 mg</td>
<td>Aramchol 600 mg</td>
</tr>
<tr>
<td>-25.0</td>
<td>-20.0</td>
<td>-15.0</td>
</tr>
<tr>
<td>-15.0</td>
<td>-10.0</td>
<td>-5.0</td>
</tr>
<tr>
<td>0.0</td>
<td>5.0</td>
<td>10.0</td>
</tr>
<tr>
<td>15.0</td>
<td>20.0</td>
<td>25.0</td>
</tr>
</tbody>
</table>

**ALT normalization, %**

<table>
<thead>
<tr>
<th>Placebo</th>
<th>Aramchol 400 mg</th>
<th>Aramchol 600 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>13.3</td>
<td>21.9</td>
<td>29</td>
</tr>
</tbody>
</table>

### Change from Baseline in AST (U/L)

- **Aramchol 400 vs. Pbo**: p=0.001
- **Aramchol 600 vs. Pbo**: p<0.0001

<table>
<thead>
<tr>
<th>Week 24</th>
<th>Week 40</th>
<th>Week 52</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>Aramchol 400 mg</td>
<td>Aramchol 600 mg</td>
</tr>
<tr>
<td>-15.0</td>
<td>-10.0</td>
<td>-5.0</td>
</tr>
<tr>
<td>0.0</td>
<td>5.0</td>
<td>10.0</td>
</tr>
<tr>
<td>15.0</td>
<td>20.0</td>
<td>25.0</td>
</tr>
</tbody>
</table>

**AST normalization, %**

<table>
<thead>
<tr>
<th>Placebo</th>
<th>Aramchol 400 mg</th>
<th>Aramchol 600 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.4</td>
<td>18.8</td>
<td>22.6</td>
</tr>
</tbody>
</table>
Change From Baseline - HbA1c

Week 52 Analyses
Aramchol 400 vs. Pbo: p=0.006
Aramchol 600 vs. Pbo: p<0.001

Aramchol, a SCD 1 modulator, improves liver glucose homeostasis in NASH. EASL 2019 poster
Dose Response Pattern in ARREST Study

**MRS**

Liver fat - Mean Change from Baseline

Placebo (N=41)  | Aramchol 400 (N=90)  | Aramchol 600 (N=83)

**MRI Responders - Reduction ≥ 5% absolute change**

Placebo (N=41)  | Aramchol 400 (N=90)  | Aramchol 600 (N=83)

24.4%  | 36.7%  | 47.0%

**Biopsy**

NASH Resolution without Worsening of Fibrosis

Placebo (N=40)  | Aramchol 400 (N=80)  | Aramchol 600 (N=78)

5.0%  | 7.5%  | 16.7%

**Liver Enzymes**

ALT – mean change from Baseline

Week 24  | Week 40  | Week 52

AST – mean change from Baseline

Week 24  | Week 40  | Week 52

Proportion of patients

Fibrosis Improvement Without Worsening of NASH

Placebo (N=40)  | Aramchol 400 (N=80)  | Aramchol 600 (N=78)

17.5%  | 21.3%  | 29.5%
Aramchol – Liver Targeted SCD 1 Modulator

- **FABAC- fatty acid Bile acid conjugate**
  - MW = 702.12
  - BCS Class IV
  - T1/2 ss = 72.4 hrs

- **Aramchol in pre clinical models:**
  - Down regulation of liver FA in multiple dietary models
  - Down regulation of collagen in TAA animal models for liver fibrosis
  - Target directly HSC to down regulate collagen and α SMA production
    (Friedman S et al. Poster 2060 AASLD 2018)

- **Aramchol in Phase 2a showed significant reduction in liver fat: relative change in MRS**

