OUR VISION

type none
OUR PURPOSE
JDRF was Founded by Families Driven to Cure T1D

Lee Ducat, Lester Salans, M.D. (NIH), Carol Lurie
THE PLAN

Doing the Greatest Good, for the Largest Number of People, in the Shortest Period of Time
THE PLAN

Accelerating Progress Across the Pipeline
THE PLAN
Accelerating Progress Across the Pipeline

TO DELIVER LIFE-CHANGING BREAKTHROUGHS

CURE
Restoring Insulin Independence

PREVENT
Preventing Symptomatic T1D

TREAT
Improving Glucose Control
WE’VE COME A LONG WAY...
We used to measure urine glucose, there was no home blood glucose testing!
This was my first lancet device!
And my first test strips...
The first artificial pancreas circa 1964...
One of the first commercial insulin pumps, the “blue brick”
BUT NOT FAR ENOUGH...
Limited Success Achieving HbA1c Targets

A1c Goal = <7.5%

A1c Goal = <7.0%

Mean HbA1c (%) by Age (years):
- <6: 21%
- 6-<13: 21%
- 13-<18: 17%
- 18-<26: 13%
- 26-<50: 32%
- ≥50: 29%
Average Current HbA1c by Age

Mean HbA1c by Age, years*

6yo, 17yo, 30yo

*≤2 years old and ≥80 years old are pooled
Hypo is still common – even with incredible efforts to avoid it.

### Predictive Low Glucose Suspend in Children

<table>
<thead>
<tr>
<th></th>
<th>11 -14 Year Olds</th>
<th></th>
<th>4 – 10 Year Olds</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>System Active</td>
<td></td>
<td>Control</td>
</tr>
<tr>
<td># nights</td>
<td>941</td>
<td>955</td>
<td></td>
<td>755</td>
</tr>
<tr>
<td>% nights &lt;60 for 120 min</td>
<td>8%</td>
<td>3%</td>
<td>&lt; 0.001</td>
<td>5%</td>
</tr>
<tr>
<td>Mean Overnight Glucose (mg/dl)</td>
<td>144 ± 18</td>
<td>152 ± 19</td>
<td>&lt; 0.001</td>
<td>153 ± 14</td>
</tr>
</tbody>
</table>

Buckingham et al. 2015.
INSIDE THE PIPELINE

Continuous Therapeutic Improvements

Targeted programs to deliver better outcomes.......
Moving Forward, New Therapies Must Improve Diabetes Health and Diabetes Happiness!

Diabetes Health

Work/Effort/Burden

Diabetes Happiness (QoL)

ROI
THE PLAN
Artificial Pancreas

Our plan is to create a future where...

Artificial Pancreas

The burden is eased all day, and you sleep safely through the night.
Artificial Pancreas
TIGHTER CONTROL OF BLOOD GLUCOSE WITH REDUCED BURDEN
We are making progress, fast.....

Veo-worldwide

640G Australia, Denmark UK – USA soon

670g Anticipated NOW!!!

Next steps:
- Faster insulin action, miniaturization, integration, individualized control

Next steps:
- Glucagon: Soluble pumpable glucagon, chronic glucagon exposure studies, dual-chamber pump development, algorithm finalization, head-to-head vs. AID
- Amylin: Coformulation vs. dual-chamber pump, ratio determination, algorithm finalization, head-to-head vs. AID

Suspend

Predictive Suspend

Automated Insulin Delivery (AID)

Multihormone (MH)
First AP-CL system on the market in 2017!

Pivotal 670G - 3 months

n=124, 72.2% in range 70-180 mg/dL, A1C 7.4% to 6.9% (All)

- BS range using open loop
- BS range using closed loop
First AP-CL system on the market in 2017!

**Pivotal 670G - Adults**

- BS range using open loop
- BS range using closed loop

n=90, 73.8% in range 70-180 mg/dL, A1C 7.3% to 6.8%

Ref - Bergenstal et. al. LB Poster Presentation ADA 2016
First AP-CL system on the market in 2017!

