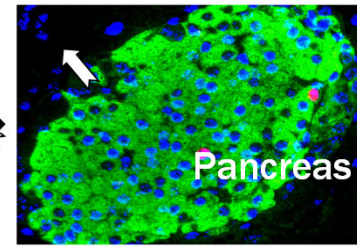
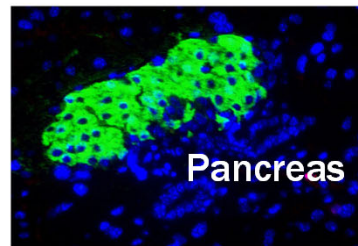




RESTORING PANCREATIC ISLET TO REVERSE DIABETES



ORAL

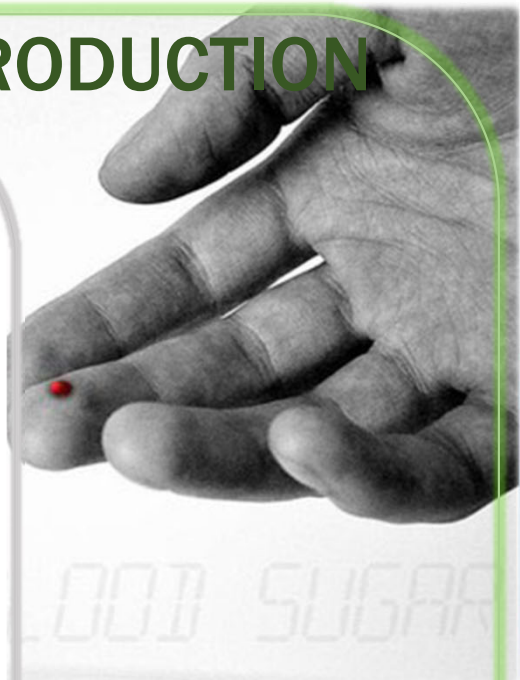


Frank Leu, Ph.D., Co-Founder & CEO
Email: frankleu@novapeutics.com
Phone: 646-275-9002

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COMPANY INTRODUCTION

- Novapeutics LLC is a preclinical biopharma company spun-out from the UPstart program at the University of Pennsylvania.
- We are developing a first-in-class small molecule oral cure for type 2 diabetes (T2D) patients via regeneration of their own insulin-producing beta cells.
- Our diabetes cure will be especially beneficial for treating mid to advanced stage T2D patients, many of whom suffer from inadequate and non-responsive pancreatic beta cells.
- Our technology could also treat type 1 diabetes (T1D).



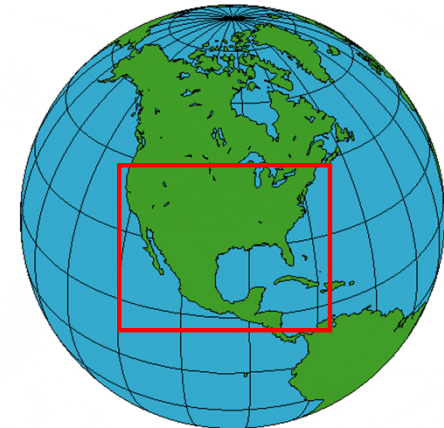
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PROBLEM

HOW BIG IS IT ?



Global Map Projection • North America

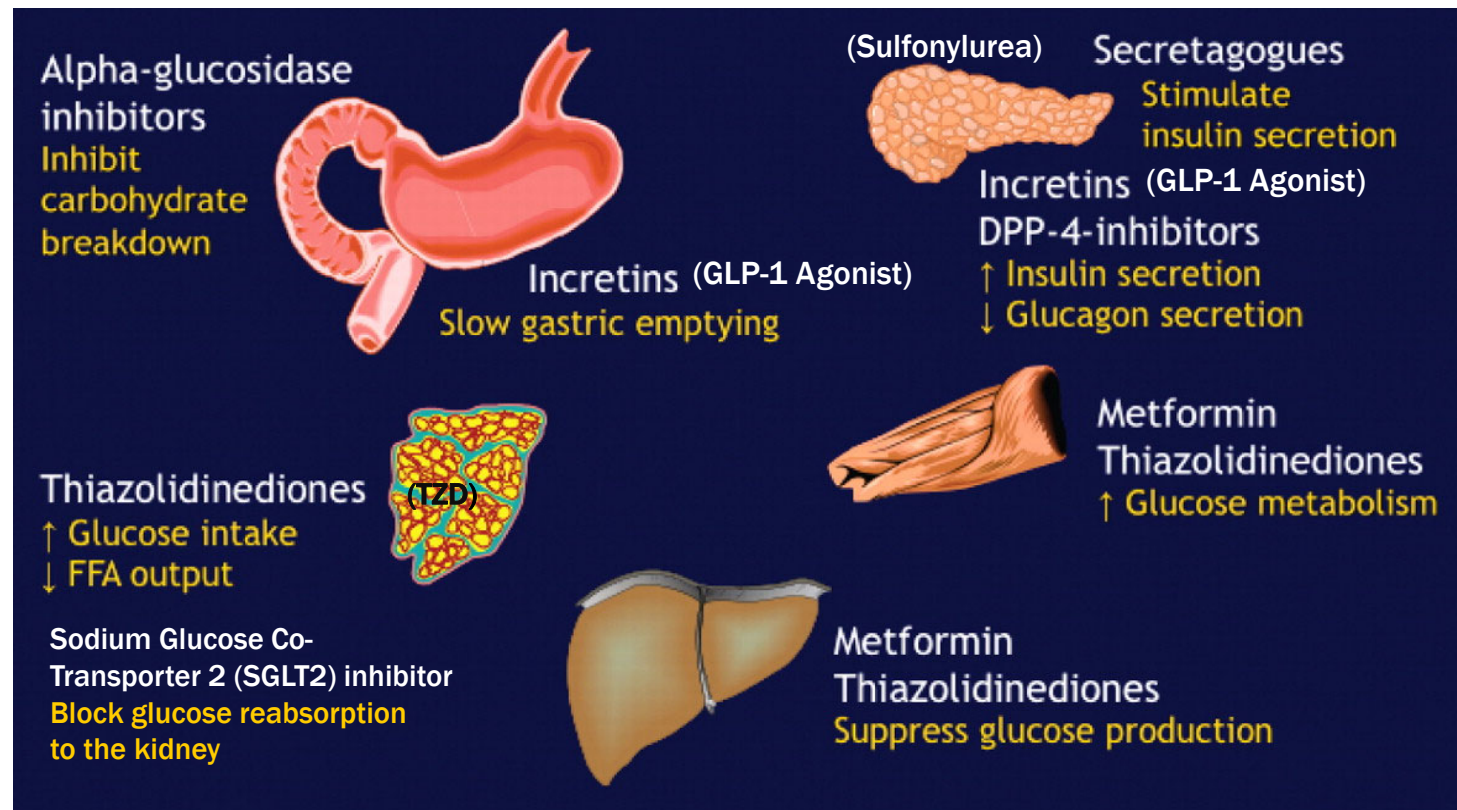
In the Year 2014, greater than 400 million people worldwide have diabetes.
- World Health Organization