---

1. Aramchol Reduces Established Fibrosis in MCD Diet Animal Model, EASL 2017 poster
2. Role of Aramchol in steatohepatitis and fibrosis in mice. Mato et al. Accepted to Hepatology Communications. 2017
3. R. Golan-Gerstl1, M. Valitsky1, R. Oren1, E. Brazovski2, L. Hayardeny1, S. Shimon Reif. "The anti-fibrotic effect of Aramchol on liver fibrosis in TAA animal model" (2017); The international liver congress (EASL), Amsterdam, the Netherlands.
Significant Increase in Exposure Using “Dose Split” Method

AUC_{0-24} ng*h/mL summary data by treatment regimen

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
<th>Geometric Mean</th>
<th>90% Lower CI</th>
<th>90% Upper CI</th>
<th>CV%</th>
</tr>
</thead>
<tbody>
<tr>
<td>300mg BID</td>
<td>16</td>
<td>110860</td>
<td>97000</td>
<td>126701</td>
<td>25.1</td>
</tr>
<tr>
<td>600 mg QD</td>
<td>16</td>
<td>72537</td>
<td>63468</td>
<td>82902</td>
<td>34.6</td>
</tr>
<tr>
<td>Ratio</td>
<td></td>
<td>1.53</td>
<td>1.38</td>
<td>1.69</td>
<td></td>
</tr>
</tbody>
</table>
In ARREST - Increasing the exposure by 22% change the response rate significantly.

Dose split results in 53% increase in exposure with the potential of pushing efficacy even higher in ARMOR.
ARREST - Excellent Safety and Tolerability Profiles

- Discontinuation due to adverse events was less than 5%:
  - 4.2%, 3% and 4.1% of patients in placebo, Aramchol 400mg and 600mg arms respectively
- SAEs reported in 12.5%, 8.9% and 9.2% of patients in placebo, 400mg and 600mg arms respectively; no deaths
- No signal for hepatotoxicity
- Weight neutral and no changes in lipid parameters

<table>
<thead>
<tr>
<th>Adverse event N (%)</th>
<th>Placebo (N=48)</th>
<th>400 mg (N=101)</th>
<th>600 mg (N=98)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constipation</td>
<td>6 (12.5)</td>
<td>5 (5)</td>
<td>8 (8.2)</td>
</tr>
<tr>
<td>Cough</td>
<td>4 (8.3)</td>
<td>4 (4)</td>
<td>5 (5.1)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>4 (8.3)</td>
<td>8 (7.9)</td>
<td>3 (3.1)</td>
</tr>
<tr>
<td>Headache</td>
<td>6 (12.5)</td>
<td>14 (13.9)</td>
<td>15 (15.3)</td>
</tr>
<tr>
<td>Influenza</td>
<td>2 (4.2)</td>
<td>8 (7.9)</td>
<td>5 (5.1)</td>
</tr>
<tr>
<td>Nausea</td>
<td>6 (12.5)</td>
<td>10 (9.9)</td>
<td>9 (9.2)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>3 (6.3)</td>
<td>7 (6.9)</td>
<td>11 (11.2)</td>
</tr>
<tr>
<td>UTI</td>
<td>3 (6.3)</td>
<td>15 (14.9)</td>
<td>13 (13.3)</td>
</tr>
</tbody>
</table>

Most frequent AEs (≥7% of subjects in at least one study arm)
ARMOR – Global Distribution

- **150 Sites**
- **15 Countries**
- **5 Continents**
• **Aramchol is a novel, first in class liver targeted, SCD1 modulator:**
  • Down regulation of SCD 1 in hepatocytes and HSC’s results in reduction in FFA and collagen production

• **ARREST results:**
  • Aligned with MoA and show effect on NASH resolution & fibrosis improvement

• **The ARMOR study**
  • Based on ARREST results and FDA recommendations (F2F meeting March 20)
  • Powered for both endpoints; NASH resolution and fibrosis improvement at 52 weeks
  • Employs a dose split method (300mg BID) to increase exposure and potential for even better efficacy
  • Designed to be a robust global study
Thank You!

NASDAQ: GLMD