Pivotal 670G - Adolescents
n=34, 67.2% in range 70-180 mg/dL, A1C 7.7% to 7.1%

BS range using open loop
BS range using closed loop
PATHWAYS TO ARTIFICIAL PANCREAS SYSTEMS

AP Systems are coming......Commercialization

- MDT: Hybrid CL: 2017
- Animas HHM
- Bigfoot Biomedical: Hybrid CL
- Type Zero: Hybrid CL
- Boston University: Dual-hormone
- Inreda: Dual-hormone
- Tandem
- Insulet
- Roche
Bigfoot Biomedical System
Sensor Will Get Smaller and Smaller
And Fingersticks Will Become Obsolete

Google Partnership Objectives

Develop a simple, low-cost, disposable body-worn sensor system integrated into an advanced data analytics platform to drive entry into Type 2 market and to expand CGM use in Type 1 market.
THE PLAN

Glucose Control

Our plan is to create a future where...

Glucose Control

Highs and lows are kept in check
Insulin on demand → Activity proportional to blood glucose levels

Improve Outcomes:
- **Glucose Control**: Reduce highs and lows; increase Time-in-Range (TIR); reduce complications
- **Quality of Life (QoL)**: Reduce burden, anxiety/fear, human errors

Priorities:
- Support discovery and development of GRI therapies for individuals with insulin-dependent diabetes
- Bring together individuals with diverse expertise required for GRI design
- Partner to ensure accelerated translation into human studies
EVEN AN INSULIN THAT STOPS WORKING WHEN GLUCOSE LEVEL IS LOW IS A WIN

GRI: A Design Concept

**An insulin that stops working when glucose levels are low**

**Increasing Glucose Level**

**Increasing Insulin Activity**
THE PLAN

Complications

Our plan is to create a future where...

Complications

Diabetes doesn’t bring other health problems
Notes: * The 2011 Scottish Diabetes Survey did not have % of T1D patients that reached all three targets
Source: NHS Scotland, L.E.K. interviews and analysis
JDRF Research and Advocacy efforts lead to pivotal trial by NIH (SDP)

- High blood uric acid levels predict progression of nephropathy in T1D
- Allopurinol is a widely used generic drug that reduces uric acid levels
- JDRF-funded PERL pilot clinical study initiated to see if allopurinol can reduce progression of nephropathy in T1D
- SDP now funding pivotal study recruiting 450 people with T1D and nephropathy
Extracellular carbonic anhydrase mediates hemorrhagic retinal and cerebral vascular permeability through prekallikrein activation

Ben-Bo Gao, Allen Clermont, Susan Rook, Stephanie J Fonda, Vivek J Srinivasan, Maciej Wojtkowski, James G Fujimoto, Robert L Avery, Paul G Arrigg, Sven-Erik Bursell, Lloyd Paul Aiello, and Edward P Feener

Phase 1 study completed 2Q2016
THE PLAN

Prevention

Our plan is to create a future where...

Prevention

T1D can be prevented and will never threaten anyone again
WHY SHOULD I CARE ABOUT PREVENTION?

T1D can affect family members and others

- What is the risk for developing type 1 diabetes among family members compared to the rest of the population?
  - No difference
  - 3X greater risk
  - 15X greater risk

- ....but ~85% of newly diagnosed T1D do NOT have a family history!
IT IS NOT A QUESTION OF “IF” BUT “WHEN”……
Risk of T1D progression with autoantibodies

George Eisenbarth: „The clock to T1D has started when islet antibodies are first detected“. Paradigm shift for staging of type 1 diabetes before clinical onset

And the Lifetime Risk approaches 100%

[JAMA. 2013;309(23):2473-2479]
T1D happens in stages and starts with 2 antibodies

- Stage 1: Presence of 2 or more autoantibodies with normal blood sugar
- Stage 2: Presence of 2 or more autoantibodies with abnormal blood sugar
- Stage 3: Clinical diagnosis of T1D

Staging Presymptomatic Type 1 Diabetes: A Scientific Statement of JDRF, the Endocrine Society, and the American Diabetes Association

MULTIPLE CAUSES WITH MANY UNKNOWNS
Multi-pronged strategy to eradicate T1D

- **Enteroviruses**: Virus and islet cell damage in pancreas, viral antibodies and infection detected before onset of autoimmunity/disease
  - T1D Genetics: IFIH1 gene affects response to enterovirus