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PROBLEM No T2D CURE



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CURRENT TREATMENTS INDUCE DIABETES COMPLICATIONS

Amputations



Wound



Heart disease



Blindness & Eye Problems



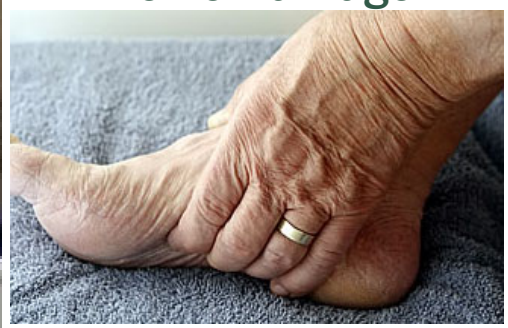
Stroke & Hypertension



Kidney Failure



Nerve Damage



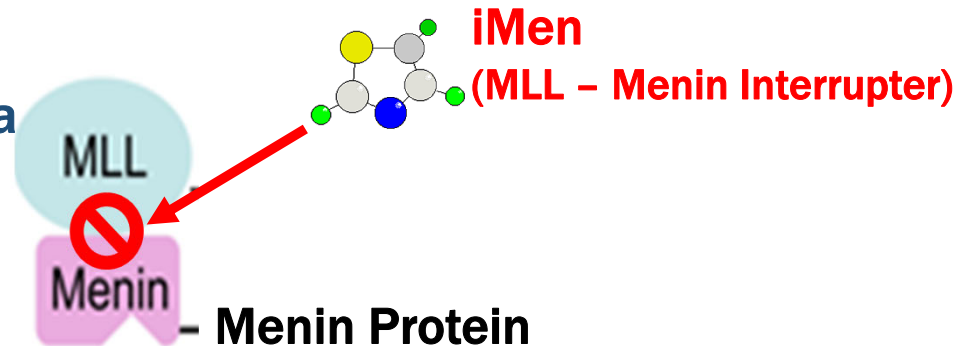
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OUR SOLUTION

SMALL CHEMICAL INDUCED PANCREATIC ISLET RESTORATION

Mix-Lineage Leukemia
Protein (MLL)



- Menin Protein

Has been reported to
interact close to **40**
different binding partners.

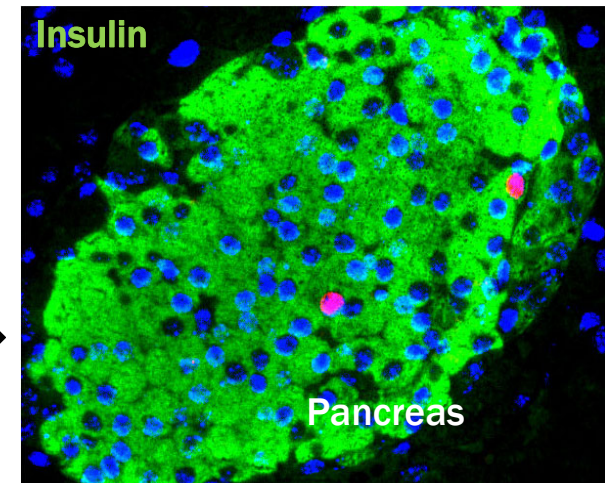
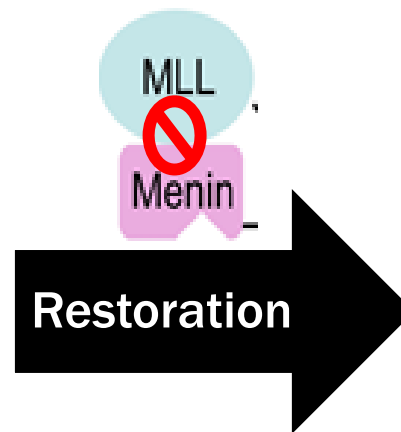
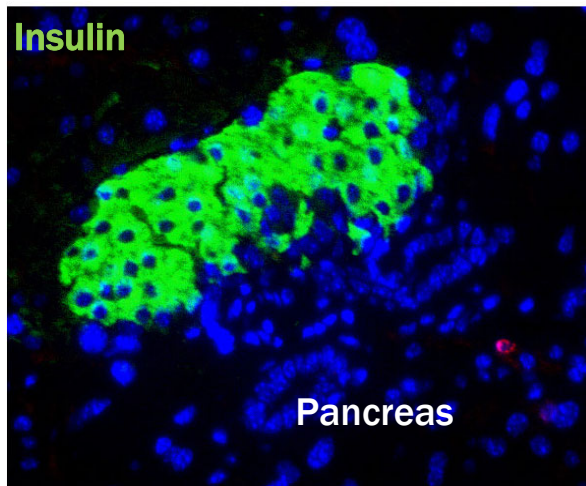
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OUR SOLUTION

