miRagen Therapeutics
NASDAQ: MGEN

May 2020
Cautionary Note Regarding Forward-Looking Statements

This presentation contains forward-looking statements relating to Miragen Therapeutics, Inc., including statements about our plans to obtain funding, develop and commercialize our therapeutic candidates, our planned clinical trials, the timing of and our ability to obtain and maintain regulatory approvals for our therapeutic candidates, the clinical utility of our therapeutic candidates and our intellectual property position. You can identify forward-looking statements by the use of forward-looking terminology including “believes,” “expects,” “may,” “will,” “should,” “seeks,” “intends,” “plans,” “pro forma,” “estimates,” or “anticipates” or the negative of these words and phrases or other variations of these words and phrases or comparable terminology. All statements other than statements of historical fact are statements that could be deemed forward-looking statements. These statements involve substantial known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. These forward-looking statements should not be relied upon as predictions of future events as we cannot assure you that the events or circumstances reflected in these statements will be achieved or will occur. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements that we make due to a number of important factors, including those risks discussed in “Risk Factors” and elsewhere in our Annual Report on Form 10-K for the year ended December 31, 2018 and our other reports filed with the U.S. Securities and Exchange Commission. The forward-looking statements in this presentation represent our views as of the date of this presentation. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this presentation.

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miRagen Therapeutics

- Leading the development of what we believe is the most advanced microRNA targeting therapeutics platform currently in development
- Favorable safety and tolerability profile has been observed in multiple product candidates
- 3 clinical stage product candidates and a recently unveiled preclinical program
- Aims to advance multiple product candidates through collaborations, while driving future expansion opportunities for the company

COBOMARSEN
- miR-155 elevated blood cancers
- Phase II (CTCL, ongoing)
- Phase I (ATLL, ongoing)

REMLARSEN
- Pathological fibrosis
- Phase II (skin, ongoing)
- Preclinical (ocular, Ph 1 ready)

MRG-110
- Tissue repair and heart failure
- Phase I (two completed clinical trials)
- Phase II ready for intradermal administration

MRG-229
- Antifibrotic effects for systemic applications
- Lung (IPF) focus (preclinical)
- Liver and kidney expansion (preclinical)
Why microRNAs?

microRNAs Regulate Network Biology to Maintain Homeostasis

- microRNAs have been evolutionarily selected to regulate networks of genes
- microRNAs are dysregulated in many diseases
- Dysregulation of microRNAs is associated with alteration of downstream gene networks and disease
- microRNA-targeted therapy is focused on disease modification by restoring homeostasis to dysregulated processes
- microRNA therapeutics are particularly suited for complex, multigenic disorders

Conventional Therapies (Small molecules, Antibodies, siRNA, etc)
Single molecule as target

microRNA-based Therapies
Network (pathway) as target
miRagen Approach to Clinical Development

- Chemical modification design appears to blunt toxicity
- Stable molecules
  - Infrequent dosing
  - No complex formulations

- Identification of PD biomarker “genetic fingerprint” for each miRNA modulator
- Selectivity for disease specific pathways

- Incorporate mPOC endpoints such as PD biomarker regulation into Ph I trials to confirm biological activity in humans

- mPOC and target validation from in-vitro to in-vivo disease models
- Validate assays for translation to the clinic

SAFETY

PD

CLINICAL

TRANSLATIONAL
# The Most Advanced microRNA Targeting Pipeline

<table>
<thead>
<tr>
<th>Candidate (Target)</th>
<th>Disease Area</th>
<th>Pre-clinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cobomarsen (miR-155)</td>
<td>Blood Cancers</td>
<td><strong>Cutaneous T-cell Lymphoma (CTCL)</strong></td>
<td><strong>Adult T-Cell Lymphoma/Leukemia</strong></td>
<td></td>
</tr>
<tr>
<td>Remlarsen (miR-29)</td>
<td>Pathologic Fibrosis</td>
<td><strong>Cutaneous Fibrosis</strong></td>
<td></td>
<td><strong>Ocular Fibrosis</strong></td>
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<tr>
<td>MRG-110 (miR-92)</td>
<td>Tissue Repair</td>
<td><strong>Heart Failure</strong></td>
<td></td>
<td><strong>Wound Healing</strong></td>
</tr>
<tr>
<td>MRG-229 (miR-29)</td>
<td>Pathologic Fibrosis</td>
<td><strong>Idiopathic Pulmonary Fibrosis</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Anticipated Milestones

