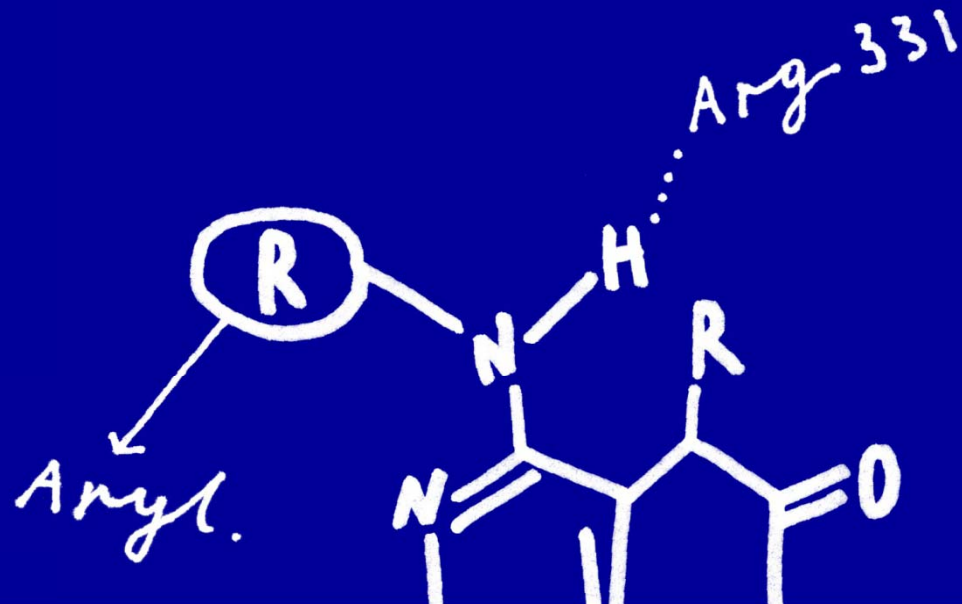


# Addressing causes not symptoms in diabetes

## CUREBETA



## Forward-looking statements

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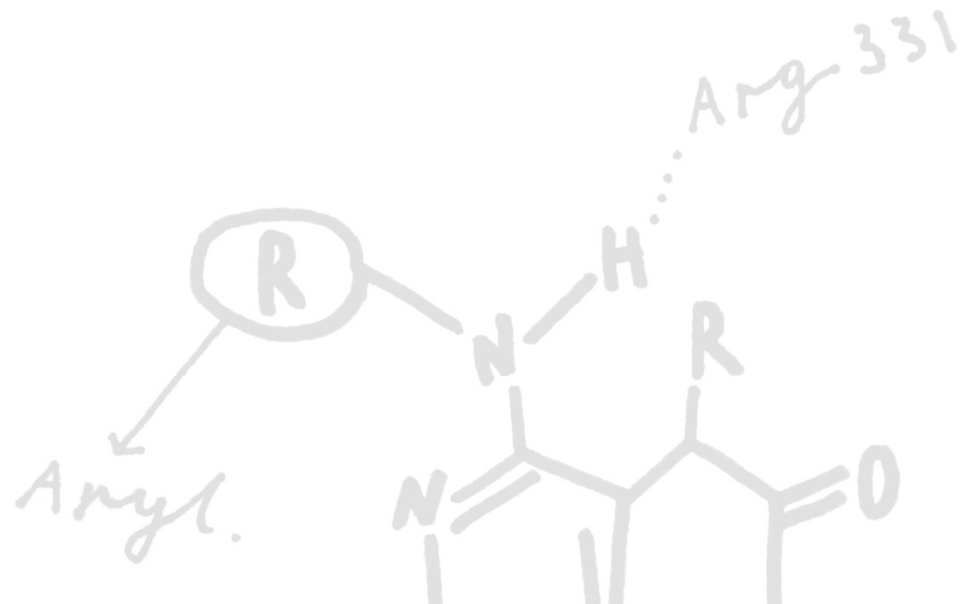
*Information set forth in this presentation contains forward-looking statements, which involve a number of risks and uncertainties. The forward-looking statements contained herein represent the judgement of Evotec as of the date of this report. Such forward-looking statements are neither promises nor guarantees, but are subject to a variety of risks and uncertainties, many of which are*

*beyond our control, and which could cause actual results to differ materially from those contemplated in these forward-looking statements. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any such statements to reflect any change in our expectations or any change in events, conditions or circumstances on which any such statement is based.*

## Agenda

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- **CUREBETA & Strategic background**
- Scientific vision and discovery background & other Cure X initiatives
- Next steps



# Cure X - First-in-class science a key building block of Action Plan 2016

Evotec's offering for Innovation Efficiency

## 3 EVT Innovate (Cure X initiatives)

- First-in-class discovery and product development innovations
- Modest R&D investments for high upfront, higher milestone and higher royalty alliances