A SMALL MOLECULE ORAL CURATIVE BY RESTORING BETA CELLS IN THE PANCREATIC ISLET



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DRUG DEVELOPMENT

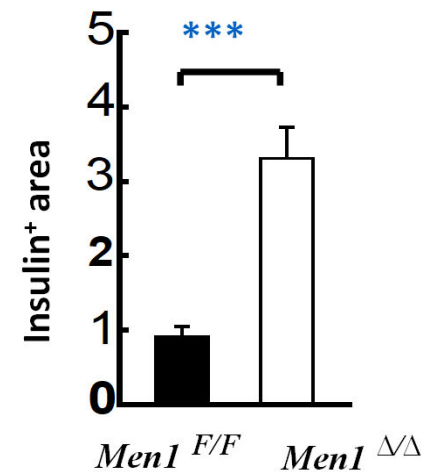
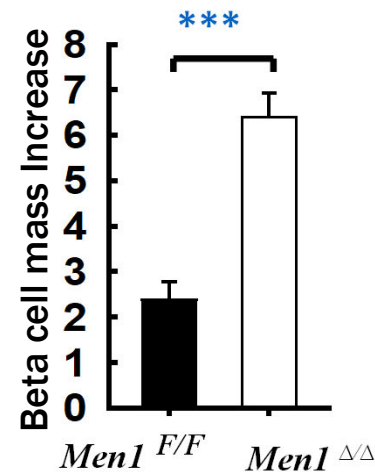
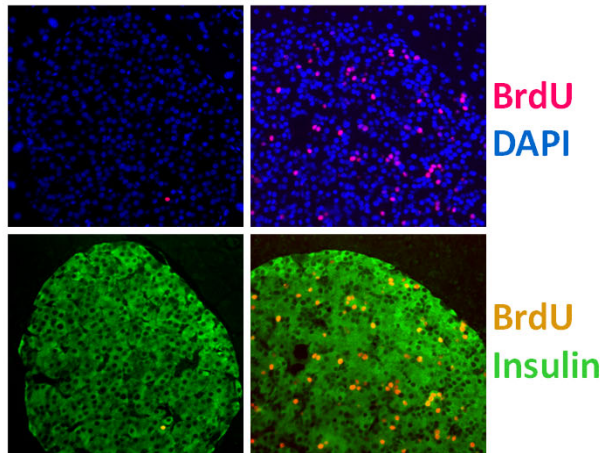
MENIN AS A DIABETES DRUG TARGET

Men1 gene excision significantly increases pancreatic beta cell regeneration and restores beta cell mass in the *db/db* mice, ultimately reverse diabetes. This menin dependent diabetes reversal also has been shown in the streptozotocin induced diabetes mouse.

Immunostaining

Men1^{F/F}

Men1^{ΔΔ}



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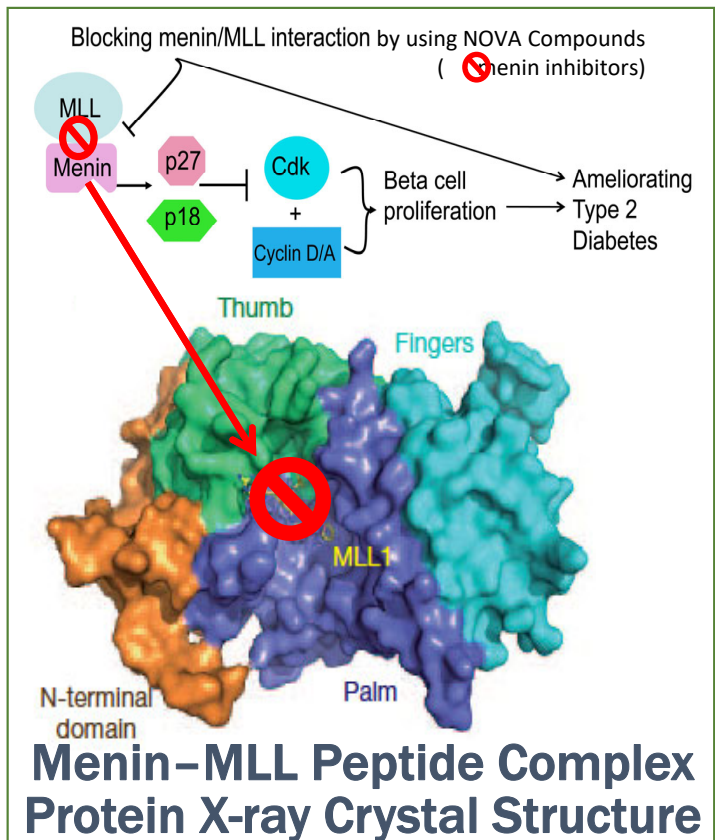
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DRUG DEVELOPMENT MECHANISM OF ACTION

iMen Interrupts the Menin-MLL Interaction and Regenerates Beta Cells

- Menin plays a major role in *in vivo* beta-cell regeneration.
- By selectively interrupting the menin-MLL protein interaction, iMen regenerates beta cells & restores pancreas function by down regulating cell cycle suppressors.
- We utilized structure based rational computational drug design to yield several potent leads.



