There is an enormous pipeline of drugs and products for the management of diabetes and related comorbidities. Some recent reports provide listings of 221 companies with development programs in type 2 diabetes alone. Near term there are no new classes of antihyperglycemic medications on the horizon though a variety of novel and theoretically advantageous application of currently available classes of medications. About ½ my presentation with focus on those drugs that are likely to be available in the next 24 months and about ½ my presentation on new classes of drugs where the potential to address unmet needs seems reasonable.

References:

**New Drugs: What’s in the Pipeline?**

John B. Buse, MD, PhD  
Verna S. Caviness Distinguished Professor  
Chief, Division of Endocrinology  
Director, NC Translational and Clinical Sciences Institute  
Executive Associate Dean, Clinical Research  
University of North Carolina School of Medicine

Thanks to Jay Skyler

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**Type 2 Diabetes Companies**

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**P&T “Pipeline Plus”**

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**Ertugliflozin**

**DIABETES, OBESITY AND METABOLISM**

A Phase 3, Efficacy and Safety Study of Ertugliflozin Monotherapy in Patients with Type 2 Diabetes Mellitus Inadequately Controlled with Diet and Exercise Alone

Steven G. Terra, Kristin Foodt, Melanie Daniel, Juan Pellas, Giuseppe Dietera, Amanda Drokulc, Gregory Clinton, Jeremy Johnson, Didier Sabar, Scott Lrward, Sam Diagono-Jack.

1Pfizer, 60 Lovett Avenue Road, Andover, MA, USA

Investigational. Not FDA approved.

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**Duality of Interest Declaration**

I report the following potential duality/dualities of interest:

**Board Member/Advisory Panel:** None

**Speaker’s Bureau:** None

**Consultant:** PhaseBio, Insulin Algorithms

**Stock/Shareholder:** PhaseBio, Insulin Algorithms

**Research Support:** AstraZeneca, Bayer, Boehringer-Ingelheim, Eli Lilly, J&J, Lexicon, Novo Nordisk, Sanofi, Theracos

Other (advisor under contract between UNC and the company): Adocia, AstraZeneca, Dance Biopharm, Dexcom, Eli Lilly, Elcyte, Eli Lilly, Farley, Gil Dynamics, Shenzhen HighTide, Intarcia, Lexicon, Merck, Metavention, Novo Nordisk, Orexigen, Quest, vTv Therapeutics

**Travel Support:** in conjunction with above-mentioned activities


Investigational. Not FDA approved.
Investigational. Not FDA approved.

New insulins

- **Rapid**
  - Technosphere (inhaled)
  - Lispro U-200
  - Human U-500 pen (not so rapid)

- **Long**
  - Degludec (U-100, U-200)
  - Glargine (biosimilar U-100, U-300)

- **Patch pumps**

- **GLP-1RA plus basal insulin**

- **Future**
  - Ultra-rapid (FiAsp, Biochaperone insulin, LY900014)
  - Smart insulin

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**Combination Therapy:**

**GLP-1RA + Insulin**

- 3:1 ratio of insulin glargine to lixisenatide
- provides a glargine dose range of 30 to 60 units and a lixisenatide dose range of 10 to 20 ug.

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**IGlarLixi Pen Injection**

- SGLT1 inhibitor (啉格列净)
- reduces glucagon and increases GLP-1 levels
- reduces body weight and fat mass

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**IGlarLixi vs IGlar and vs Lixi in T2DM on Metformin: LixiLan-O Trial**

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**A1c Targets at 30 weeks**

- HbA1c <7%
- HbA1c ≤6.5%

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Rosenstock J et al. Diabetes Care 2016; 39:2026-2035
**DUAL 2: Daily dose of IDeg component**

- **End of trial dose:**
  - IDegLira: 45U
  - IDeg: 45U

- **Treatment difference:** -0.02 U
- **p = ns**

- ~65% at max dose of IDegLira, of which ~60% were at target (<7.0%).

**Mean values with error bars (standard error mean) based on safety population and LOCF imputed data**

**Estimated treatment differences are from an ANCOVA analysis**

**NN9068-3912; IDegLira vs IDeg in T2DM**


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**DUAL 2: Change in body weight over time**

- **Treatment difference:** -2.51 kg (5.52 lb)
  - **p <0.0001**

**Mean values with error bars (standard error mean) based on FAS and LOCF imputed data**

**Estimated treatment differences are from an ANCOVA analysis**

**NN9068-3912; IDegLira vs IDeg in T2DM**


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**DUAL 2: Confirmed hypoglycaemia**

- **Rate ratio:** 0.66
  - **p =0.13**

**Cumulative episodes per subject**

**NHB (%)**

<table>
<thead>
<tr>
<th>Time (weeks)</th>
<th>IDegLira (n=199)</th>
<th>IDeg (n=199)</th>
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</table>

**Mean values based on SAS**

**Estimated treatment ratios are from a negative binomial model**

**NN9068-3912; IDegLira vs IDeg in T2DM**


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**DUAL 2: Percentage of subjects with nausea**

**Subjects (%)**

**Time (weeks)**

<table>
<thead>
<tr>
<th>Time (weeks)</th>
<th>IDegLira (n=199)</th>
<th>IDeg (n=199)</th>
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</table>

**Data are from SAS**

**NN9068-3912; IDegLira vs IDeg in T2DM**


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**Combination Therapy:**

**GLP-1RA + SGLT2 Inhibitor**

**GLP1-RA + SGLT2 Inhibitor**

**Exenatide-QW and Dapagliflozin**

**Change in HbA1c (%)**

**Time (weeks)**

- **Mean values with error bars (standard error mean)** based on FAS and LOCF imputed data

- **Estimated treatment differences are from an ANCOVA analysis**

- **NN9068-3912; IDegLira vs IDeg in T2DM**


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**Frias et al. Lancet Diabetes Endocrinology 2016; 4:1004-1016**
Implanted GLP1 RA Preparation

Continuous Subcutaneous Exenatide with ITCA 650* Intarcia Delivery Technology

- Mini-Pump Size of a matchstick!
- Continuous Subcutaneous Delivery of Exenatide

Continuous Subcutaneous Exenatide with ITCA 650* Intarcia Delivery Technology

- Osmotic Mini-Pump
- Continuous zero order delivery for up to a full 12 months
- Novel formulation stabilizes peptides at body temps for years

Continuous Subcutaneous Exenatide with ITCA 650* Intarcia Delivery Technology

- Sub-cutaneous placement once/twice yearly
- Done in a brief, in-office, sterile procedure by MD or NP/PAs
- Approved reimbursement codes for similar procedures

Oral GLP1 Preparations
Investigational. Not FDA approved.
“Prediction is very difficult, especially about the future.”

Robert Børne Petersen (1882-1968)
Danish cartoonist, writer, animator, illustrator, poster and Humorist.