## 2 EVT Integrate

- Integrated drug discovery alliances on partner targets
- Best-in-class integrated drug discovery alliances (multi-target projects)
- Risk-shared performance-based alliances with research fees, milestones and royalties

## 1 EVT Execute

- Stand alone screening, medicinal chemistry, compound management, compound profiling,...
- Highest quality solution tools and processes
- No risk-exposure, lower margin, but long-term repeat business

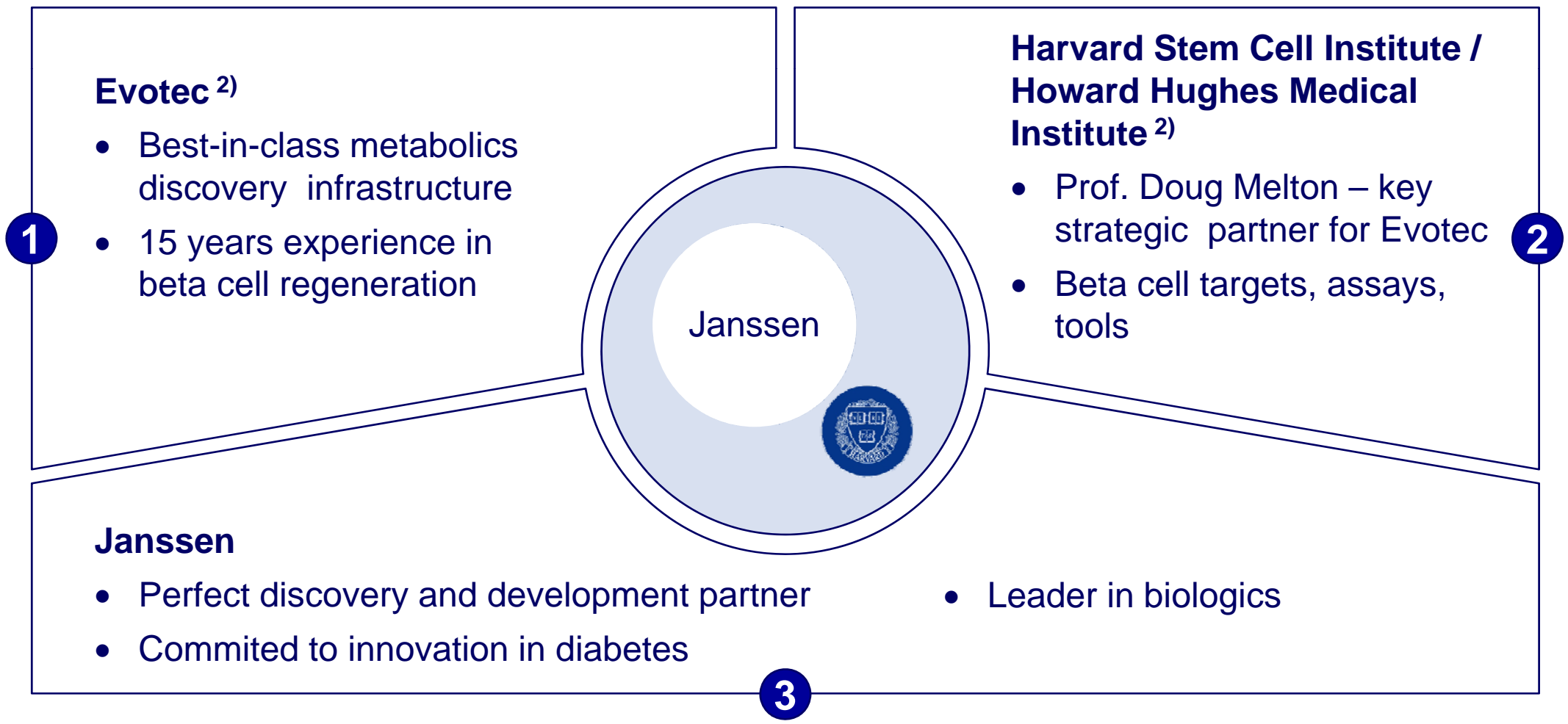
# CUREBETA

## Summary – “Win – Win – Win” Situation

<p><b>CureBeta terms</b></p>	<ul style="list-style-type: none"> <li>• Upfront US \$ 8 Mio, potential milestones about US \$ 200 - 300 Mio per product (pre-clinical, clinical, regulatory, commercial),</li> <li>• Royalties</li> <li>• Research payments</li> </ul>
<p><b>Win/Win/Win alliance</b></p>	<ul style="list-style-type: none"> <li>• <b>Janssen:</b> Access to an exclusive portfolio of small molecule and biologic research programs focused on the regeneration of insulin-producing beta cells in people with diabetes</li> <li>• <b>Evotec:</b> Expanding leadership in beta cell regeneration - highly systematic, unbiased and comprehensive approach to beta cell replication</li> <li>• <b>Harvard:</b> Accelerating development of innovative science with commercial upside</li> </ul>
<p><b>Starting point for innovation efficiency and external innovation</b></p>	<ul style="list-style-type: none"> <li>• Pharma industry appreciates the approach &amp; seems keen to enter these type of deals</li> <li>• Optimal translational strategy for academia or early biotech ideas as targets get immediately on pharma grade infrastructures</li> <li>• Building Cure X platforms has dual upside             <ul style="list-style-type: none"> <li>– Building infrastructure for EVT Integrate business in new fields</li> <li>– Building early stage project portfolios for EVT Innovate alliances</li> </ul> </li> </ul>

# Great Partners

## Who is CureBeta<sup>1)</sup>?



1) The JDRF (Juvenile Diabetes Foundation) will also support CureBeta  
 2) Evotec / Harvard Alliance - initiated in Q1 2011