J Huang et al. *Nature* 000, 1-5 (012)
doi:10.1038/nature10806

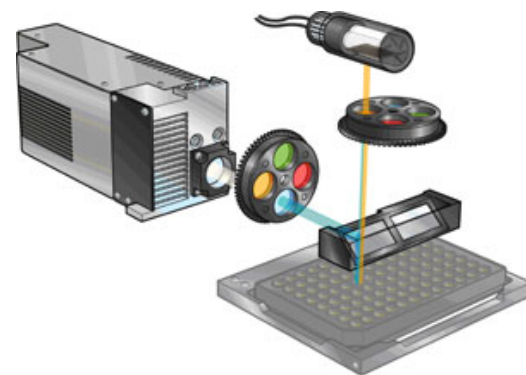
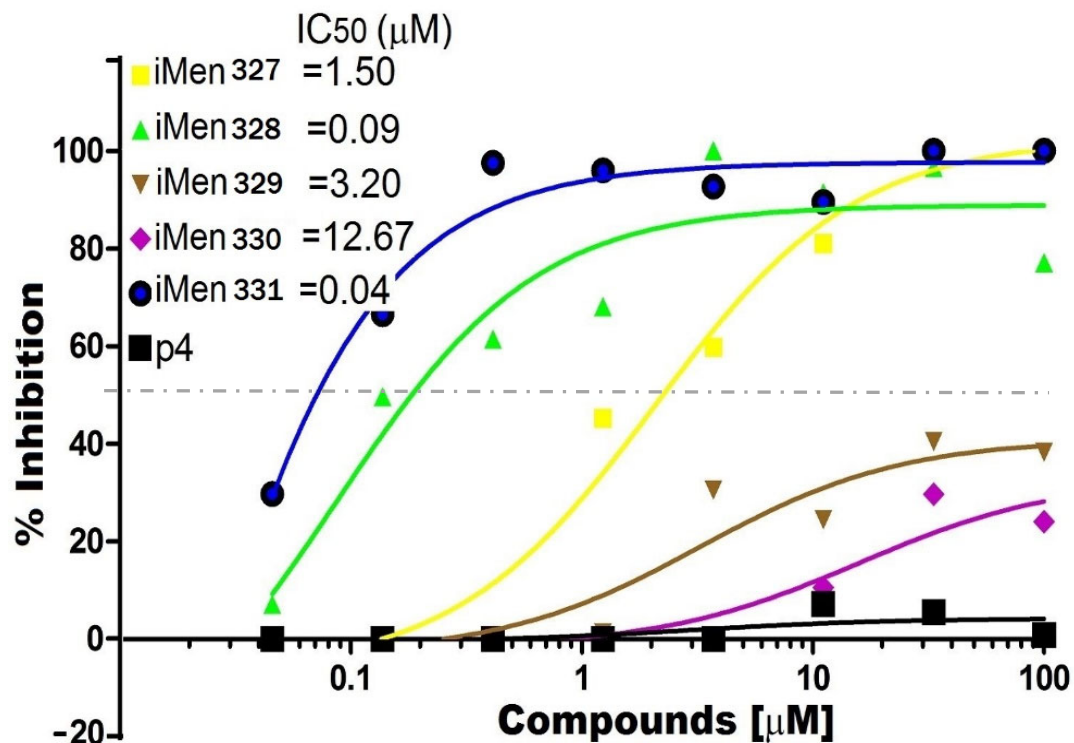
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DRUG DEVELOPMENT RAPID HIGH THROUGHPUT NOVEL COMPOUND SCREENING PLATFORM

HIGH THROUGHPUT SCREENING FLUORESCENCE-POLARIZATION ASSAY (FP ASSAY)



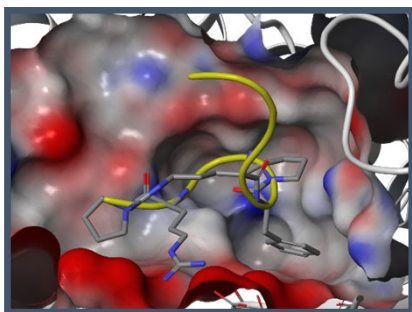
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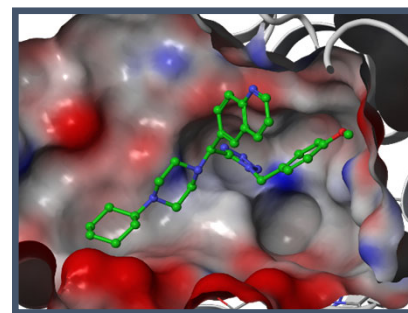
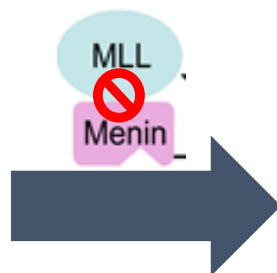


DRUG DEVELOPMENT

OUR POTENT MENIN-MLL INTERRUPTER LEADS



Menin-MLL Peptide Complex



iMen
(menin-MLL interrupter)

🚫 Couple of our best leads have excellent menin-MLL interrupter potencies with IC_{50} of 90nM and 40nM. They are ready for IND-enabling studies.



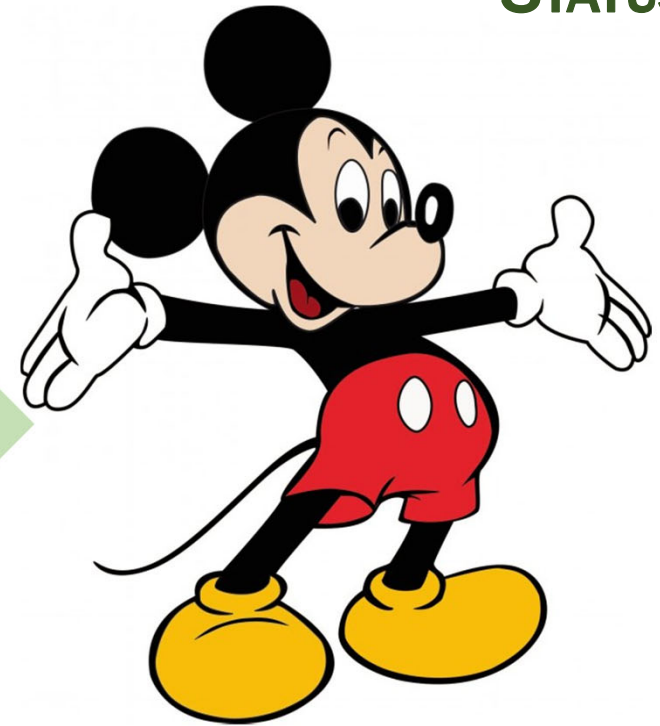
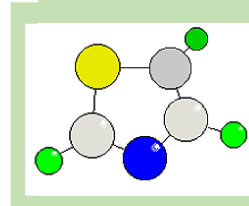
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COMPANY OVERVIEW