- Phase I ATLL Data (released Jan 20)
- MRG-229 Pre-clinical Data (2Q20)
- Regulatory Guidance in ATLL
- Phase 2 CTCL Topline Data
- Phase 2 Cutaneous Fibrosis Data
## Clinical Development Programs

*Large microRNA Therapeutics Safety Database*

<table>
<thead>
<tr>
<th></th>
<th>COBOMARSEN</th>
<th>REMLARSEN</th>
<th>MRG-110</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ROUTE OF ADMINISTRATION</strong></td>
<td>Intralesion, IV and Subcutaneous</td>
<td>Intradermal</td>
<td>Intradermal and IV</td>
</tr>
<tr>
<td><strong>DOSE</strong></td>
<td>75–1200 mg</td>
<td>Up to 14 mg</td>
<td>Up to 1.5 mg/kg</td>
</tr>
<tr>
<td><strong>EXPOSURE</strong></td>
<td>68 patients <em>(CTCL, ATLL, DLBCL, and CLL from Ph1 and CTCL SOLAR)</em> for up to 2.2 Years</td>
<td>61 patients for up to 4 weeks</td>
<td>65 subjects for up to 3 weeks</td>
</tr>
<tr>
<td><strong>CLINICAL TRIALS</strong></td>
<td>• CTCL – Phase 1 Completed <em>(n=41)</em></td>
<td>• NHV – Phase I Completed <em>(n=54)</em></td>
<td>• NHV – Phase 1 ID SAD/MAD Completed <em>(n=42)</em></td>
</tr>
<tr>
<td></td>
<td>• CTCL – SOLAR Phase 2 Ongoing <em>(n=10)</em></td>
<td>• Keloid – Phase 2 Enrollment Complete <em>(n=14)</em></td>
<td>• NHV – Phase 1 IV SAD Completed <em>(n=49)</em></td>
</tr>
<tr>
<td></td>
<td>• ATLL – Phase 1 Ongoing <em>(n=13)</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• DLBCL, CLL – Phase 1 Enrollment Suspended <em>(n=9)</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SAFETY</strong></td>
<td>• Generally safe and well tolerated</td>
<td>• Generally safe and well tolerated</td>
<td>• Generally safe and well tolerated</td>
</tr>
<tr>
<td></td>
<td>• No acute inflammatory toxicities</td>
<td>• No negative effect on healing <em>(no exaggerated pharmacology)</em></td>
<td>• No acute inflammatory toxicities</td>
</tr>
<tr>
<td></td>
<td>• No significant abnormalities in liver, kidney or blood</td>
<td>• No significant abnormalities in liver, kidney or blood</td>
<td>• No significant abnormalities in liver, kidney or blood</td>
</tr>
<tr>
<td></td>
<td>• No evidence of global immunosuppression <em>(no exaggerated pharmacology)</em></td>
<td>• No evidence of global immunosuppression <em>(no exaggerated pharmacology)</em></td>
<td>• No injection site reactions</td>
</tr>
<tr>
<td></td>
<td>• No evidence of metabolic or hematological toxicities</td>
<td>• No evidence of distal angiogenesis <em>(no exaggerated pharmacology)</em></td>
<td>• No evidence of distal angiogenesis <em>(no exaggerated pharmacology)</em></td>
</tr>
</tbody>
</table>

* data cut off of July 23, 2019
microRNA Dysregulation Can Be Associated with Poor Outcomes, Creating an Opportunity for microRNA Targeting Therapeutics

**microRNA-155**
- Overexpression of miR-155 has been associated with poor clinical outcomes in a variety of cancers

**COBOMARSEN**
- A microRNA-155 inhibitor that has demonstrated promising anticancer activity
- By affecting multiple signaling pathways in cancer, cobomarsen may provide long term benefit with few resistance mechanisms
Cobomarsen Phase 1 Clinical Trial Data Highlights

92% of the CTCL subjects in the systemic administration cohorts observed to have improvement in tumor burden as assessed by mSWAT score.

63% of subjects treated with cobomarsen administered as a 300 mg IV-infusion achieved a PR and 50% maintained the response for greater than four months (ORR4).