# Bringing best of science and industry together

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## Quotes from Evotec – Janssen - JDRF

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*"Our collaboration with Doug Melton's laboratory has been extremely successful on multiple levels. We have not only achieved our scientific goals of creating a superior beta cell drug discovery platform and generating a deep pipeline of novel and exciting targets, but we have also established a new model of collaboration between academia and industry that has proven highly efficient and effective in accelerating innovative scientific development. Janssen Pharmaceuticals perfectly complements this effort, bringing in world-leading pharmaceutical development expertise as well as the necessary resources to execute on our mission to produce first-in-class therapeutics designed to restore beta cell mass and function."*

**Dr. Cord Dohrmann**  
Chief Scientific Officer of Evotec

*"Beta cell survival and function play a critical role in maintaining normal glucose levels and when they are compromised, can contribute to the onset of diabetes. This collaboration strengthens our long term diabetes development pipeline and directly reflects our commitment to making a difference for the millions of people worldwide living with this disease."*

**Peter DiBattiste, M.D., Global Therapeutic Head, Cardiovascular and Metabolism at Janssen**

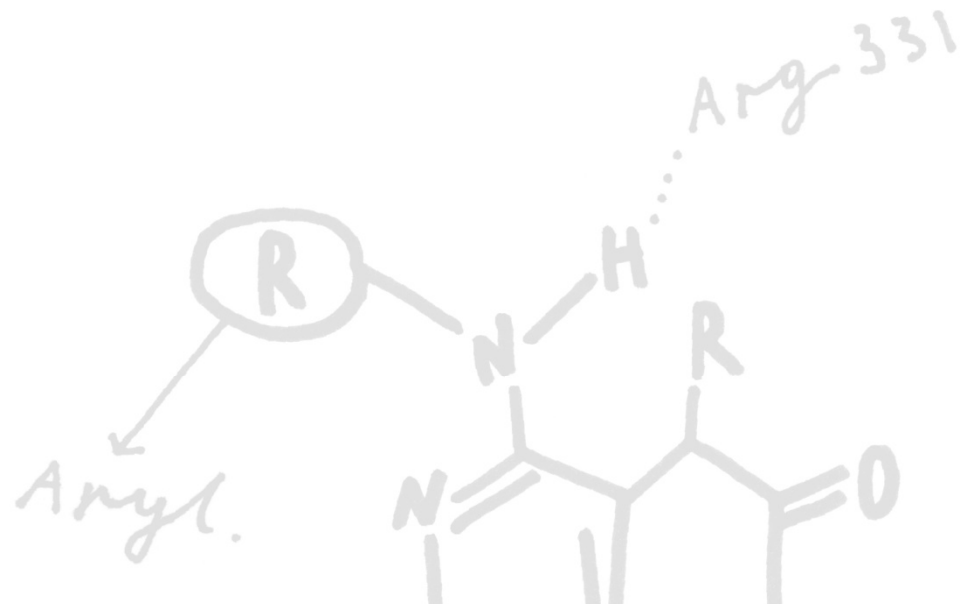
*"We are delighted to see Evotec, Dr. Doug Melton, and Janssen launch this collaborative partnership and commitment to develop innovative regenerative medicine therapies for diabetes. JDRF looks forward to supporting the CureBeta initiative."*

**Dr. Richard Insel, Chief Scientific Officer  
Juvenile Diabetes Research Foundation (JDRF)**

## Agenda

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- *CUREBETA* & Strategic background
- **Scientific vision and discovery background & other Cure X initiatives**
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# Why is there such a dramatic unmet medical need?