STATUS



Diabetes Reversal

- Non-Obese Diabetic (NOD) = T1D
- Diet Induced Obese (DIO) = T2D



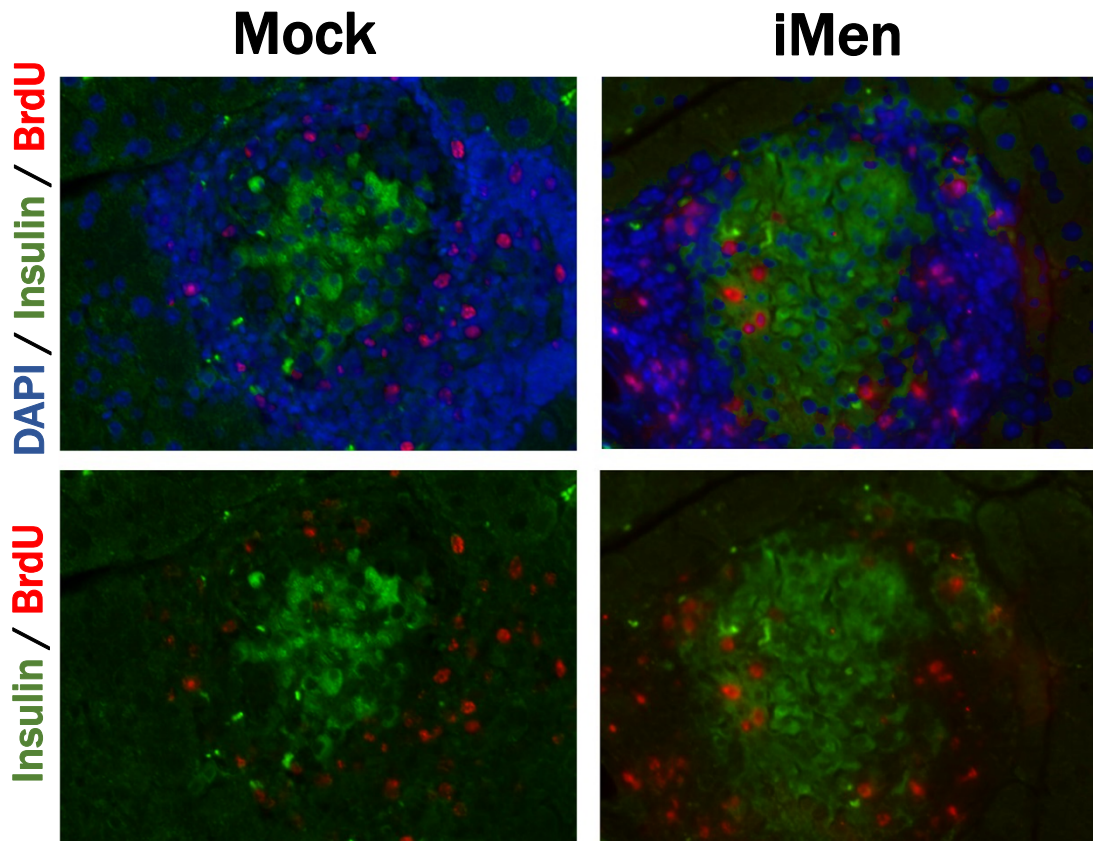
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DRUG DEVELOPMENT

iMEN RESTORES PANCREATIC ISLET



Immunofluorescence staining of Non Obese Diabetic (NOD) mouse pancreas. iMen restores Pancreatic islet mass and results in higher insulin production, showing a statistically significant ~3-fold increase with $P < 0.05$ in the number of islet cells per section of the pancreas measured.



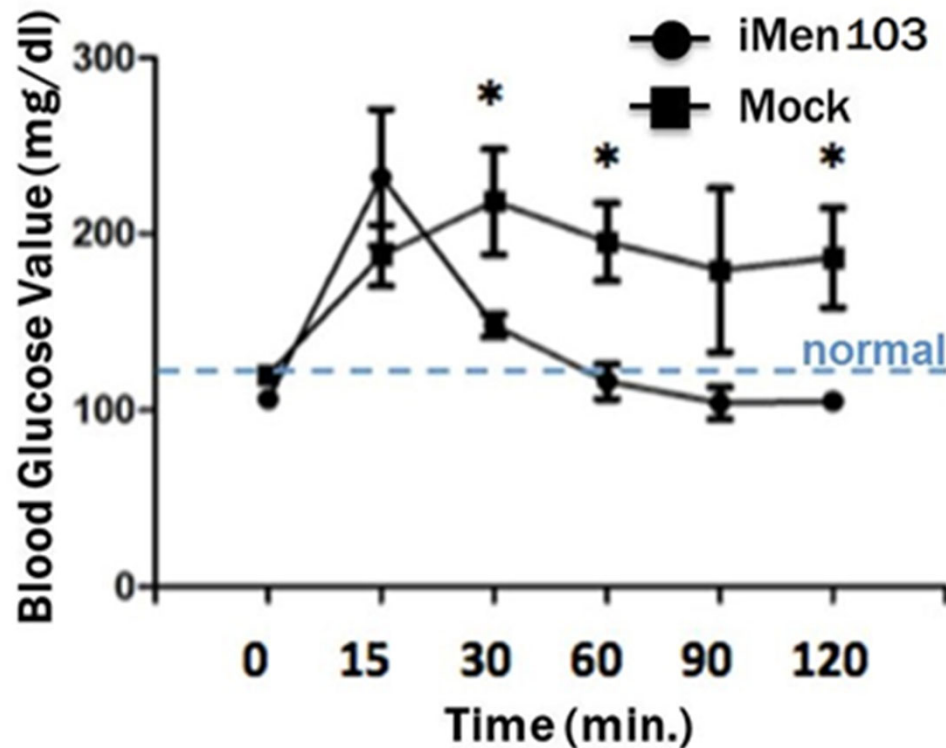
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DRUG DEVELOPMENT

