Improved Perfusion and Wound Healing in Healthy Pigs with MRG-110, an Inhibitor of microRNA-92a

Rusty Montgomery, Ph.D.
April 27th, 2018
Disclosures

- Employee of miRagen Therapeutics, Inc.
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.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.
microRNA Therapeutics Regulate Systems Biology to Modify Disease

- microRNA-targeted therapy is focused on disease modification by restoring homeostasis to dysregulated processes
- microRNAs regulate complex biological systems
- microRNA-targeted therapies are intrinsically focused on disease-relevant pathways
- microRNA therapeutics particularly suited for complex, multigenic disorders
miR-92a is a Key Regulator of Angiogenesis

Overexpression of miR-92a inhibits sprouting, network formation, and angiogenesis in multiple models.

Inhibition of miR-92a induces granulation tissue formation, angiogenesis, and accelerates wound healing in db/db model.
Dermal Tolerability and Wound Healing Studies in Pigs

- Are the effects observed in the db/db mouse translatable to non-diabetic conditions?
- What is the optimal dose/regimen necessary for these effects?

- Pig skin architecture and healing processes are similar to humans which make them one of the best animal models for wound healing and skin tolerability studies

- GLP local tolerability and wound healing study in Farm Pigs
  - Six MRG-110 treated pigs and 2 control pigs each received eight 2.5 x 2.5 cm full thickness wounds on the back
  - 3, 12, 48 mg/wound intradermally per dose day compared to no treatment except dressing changes (SOC) and vehicle treated wounds
  - Wounds were treated 3 times a week for 2 weeks then followed to complete wound closure at Day 49
  - All doses well tolerated
MRG-110 Improves Wound Perfusion and Rate of Wound Closure in Healthy Farm Pigs

• MRG-110 improved perfusion as assessed by laser Doppler imaging at day 14 for all 3 doses

• On Day 35, complete wound closure was achieved in 7 of 12 wounds (58%) with low dose MRG-110 compared to 0 of 8 (0%) Standard of Care (wound dressing changes only) and 1 of 8 (12%) vehicle control treated wounds

• All doses appeared active suggesting low dose (3 mg/wound; ~2 mg/cm²) is at the top of dose response curve
MRG-110 Improves Vascularization and Increases Granulation Tissue Formation During Healing of Full Thickness Wounds in Healthy Pigs at Day 49

All data presented as mean ± SEM
* p<0.05 and ** p<0.01 compared to SOC by Kruskal-Wallis using Dunn’s multiple comparisons test
+ p<0.05 by one-way ANOVA compared to SOC using Holm-Sidak’s multiple comparisons test

602 SOC: Granulation Tissue (dashed line) Dermal: 1+ Subcutaneous: 2+
605 High Dose: Granulation Tissue (dashed line) Dermal: 4+ Subcutaneous: 4+
MRG-110 Treatment Schedule Optimization of Wounds in Healthy Farm Pigs

Wound Closure data assessed in 3 wounds allowed to go to full closure per dosing regimen.

Study Design: 4 Pigs treated with a vehicle or MRG-110 on a different schedule

- Vehicle control doses 3x a week for two weeks,
- MRG-110 as a single dose on Day 1
- MRG-110 as 2 doses given a week apart, and
- MRG-110 dosed three times a week for two weeks

3 wounds per treatment regimen were biopsied each week to assess wound healing, granulation tissue formation and vascularization by IHC

Perfusion Units Over Time

Wound Closure Over Time

MRG-110 treatment improved perfusion and wound closure
CD31 and ITGA5 Staining of New Vasculature in Vehicle or MRG-110 Treated Wounds on Day 14 (6 days post last dose)

CD31 (PECAM-1) Staining of endothelial cells demonstrates increased density of blood vessels in healing wound with MRG-110 treatment.

ITGA5, a component of the fibronectin receptor critical for angiogenesis and a direct target of miR-92a, is upregulated in MRG-110 treated wounds and expression is sustained longer compared to VC treated wounds.

Increased markers of vascularization shown with weekly dosing of MRG-110
Conclusions

- MRG-110 improved perfusion as assessed by laser Doppler imaging at day 14 for all 3 doses tested
- On Day 35, complete wound closure was achieved in 7 of 12 wounds (58%) with low dose MRG-110 compared to 0 of 8 (0%) SOC and 1 of 8 (12%) VC treated wounds
- All doses appeared active suggesting low dose (3 mg/wound; ~2 mg/cm²) is at the top of dose response curve
- Weekly administration of MRG-110 showed improved perfusion, wound closure, and markers of vascularization (ITGA5 and CD31+ staining)
- Supports advancing into Phase 1 clinical trial in healthy, excised skin
Acknowledgments

- Linda Pestano
- Corrie Gallant-Behm
- Aimee Jackson
- Paul Rubin

Contact: RLM@miRagen.com

Poster: P.IRD4