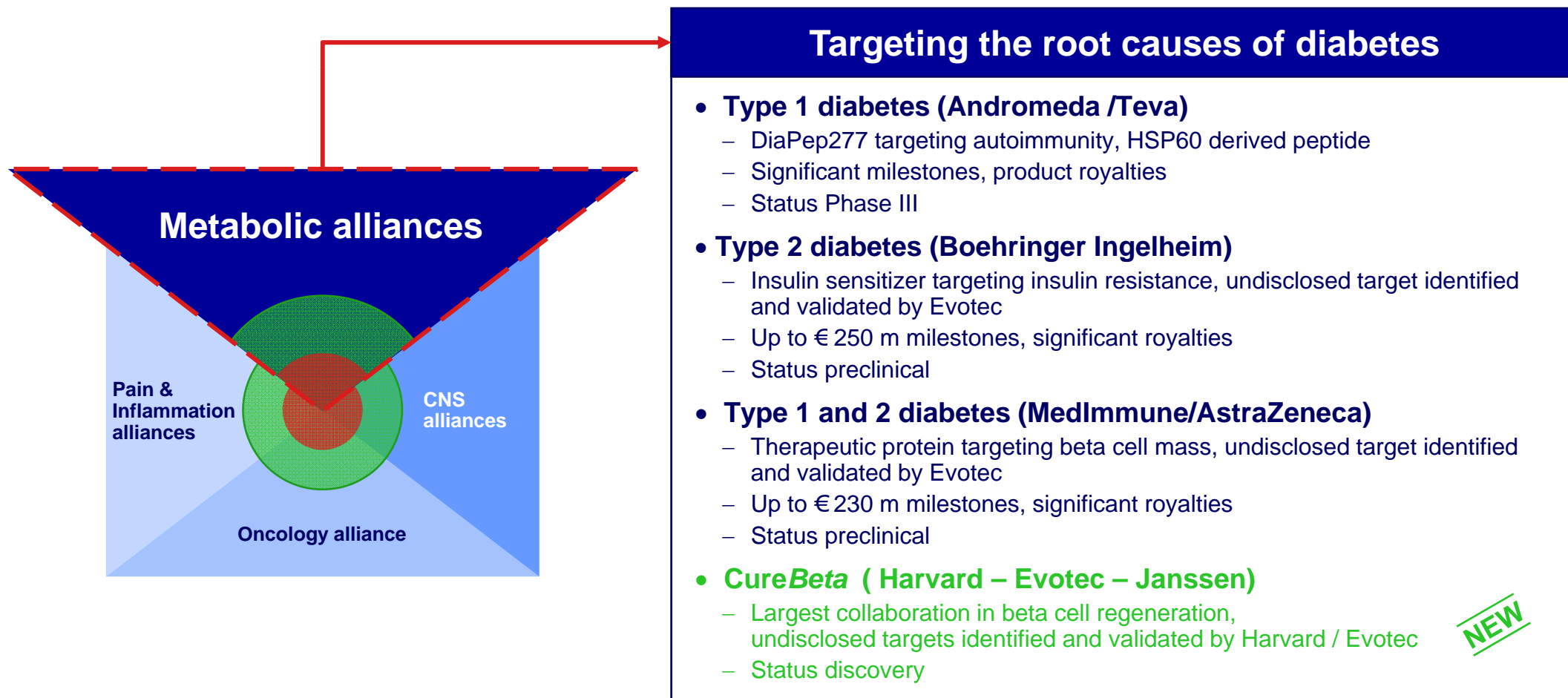
## Important Facts about Diabetes

- 1** Two major forms of diabetes type 1 and type 2  
Insufficient beta cell function common to both
- 2** More than 346 million people worldwide have diabetes  
183 million people (50%) with diabetes are undiagnosed
- 3** Diabetes caused 4.6 million deaths in 2011  
Predicted to become the 7<sup>th</sup> leading cause of death in the world by the year 2030
- 4** Diabetes is a leading cause of blindness, amputation and kidney failure  
Comorbidities associated with diabetes represent a tremendous burden to society
- 5** Diabetes caused at least USD 465 billion dollars in healthcare expenditures in 2011;  
11% of total healthcare expenditures in adults (20-79 years old)
- 6** Most people with diabetes are between 40-59 years of age  
Patient population is getting continuously younger
- 7** Top selling drug in 2011: Lantus (Insulin analogue) – \$ 4.9 billion  
Followed by Januvia – \$ 3.3 billion
- 8** U.S. is the single largest market in diabetes at roughly 37% of the global market  
Percentage will drop to 28% by 2018, primarily as a result of significant growth in Asia/Pacific
- 9** No disease modifying therapies on the market or in late stages of clinical development