iMEN NORMALIZES BLOOD GLUCOSE VALUE



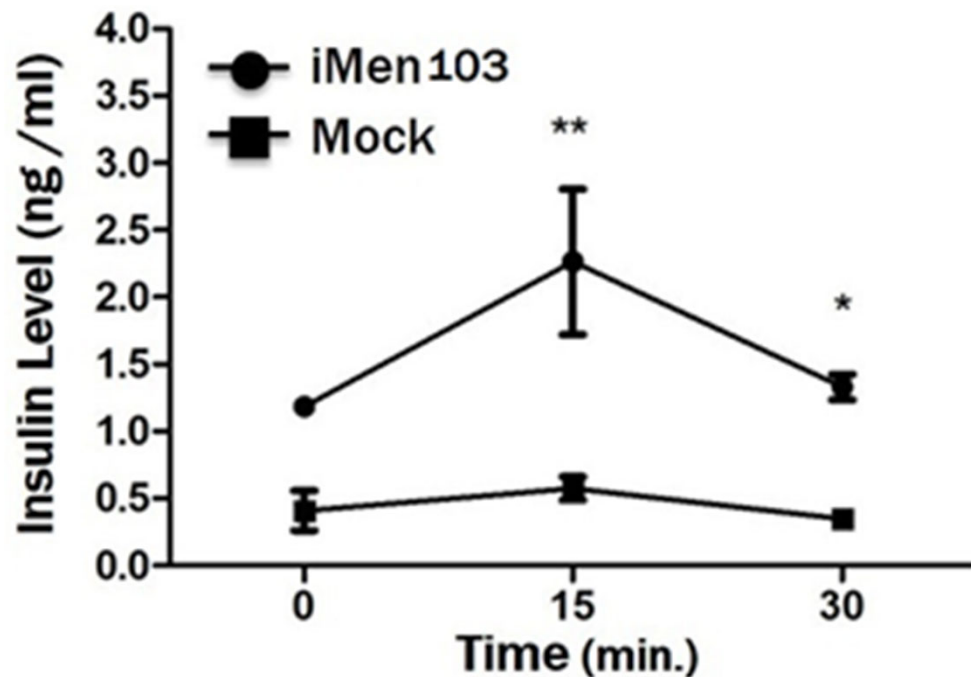
iMen significantly improves the function of the islets of NOD mice *in vivo* as shown in GTT. NOD mice were injected Intraperitoneally (I.P.) with iMen103 (●) or Mock (■) (9 week-old NOD injected daily for 9 weeks).



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DRUG DEVELOPMENT iMEN RESTORES INSULIN LEVEL



iMen markedly increased insulin levels detected in blood upon glucose stimulation in NOD diabetic mice *in vivo*. NOD mice were injected Intraperitoneally (I.P.) with iMen103 (●) or Mock (■) 9-week-old NOD mice injected daily for 10 weeks.



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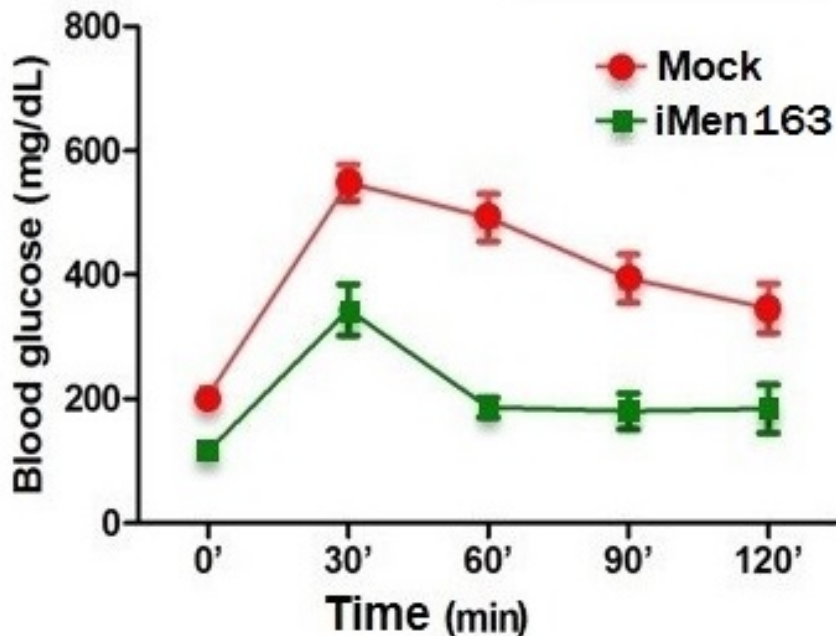
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DRUG DEVELOPMENT

iMEN REVERSES DIABETES IN T2D MICE

GTT in DIO mice after 2 weeks



iMen markedly increased insulin level detected in blood upon glucose tolerance test (GTT) in the DIO type 2 diabetic (T2D) mice *in vivo*. GTT after daily intraperitoneal injection (I.P.) with iMen163 (■) or Mock (●) at the age of 3 week-old on daily basis for 2 weeks.

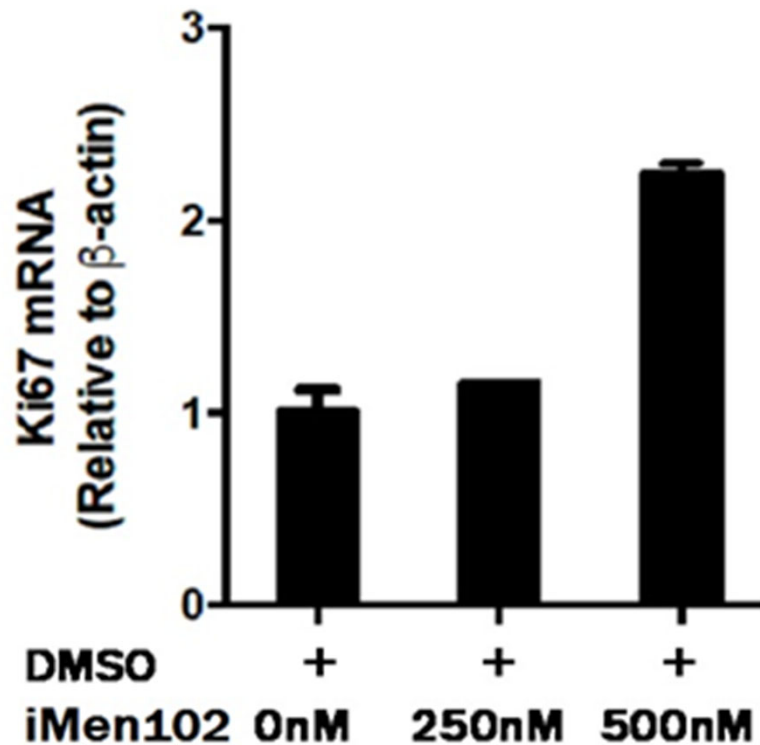


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DRUG DEVELOPMENT

iMen REGENERATES HUMAN BETA CELLS



iMen induces the regeneration of human beta cells. Treatment of human beta cells isolated from an 11-year-old donor for 7 days in culture medium, with either DMSO alone or plus iMen102 at 250nM or 500nM, followed by isolation of RNA and RT-PCR to detect the level of Ki67, a well-known marker for new cells generation.



