Harnessing the Power of microRNA Systems Biology

miRagen Therapeutics
NASDAQ: MGEN

Jefferies Global Healthcare Conference
June 8, 2017
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. 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 Highlights

• A clinical stage biopharmaceutical company with programs in Oncology and Fibrosis
  ♦ MRG-106 in CTCL → miR-155 elevated lymphoma / leukemia
  ♦ MRG-201 cutaneous fibrosis & tissue repair → pathological fibrosis & connective tissue disorders

• Expertise in nucleic acid drug discovery and development
  ♦ microRNA validation, oligonucleotide chemistry, translational medicine

• Strategic collaboration with Servier in cardiovascular disease
  ♦ miRagen retains commercial rights in the U.S. and Japan

• Current cash runway expected through 2018
  ♦ $54.3 million cash and equivalents as of March 31, 2017
Experienced Executive Leadership Team

William S. Marshall, Ph.D.
President & Chief Executive Officer

Adam Levy
Chief Business Officer

Jason A. Leverone, C.P.A.
Chief Financial Officer

Paul Rubin, M.D.
Executive Vice President, R&D
The objective of microRNA-targeted therapy is to achieve disease modification by restoring system homeostasis.

- microRNAs regulate complex biological systems
- microRNA-targeted therapies are intrinsically focused on disease-relevant pathways
- microRNA therapeutics particularly suited for complex, multigenic disorders
Foothold Clinical Development Strategy

• Biomarker driven early clinical trials
• Progressive de-risking
• May improve probability of success
• Accelerate proof of concept in humans
• Initial rare disease indication may allow more rapid commercialization
## Pipeline of Therapeutic Candidates

<table>
<thead>
<tr>
<th>Candidate</th>
<th>Disease Area</th>
<th>Pre-clinical</th>
<th>IND Enabling</th>
<th>Phase I</th>
<th>Partner/Internal</th>
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<tbody>
<tr>
<td>MRG-106</td>
<td>Hematological Malignancies</td>
<td>Cutaneous T-cell Lymphoma (CTCL)</td>
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<td>MRG-106</td>
<td>Hematological Malignancies</td>
<td>Viral Lymphomas</td>
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<td>MRG-106</td>
<td>Hematological Malignancies</td>
<td>Other miR-155 Elevated NHL</td>
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<td>MRG-201</td>
<td>Pathologic Fibrosis</td>
<td>Cutaneous Fibrosis</td>
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<td>MRG-201</td>
<td>Pathologic Fibrosis</td>
<td>Idiopathic Pulmonary Fibrosis</td>
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<td>MRG-201</td>
<td>Pathologic Fibrosis</td>
<td>Other Fibrotic Indications</td>
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<tr>
<td>MRG-107</td>
<td>Neurodegeneration</td>
<td></td>
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<tr>
<td>MRG-110</td>
<td>Ischemia</td>
<td></td>
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</tr>
</tbody>
</table>
CTCL  
Mycosis Fungoides  

miR-155  
High NHL  

Leukemia  
CLL  
ALL  

Nodular  
Diffuse  

MRG-106  
(miR-155 inhibitor)  
Hematological Malignancies
Regulating Systems Biology to Modify Disease

miR-155 is an OncomiR and a Pro-inflammatory microRNA

↑ miR-155

- CEBPβ
  - Inflammation
    - M1→M2
  - Cytokines
  - T cell activation

- SOCS
  - iNOS
  - Cytokines
  - T cell activation

- SHIP-1
  - PI3K/AKT/MAPK
  - Proliferation
  - Myeloid expansion

- Jarid2
  - Leukemic transformation

- PU.1
  - Myeloid differentiation

- Wee1
  - DNA repair

Inflammation / Immunity

Cancer
Mycosis Fungoides (MF)

- Most common form of CTCL
- United States MF prevalence of 16,000-20,000 cases
- Initially indolent but with serious quality of life detriment
- 5-year survival of approximately 90.6% in newly diagnosed CTCL patients
- Average age at onset is 45-55 years for patients and is >60 years for patients who present with tumors or significant erythroderma
- 70-80% diagnosed with early stage MF with only skin involvement