- For evaluable patients achieving a PR (n=12), the mean duration of response was 309 days at the time of the 07/30/19 data cutoff
- Cobomarsen was generally well-tolerated at all doses tested in CTCL subjects
- Data from the Phase I trial helped the company to design ongoing Phase II clinical trial
SOLAR Phase 2 Clinical Trial

A Randomized, Open-Label, Parallel-group, Active Comparator, Global Trial in Patients with Stage IB-III Mycosis Fungoides (MF)

Primary Endpoint
+ Durable Skin Response Rate of Four Months (ORR4)

Secondary Endpoints
+ Progression-free Survival in Skin

Open Label Randomized to: Cobomarsen IV Infusion vs. Vorinostat

Randomize n~37

Cobomarsen N=18

Vorinostat N=18

Potential to open additional Randomization

Follow until progression

Interim Analysis

Cobomarsen N=up to 43

Vorinostat N=up to 43

Follow until progression

Crossover to cobomarsen

EOS

Follow until progression
ATLL (Adult T-cell Leukemia/Lymphoma)

- Adult T-cell leukemia/lymphoma (ATLL) is a peripheral T-cell neoplasm caused by human T-lymphotrophic virus type 1 (HTLV-1)

- HTLV-1 is correlated with the overexpression of miR-155 during its lifecycle

- Malignant transformation leading to ATLL occurs in up to 7% of HTLV-1–infected individuals

- The aggressive form of the disease is highly morbid, with mean survival times of 4-10 months after diagnosis even with the best standard of care over the last two decades

Arch Pathol Lab Med 2014;138-282; Blood Advances, 2018 (march27); 2 (6)
RESULTS

Cobomarsen observed to have a favorable MST and PFS in Aggressive ATLL with Residual Disease, Compared to External Historical Cohort

<table>
<thead>
<tr>
<th></th>
<th>Cobomarsen-Aggressive</th>
<th>External Cohort All Aggressive</th>
<th>External Cohort-Acute</th>
<th>External Cohort-Lymphomatous</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (papers)</td>
<td>NA</td>
<td>12</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>n (patients)</td>
<td>6</td>
<td>3,739</td>
<td>3,369</td>
<td>3,369</td>
</tr>
<tr>
<td>MST (months)</td>
<td>26</td>
<td>7.4</td>
<td>6.8</td>
<td>10.4</td>
</tr>
<tr>
<td>PFS (months)</td>
<td>12.5</td>
<td>5.4</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Cobomarsen Appears to Decrease Expression of Cell Proliferation and Activation Biomarkers on ATL Cells

**BASELINE PROGNOSTIC BM**

**COBOMARSEN TREATMENT**

*Activation Markers ATL Tumor Cells*

*Proliferation Index ATL Tumor Cells*
miR-29 is an Anti-Fibrotic miRNA

- Reduced expression of miR-29 has been implicated in the development and progression of a wide range of fibrosis indications
- miR-29 inhibits TGF-β activity, EMT, fibroblast-to-myofibroblast transition and ECM synthesis
- miR-29 inhibits every step of the collagen fibrillogenesis pathway

miRagen preclinical and/or clinical data + literature support
- Literature support
Remlarsen: Reduces Fibroplasia Without Affecting Wound Healing

- Remlarsen treatment appears to inhibit the expression of dynamic and mechanistic biomarkers of fibrogenesis in humans
- This appears to result in a significant reduction in fibroplasia, a marker of scar tissue deposition
- Normal regranulation and healing of the wounds observed with treatment
- Statistically significant reduction of fibroplasia without affecting wound healing
- Justifies further exploration for broad applications in scar reduction

\[ \text{Fibroplasia} \]

16 subjects (Additional 3 subjects did not have histology assessment performed)

Hematoxylin and Eosin stain & assessment by a blinded pathologist

*Statistically significant (p=0.0086)
Remlarsen: An Anti-Fibrotic in the Eye

- Successful biodistribution to target cells in preclinical studies
  - Retina with intravitreal injection
  - Cornea with topical administration
- Compelling biomarker and antifibrotic activity in preclinical studies
**MRG-229: A Next-Gen miR-29 Mimic for Systemic Administration and Targeted Delivery in Systemic Fibrosis**

*In vitro* Screening of Extensively Modified Mimics
- Increased stability
- Improved potency

**Targeting Conjugates**
- Tissue/indication specific receptor targeting
- Improved uptake via conjugates

**Mechanism of Action Validated in Human Clinical Trials**

**Optimized for Stability and Activity**

**Optimized for Biodistribution and Delivery**

**MRG-229 (Next Gen miR-29 mimic)**
MRG-229: Potent Antifibrotic Activity Observed in Preclinical Model of IPF

Significantly Blocks Pulmonary Fibrosis in Bleomycin-Treated Mice
MRG-229 Appears to Block Fibrosis in Human Precision-Cut Lung Slices

In collaboration with Naftali Kaminski
And Maurizio Chioccioli
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