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MARKET ASSESSMENT OVERVIEW

- Our drug would be administered orally to regenerate beta cells. We anticipate our curative approach could **displace the insulin market for T2D and potentially for T1D** as well.
- Existing oral drugs for T2D are used for treating early stages of the disease while **mid to advanced T2D patients rely on injectables** (i.e. GLP-1 agonist and insulin), which have less patient compliance.
- Our drug **could also be used as a first-line anti-diabetic agent**, which maybe the best way to impose its effectiveness as a curative agent, replacing early stage diabetes treatments such as Metformin and Thiazolidinediones.



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TECHNOLOGY DEVELOPMENT

- Genetic prove of concept that via *Men1* gene deletion *in vivo* significantly increases pancreatic beta cell mass, increases insulin production by ~3.5 fold, and reverses diabetes in a genetic murine model.
- Identified several potent novel iMen via structure-based rational drug design based on the X-ray menin-MLL peptide complex structure and high throughput screening.
- Demonstrated that iMen can reverse diabetes, restore pancreatic islet by regenerating beta cells in two different murine models: (1) NOD for Type 1 Diabetes & (2) DIO for Type 2 Diabetes.
- iMen can regenerate human beta cells in an *ex-in vivo* experiment.



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MARKET ASSESSMENT OVERVIEW

- Our drug is administered orally as a cure via beta cell regeneration. We anticipate our curative approach could **displace a large part of the insulin market for T2D and potentially for T1D** as well.
- Existing oral drugs for T2D are used for treating early stages of the disease while **mid to advanced T2D patients rely on injectables** (i.e. GLP-1 agonist and insulin), which have less patient compliance.
- Our drug **could also potentially be used as a first line anti-diabetic agent**, which maybe the best way to impose its effectiveness as a curative agent, replacing early stage diabetes treatments such as Metformin and Thiazolidinediones.



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MARKET ASSESSMENT OUR UNITED STATES MARKET

- The American Diabetes Association estimates **\$245B** per year in expenditures for diabetes related health-care in 2012. The T2D market alone is estimated at **~\$40B**. Every T2D patient could spend **~\$500K** in medical treatments in their lifetime.
- Approximately **67%** of T2D patients will end up using insulin injection as the main treatment, while up to **40%** of the T2D patients use insulin at any given time. It is estimated that our initial projected market for displacing injected Insulin alone would be **~\$10.7B**.

\$245B

Diabetes total
healthcare
expenditures

~\$40B

T2D drugs

\$15.6B

Our Market



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FINANCIALS SUMMARY

NON-DILUTIVE FUNDING

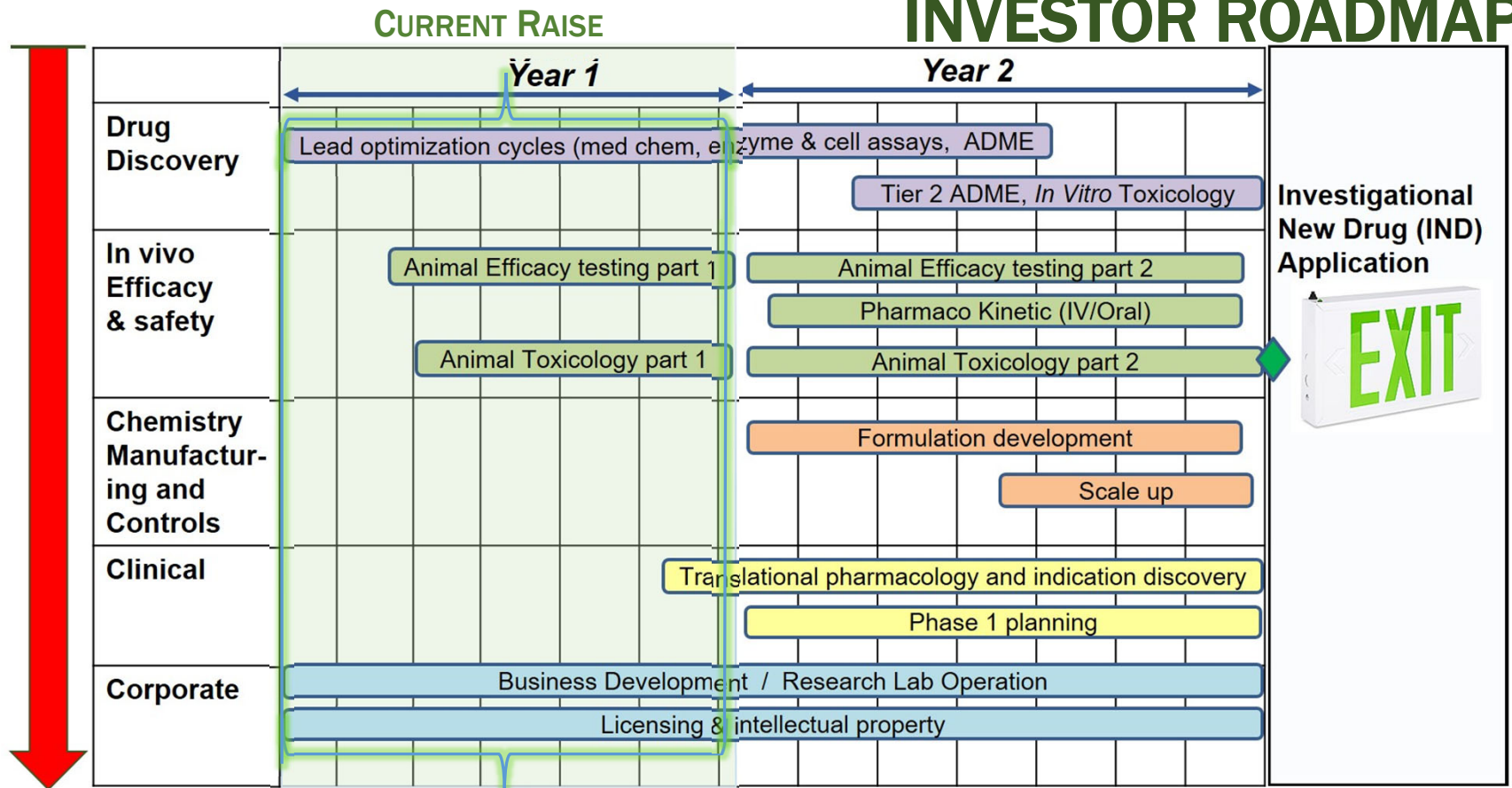
- \$10M of R&D grants (i.e. NIDDK and JDRF) were invested before and some during to formation of the company.
- \$252K Small Business Innovative Research Grant Phase 1 from the National Institute of Diabetes, Digestive and Kidney Diseases (NIDDK).
- \$100K plus the equivalent of in-kind support from Penn Center of Innovation Ventures since 2011.
- Harrington Innovator program funded ~\$300k up-to-date for technology development.