**Early Stage MF**

**Late Stage MF**
MRG-106: Two-Part Phase 1 CTCL Study

Objectives:
- **Primary**: Investigate safety & tolerability of multiple injections
- **Secondary**: Characterize the pharmacokinetic profile
- **Explanatory**:
  - Pharmacodynamic profile
  - Gene expression alterations
  - Histopathology of lesion biopsy
  - Imaging of tumor morphology

**Part A**
Intra-tumoral delivery of inhibitor of miR-155. **75 mg dose**

- Pretreatment biopsy
- Placebo biopsy
- MRG-106 biopsy

**Part B**
Systemic SC or IV delivery to determine optimal potential dose. **300, 600 and 900 mg+ dose**

- MRG-106 Sub-cut.
- Biopsy
Exploratory Efficacy Measurements in Part A: Intra-tumoral Injection

<table>
<thead>
<tr>
<th>Patient</th>
<th># of Doses</th>
<th>Dose Schedule</th>
<th>CAILS Score (Max/Min)</th>
<th>Maximal % Reduction in CAILS</th>
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</thead>
<tbody>
<tr>
<td>107-001</td>
<td>3</td>
<td>-7, 1, 2</td>
<td>18 → 12</td>
<td>33%</td>
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<tr>
<td>102-001</td>
<td>5</td>
<td>-7, 1, 3, 5, 8</td>
<td>26 → 6</td>
<td>77%</td>
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<tr>
<td>101-001</td>
<td>5</td>
<td>-7, 1, 3, 5, 8</td>
<td>12 → 4</td>
<td>67%</td>
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<tr>
<td>105-001</td>
<td>4</td>
<td>1, 3, 5, 8</td>
<td>16 → 8</td>
<td>50%</td>
</tr>
<tr>
<td>102-003</td>
<td>4</td>
<td>1, 3, 5, 8</td>
<td>12 → 6</td>
<td>50%</td>
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</tbody>
</table>

○ = Last Dose
Exploratory Efficacy Measurements in Part B: Systemic Administration

Note: Numbers in the bars are the number of doses administered
Potential Clinical Benefit of MRG-106 on Disease Observed as Early as Study Day 19

Grey shading = drug administration period, white = pause in drug administration
Patient with Extensive Skin Disease (Baseline mSWAT of 180) Showed mSWAT Score Improvement
Improvement in Total Skin Disease Score Correlates with MRG-106 Treatment

Grey shading = drug administration period, white = pause in drug administration

Day 1
CAILS: 13

Day 19
CAILS: 10

Day 27
CAILS: 8

Day 57
CAILS: 5

Day 103
CAILS: 10

Day 131
CAILS: 8

Day 159
CAILS: 7

Day 186
CAILS: 6
Alterations to Gene Expression Pathways Consistent with Intended Mechanism of Action

MRG-106 treatment believed to decrease CTCL associated disease pathways including STAT and NFkB Pathways
MRG-106 Potential Clinical Development Plan

Dose and Schedule Optimization in CTCL

Ph 1 CTCL

mPoC
Interim Analysis

cPoC*

Parallel Indication Expansion in Ph1

ATLL

DLBCL / CLL

Other

Ph 2 in NHL / Leukemia**
MRG-201
(miR-29 replacement)

Pathological Fibrosis & Tissue Repair
miR-29 is a Regulator of Biological Pathways Implicated in Fibrosis

- **Growth factors**: TGF-β2, TGF-β3, EGF, IGF2, IGFBP5, PDGFA, PDGFC
- **Collagen transcription/translation**: COL1A1, 1A2, 3A1, 5A1, 5A2, 5A3, 6A4, 6A5, 6A6, 8A1, 8A2, 9A1, 11A1, 12A1, 14A1, 22A1, 28A1
- **Post-translational modification & triple helix formation**: HSP47, P4HA2, P4HA3, PLOD2
- **N- and C-terminal cleavage & secretion**: PCOLCE2
- **Fibril cross-linking**: LOXL2
- **Mature collagen fibrils**:
MRG-201 First-In-Human Phase 1 Study in Induced Cutaneous Fibrosis