# Multiple highly innovative, potentially disease modifying approaches

## Evotec's unique diabetes franchise



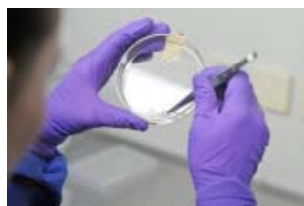
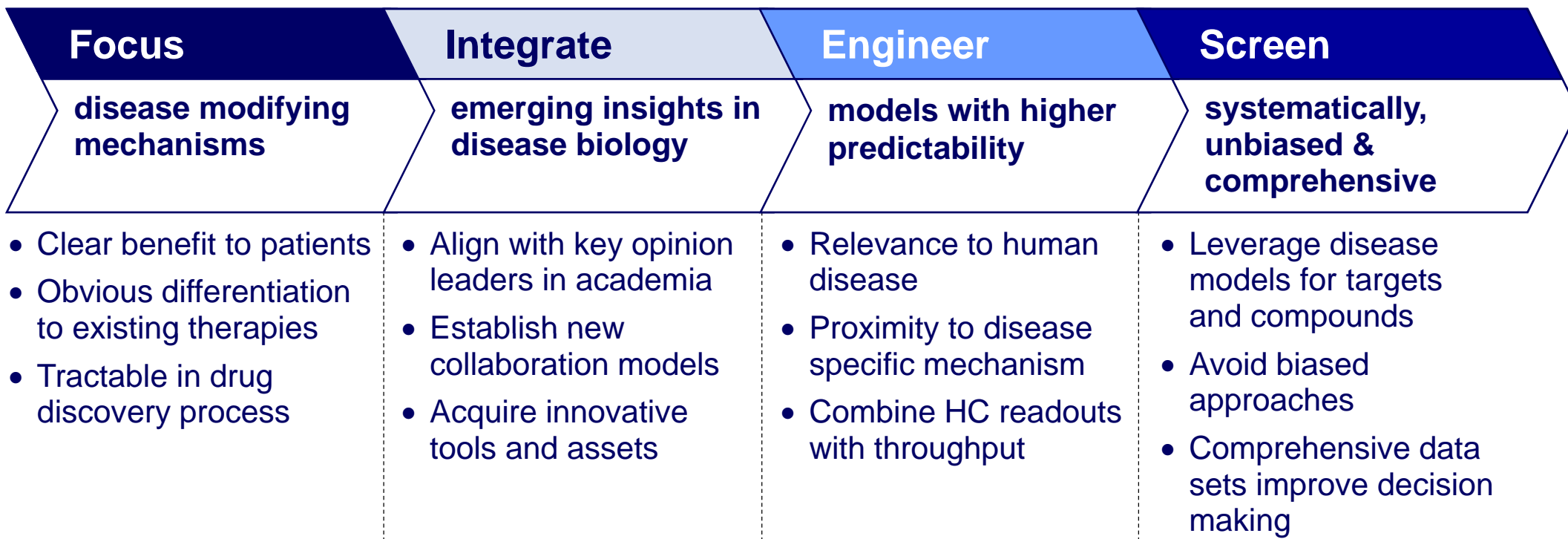
### Targeting the root causes of diabetes

- **Type 1 diabetes (Andromeda /Teva)**
  - DiaPep277 targeting autoimmunity, HSP60 derived peptide
  - Significant milestones, product royalties
  - Status Phase III
- **Type 2 diabetes (Boehringer Ingelheim)**
  - Insulin sensitizer targeting insulin resistance, undisclosed target identified and validated by Evotec
  - Up to € 250 m milestones, significant royalties
  - Status preclinical
- **Type 1 and 2 diabetes (MedImmune/AstraZeneca)**
  - Therapeutic protein targeting beta cell mass, undisclosed target identified and validated by Evotec
  - Up to € 230 m milestones, significant royalties
  - Status preclinical
- **CureBeta ( Harvard – Evotec – Janssen)**
  - Largest collaboration in beta cell regeneration, undisclosed targets identified and validated by Harvard / Evotec
  - Status discovery



# Combining top science with platforms for big unmet medical need

What defines first-in-class innovation infrastructure?




# Systematic, unbiased and comprehensive mechanism-focused infrastructures

The *CUREBETA* “Autobahn”

<b>High Resolution Expression Profiling</b>	<ul style="list-style-type: none"> <li>• Transcriptome / proteome analysis</li> <li>• Profiling of specific cells and tissues               <ul style="list-style-type: none"> <li>– Disease relevant mechanisms</li> <li>– Longitudinal analysis of disease progression</li> </ul> </li> </ul>
<b>Mechanism Focused Chemical Genomics</b>	<ul style="list-style-type: none"> <li>• Mechanisms focused cellular assay               <ul style="list-style-type: none"> <li>– Primary cells / tissues</li> <li>– Immortalized cells</li> </ul> </li> <li>• High content screening of               <ul style="list-style-type: none"> <li>– Annotated libraries</li> <li>– Diverse libraries</li> <li>– Natural products</li> </ul> </li> </ul>
<b>High Content Functional Genetics</b>	<ul style="list-style-type: none"> <li>• Sophisticated high content cellular assay</li> <li>• Loss of function</li> <li>• Gain of function</li> <li>• High content readouts</li> </ul>