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INVESTOR ROADMAP



- ★ \$10M Plus in R&D
- ★ \$252K NIH SBIR Phase 1 award in 2013
- ★ \$300K Harrington Innovator Project Grant

\$1.0M

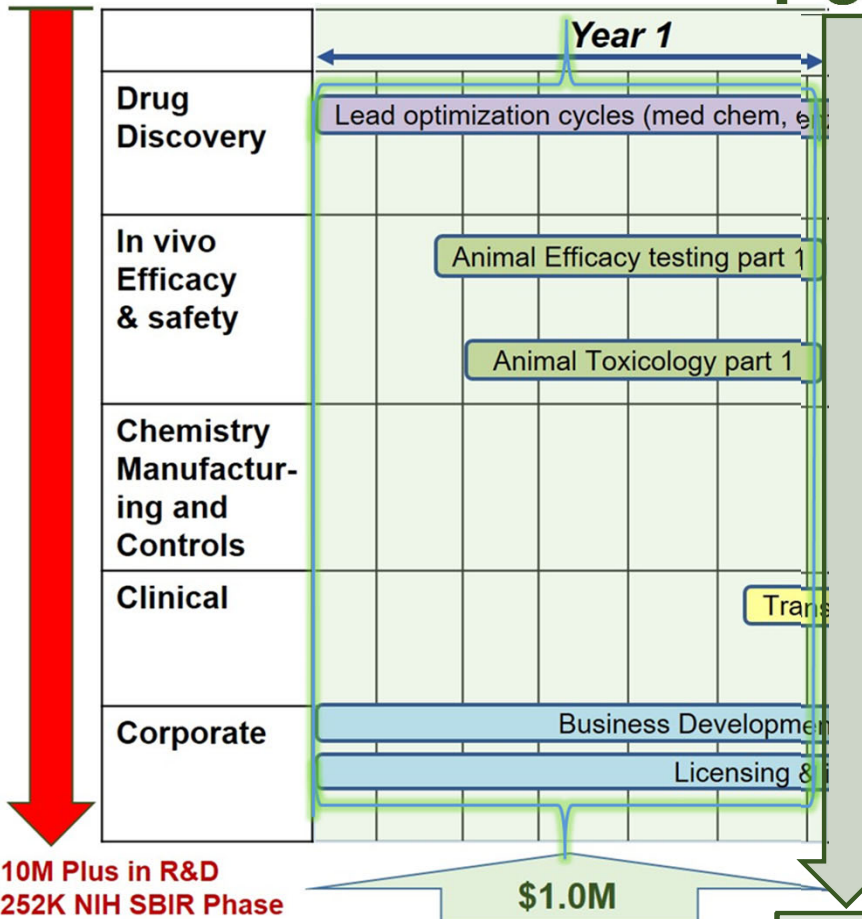
\$2.0 million



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POTENTIAL EXIT COMPARABLE



In 2010, CureDM an early preclinical stage company, with a beta cells regenerative peptide targeting an intracellular target did a global licensing deal with Sanofi for \$335 million at the stage of non-GLP murine studies. Our small molecule acts through an independent mechanism of action to regenerate beta cells and can be orally delivered instead of injection. Based on this demonstrated interest in the beta cell regenerative therapeutics, we anticipate that an exit could occur as early as anytime during the IND-enabling studies. Prior to the start of a Phase I clinical trial, which is scheduled to occur in 2 years.

- ★ \$10M Plus in R&D
- ★ \$252K NIH SBIR Phase 1 award in 2013
- ★ \$300K Harrington Innovator Project Grant

\$1.0M

CureDM global licensing deal with Sanofi for \$335M



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COMPETITIVE ADVANTAGE SUMMARY

- **Curative solution** restoring pancreatic islet via regenerating depleted beta cells
- **First-in-class drug mechanism**, Menin-MLL interrupter.
- **Administered orally** rather than by injection, thus increase patient compliance.
- **Does not need constant self-monitoring** of glucose levels and the use of an insulin pump.



BUSINESS DEVELOPMENT TECHNOLOGY & BUSINESS PARTNERS

- FoxChase Chemical Diversity Center for medicinal chemistry development.
- Absorption Systems (a potential stake holder) for our preclinical development / INDenabling studies partner.
- Fox Rothschild LLP for Legal Counsel.
- Stephano Slack LLP for Accounting. ➤ RSM US LLP for Strategic.
- Penn Center for Innovation Ventures (PCIV) is a stake holder and we have access to all of its partners and resources.
- Access and technical support from the Institute of Diabetes, Obesity and Metabolism at the University of Pennsylvania.



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Thank You !

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- Diabetes Curative
- Regeneration therapeutic
- Orally Delivered
- Small Molecule

Frank Leu, Ph.D., CEO, Co-Founder
Email: frankleu@novapeutics.com
Phone: 646-275-9002