• Normal healthy volunteers at a single trial site (Montreal)

• 4 cohorts (n=3-10 per cohort):

  ♦ A – establish PD marker kinetics in skin incision ✔
  ♦ B – single ascending dose in intact skin ✔
  ♦ C – single ascending dose around skin incision ✔
  ♦ D – multiple ascending doses around skin incision ✔

• MRG-201 at doses of 0.5-14mg in all cohorts has been well tolerated

Final data anticipated by end 2Q 2017
MRG-201 Mechanistic Proof of Concept: PD Biomarkers Are Regulated in Human Incised Skin

- Evidence of PD activity after single administration of MRG-201
- PD biomarkers that are up-regulated in incised skin are down-regulated by MRG-201
- PD biomarkers that are down-regulated in incised skin are up-regulated by MRG-201

Incision vs. unwounded skin

Drug vs. saline at Day 5
Blinded Histology Analysis Shows Statistically Significant Reduction of Fibroplasia with MRG-201 vs Saline

**Fibroplasia**

- **Width**
  - Saline
  - MRG-201

- **Depth**
  - Saline
  - MRG-201

- **Area**
  - Saline
  - MRG-201

**P-values**:
- **Width**: p = 0.0464
- **Depth**: p = 0.0078
- **Area**: p = 0.0078

**Graph**

- Depth/Width (mm) or Area (mm²)
  - Saline
  - MRG-201
**Keloids – Cutaneous Pathologic Fibrosis**

- Benign scar at the site of minor or major skin injuries (acne, trauma, surgery, burns)
- Results from an overgrowth of scar tissue
  - Excessive collagen I and III deposition
  - TGFβ has been implicated in the pathogenesis
- Available treatments: steroids, radiation, excision, cryosurgery, laser ablation, 5FU, interferon, triamcinolone acetonide, methotrexate…
  - Poor treatment response
  - High reoccurrence rate post-excision
  - High unmet medical need
miR-29 in IPF
Nebulized MRG-201 Attenuates Fibrosis Induced by Bleomycin in Preclinical Model

MRG-201 or control dosing started 10 days after bleomycin administration - administered daily for 7 days

Note: Performed at Yale.
MRG-201 Potential Clinical Development Plan

Ph 1 Healthy Vol. → IND Keloids → Ph 2 Keloids

Ph 1 Healthy Vol. → mPoC Interim Analysis

Ph 1 IPF

Ph 1 Hepatic
# Upcoming Events and Milestones

<table>
<thead>
<tr>
<th>Program</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematological Malignancies</td>
<td>✓ Interim Phase 1 CTCL data presentation at ASCO (Q2)</td>
<td>✓ Phase 1 trial expansion to include 3rd indication (H1)</td>
</tr>
<tr>
<td>(MRG-106)</td>
<td>☐ Phase 1 trial expansion to include 2nd indication (H2)</td>
<td>☐ Initiation of Phase 2 trial in CTCL / NHL (H2)</td>
</tr>
<tr>
<td></td>
<td>☐ Interim Phase 1 CTCL data presentation at ASH (Q4)</td>
<td></td>
</tr>
<tr>
<td>Pathologic Fibrosis</td>
<td>✓ Last patient dosed in Phase 1 dermatologic fibrosis trial (H1)</td>
<td>☐ Initiation of Phase 1 with inhaled formulation</td>
</tr>
<tr>
<td>(MRG-201)</td>
<td>☐ Preclinical inhalation feasibility study results presentation at scientific conference (H2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>☐ Phase 1 results presentation at scientific conference (H2)</td>
<td></td>
</tr>
<tr>
<td>Revascularization</td>
<td>☐ Completion of IND/CTA enabling studies (Q4)</td>
<td>☐ Initiation of Phase 1</td>
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<tr>
<td>(MRG-110)</td>
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Intellectual Property Portfolio

- Owner / exclusive licensee of 113 issued patents over 100 pending applications
  - Composition of matter patents on all compounds
- Exclusive licensee to LNA technology for multiple targets
- Freedom to operate with targeted miRNAs based on current claims and likely allowances
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