- **Hygiene Hypothesis and Gut Microbiome**: The JDRF Microbiome Consortium created in 2011 to engage the community, create collaborations and drive the field forward
  - Several vaccine projects, including vaccines to induce normal microorganisms in the GI tract

- **Insulin Resistance and Dysglycemia**: Cause or Accelerator?
  - Evaluate glycemic, β-cell specific and metabolic agents in preventing progression in at-risk and preclinical stages
WHY SHOULD I CARE ABOUT PREVENTION?

T1D can affect family members and others

- Risk of T1D in relatives of individuals with T1D:
  - Identical Twin: 30-70%
  - Multiple Affected First Degree Relatives: 20-50%
  - Sibling: 8% (but if HLA risk genes identical: 30-70%)
  - Offspring:
    - Father: 5%
    - Mother: 3%

- If no Family Hx - General Population: 0.4% (but if HLA risk genes: 4%)

*JDRF supporting activities toward regulatory acceptance and cost-effective screening tools for global implementation*
THE PLAN
Beta Cell Replacement

Our plan is to create a future where...

Beta Cell Replacement

You can skip counting carbs for months at a time
Replacement program priorities

- β cell sources from stem cells and pigs are available but need optimization
- Encapsulation Systems that provide complete immunoisolation
- Retrievable scaffold (open concept)
  - Reliant on cell engineering or other forms of immune tolerance to confer immune protection

Macro-encapsulation

Micro & nano encapsulation

Scaffold/Hydrogels
Engineered cell source: with genetic modification
Local immune modulators
THE PLAN

Restoration

Our plan is to create a future where...

Restoration

Producing your own insulin doesn’t require a second thought
INNOVATIVE SOLUTION FOR PUTTING BETA CELLS BACK IN THE BODY
Generating Improved β/Islet Cells through Genetic Modifications

- Recent advances in gene editing technologies open up the intriguing possibility of generating modified cell sources that have improved survival, function and can protect themselves from the immune system without encapsulation or immunosuppressive drugs, leading to new program focus.

- 7 new projects to use this approach to both human and porcine islet sources.

Genes to confer immune protection or increase β cell function
JDRF Changes Dogma in β Cell Health and Survival

Healthy β cell

Glucose
Normal, processed insulin

Stressed β cell

Glucose
Inactive, misfolded insulin

Dead β cell

No insulin

Relieve β cell stress -> restore β cell function and slow/stop autoimmune process

• Stress feedback loop
• β cell demise
• Accelerates autoimmunity
Multiple clinical studies in β cell survival

- **Healthy β cell**: Normal, processed insulin
- **Stressed β cell**: Inactive, misfolded insulin
- **Dead β cell**: No insulin

**Compounds**:
- TUDCA
- Verapamil
- DFMO
INSIDE THE PIPELINE
Continuous Therapeutic Improvements

Right Individual → Right Stage → Right Therapy → Right Dose

ARTIFICIAL PANCREAS | COMPLICATIONS | BETA CELL REPLACEMENT | GLUCOSE CONTROL (INCLUDING SMART INSULIN) | RESTORATION | PREVENTION

The Plan for a World without T1D
YOUR SUPPORT

Raising Awareness. Raising Funds.

AN IN-SCHOOL PROGRAM GEARED TOWARD AWARENESS, EDUCATION AND FUNDRAISING FOR T1D RESEARCH

BIKE RIDERS REACH PERSONAL TRAINING GOALS AS THEY RAISE FUNDS FOR CRITICAL RESEARCH

THE FUNDS RAISED BY JDRF ONE WALK® – OUR FLAGSHIP FUNDRAISING EVENT AND THE LARGEST T1D EVENT IN THE WORLD – HELP US TURN TYPE ONE INTO TYPE NONE.

AN OPPORTUNITY TO TURN A FAVORITE SPORT, HOBBY OR LIFE EVENT INTO A JDRF FUNDRAISER
CONTACT
Here’s Where You Can Find Us

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THANK YOU

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