**First in class Candidate Leads / Targets**

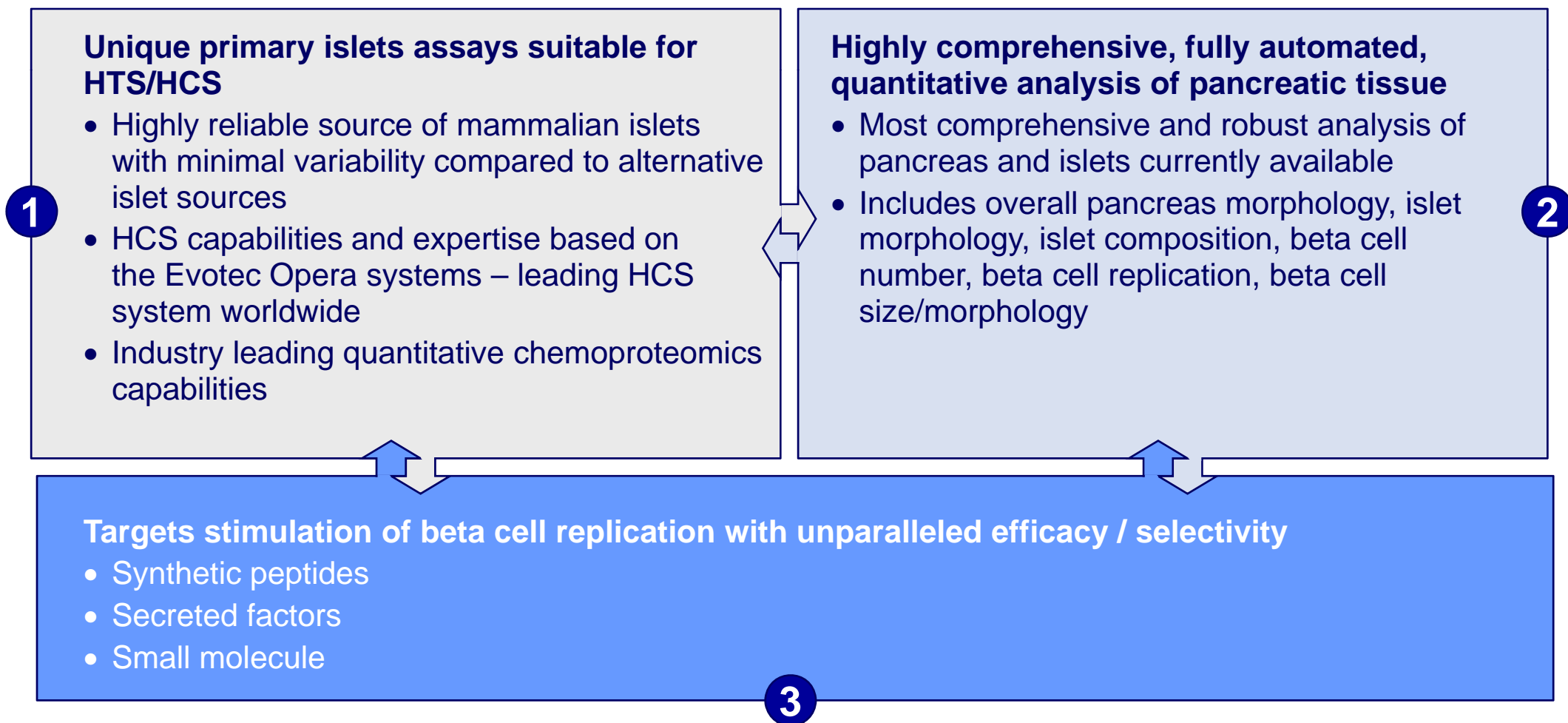



**Pipeline of selected Targets and Leads advance into Drug Discovery Process**



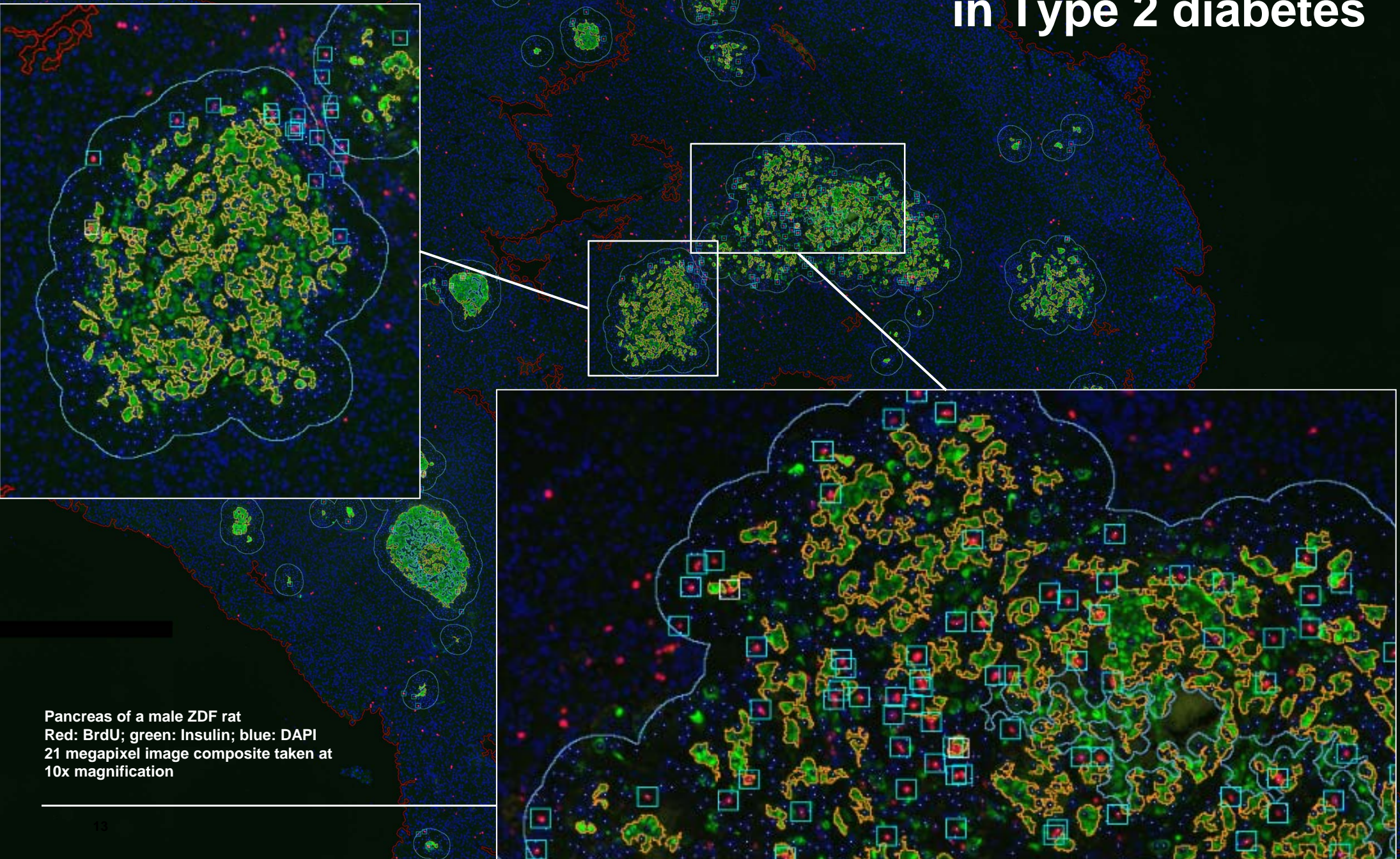
# CUREBETA – Establishing infrastructure standards

Targets, assays, models, analysis...



evotec

# Islets Degeneration in Type 2 diabetes

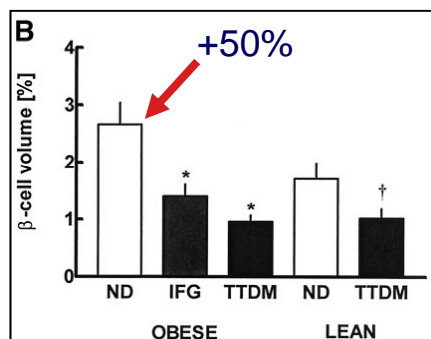


Pancreas of a male ZDF rat  
Red: BrdU; green: Insulin; blue: DAPI  
21 megapixel image composite taken at  
10x magnification

# Key mechanisms regulating beta cell mass

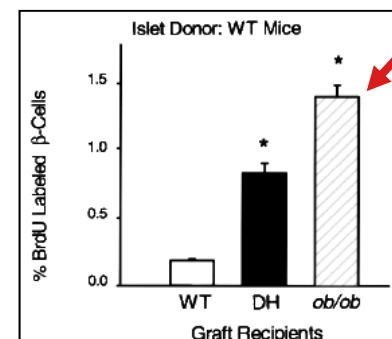
## Beta cell replication and insulin resistance

### Increased beta cell mass in *obese humans*



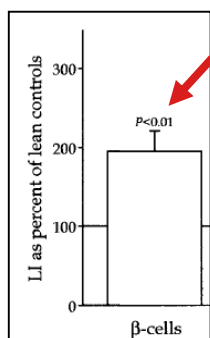
Butler et al.,  
Diabetes 2003

### Mouse islets transplanted into insulin resistant mice



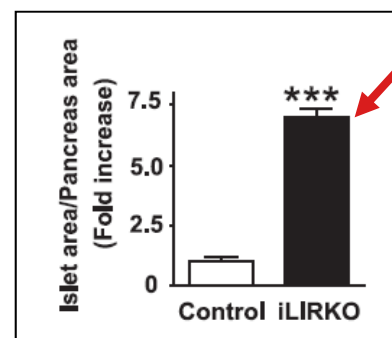
Flier et al.,  
PNAS 98, 2001

### Human islets transplanted under *ob/ob* kidney capsule



Tyrberg et al.,  
DIABETES, 2001

### Increased beta cell mass in *iLIRKO* mice



Escribano et al.,  
Diabetes 2009

## Building a Cure X pipeline

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High unmet medical need and paucity of disease modifying targets...

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### **CureBeta**

- Started collaboration with Harvard University in March 2011
- Partnered with Janssen in July 2012

### **CureNephron**

- Started collaboration with Harvard University in February 2012
- Highly productive in generating candidate targets & compounds
- Marketing efforts will start in September 2012

### **CureNeuron**

- Concept phase for internal projects
- Exploring potential collaboration opportunities

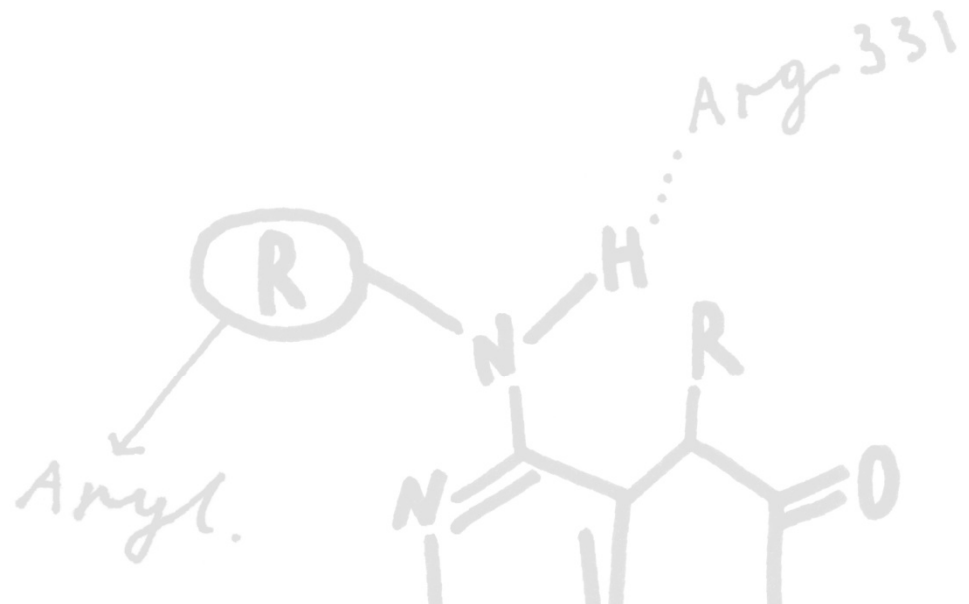
### **CureHeart**

- Concept phase for internal projects
- Exploring potential collaboration opportunities

## Agenda

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- **CUREBETA** & Strategic background
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# CUREBETA - disruptive innovation in diabetes

BETALunch in Harvard: The root cause – Not the symptoms

## BETALunch, Scientific Workshop, Fall 2012<sup>1)</sup>

### Workshop / Scientific Seminar on

- Disease modifying drugs in diabetes
- Beta cell mass and function are pivotal for the development of disease modifying drugs
- Systematic, unbiased and comprehensive approach to beta cell regeneration
- Unique tools and models for the target/drug discovery and rapid development
- Combining leading expertise in academic beta cell biology, biotech discovery and pharma development

### Key Contributions

Doug Melton, others



Prof Doug Melton

## Strong news flow to come

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Outlook and next steps for 2012 ff

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### Key milestones for 2012

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#### 1 EVT Execute

- Double digit revenue growth 2012 – 2016
- Expansion success of existing alliances
- Significant long-term deals with major pharma ✓

#### 2 EVT Integrate

- At least 2 significant new integrated technology/disease alliances
- Deliver significant and accelerated preclinical/clinical milestones
- Show operational synergies of recent acquisitions ✓

#### 3 EVT Innovate

- At least 1 strategic deal for early assets ✓
- Even more innovation upsides (e.g. Cure X, ...) ✓
- Phase III data in DiaPep277 ✓ and Phase IIb start within product development partnerships ✓

**Your contact:**

Dr Werner Lanthaler  
*Chief Executive Officer*

+49.(0).40.560 81-242  
+49.(0).40.560 81-333 Fax  
werner.lanthaler@evotec.com

