# Broadening Indications For Diabetes Drugs

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Sulfonylureas

# Sulfonylureas

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Chlorpropamide - 1958
Acetohexamide - 1960
Tolbutamide - 1982
Tolazamide - 1983
Glyburide - 1984
Glipizide - 1984
Glimepiride - 1995
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### Sulfonylureas

Metformin

1990 1990

# Biguanides Metformin

Weight neutral
Reduces LDL and triglycerides

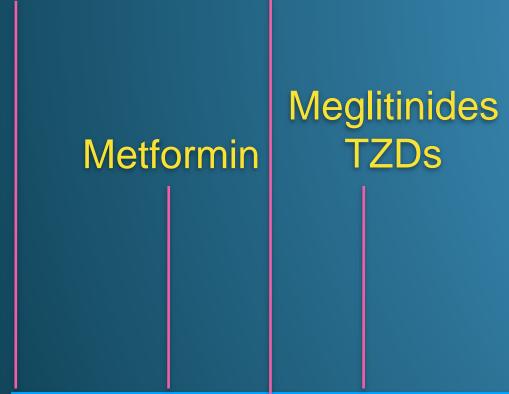


1990 19931995

# a-Glucosidase Inhibitors

Acarbose - 1995





1990 19931995 1997

# Meglitinides

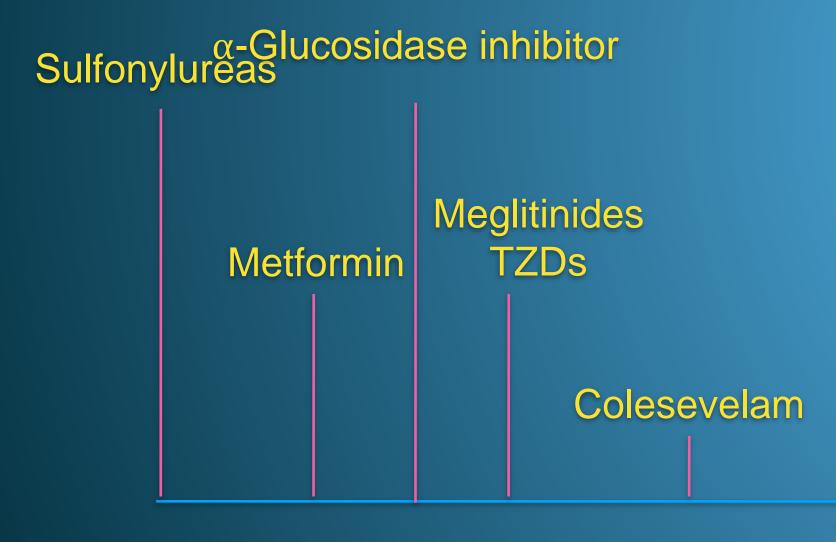
Repaglinide - 1997

Nateglinide - 2000

# Thiazolidinediones

Troglitazone - 1997, 1999 (3x transaminases) Rosiglitazone - 1999, 2007 (CHF?)

Pioglitazone - 1999, 2011 (ACT NOW), 2018 (NASH/NAFLD)



1990 19931995 1997 2000

# Bile Acid Sequestrant

Colesevelam - 2000, 2008



Exenatide - 2005, 2014

# Exenatide

Glucose-mediated insulin secretion
Restores 1st-phase insulin secretion
Glucose-mediated glucagon suppression
Slows gastric motility
Reduces appetite
Stimulates beta cell proliferation

Exenatide - 2005, 2014 Liraglutide - 2010, 2014 (LEADER)

# Liraglutide

- Adjunct to diet and exercise to improve glycemic control in patients 10 years or older with type 2 diabetes mellitus
- For adults with excess weight (BMI≥30 or 27 with a weight-related comorbidity), and children aged 12-17 years with body weight > 60 kg to help lose weight and keep it off

Exenatide - 2005, 2014 Liraglutide - 2010, 2014 (LEADER) Dulaglutide - 2014, 2020 (REWIND, AWARD-11)

# Dulaglutide

### Indications

- Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
- To reduce the risk of MACE in adults with type 2 diabetes mellitus who have established CV disease or multiple CV risk factors
- <u>Primary prevention</u> of MACE in adults with type 2 diabetes mellitus who have established CV disease or multiple CV risk factors

Not recommended as first-line therapy for patients not controlled by diet and exercise

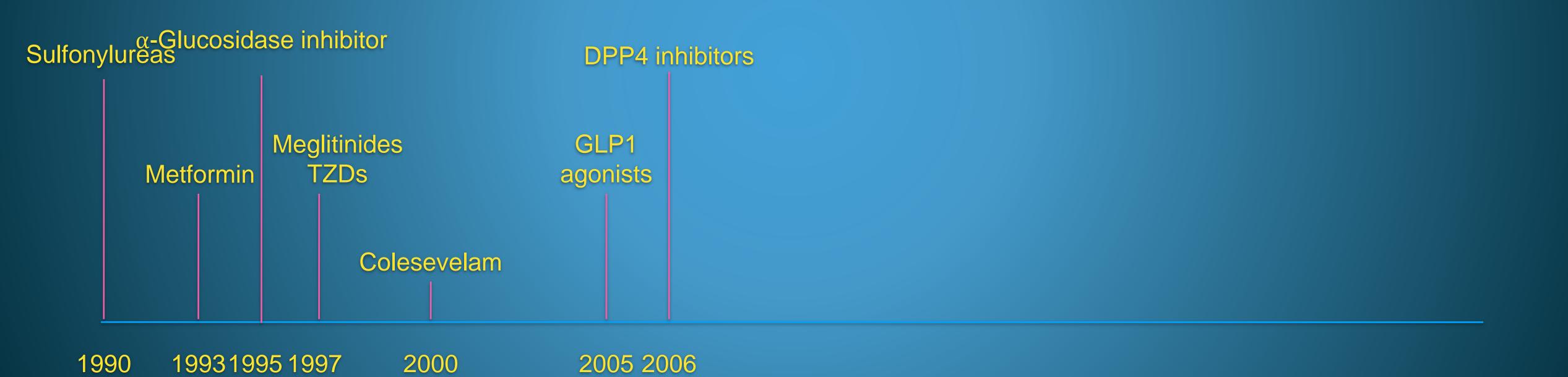
Exenatide - 2005, 2014
Liraglutide - 2010, 2014 (LEADER)
Dulaglutide - 2014, 2020 (REWIND, AWARD-11)
Albiglutide - 2014

Exenatide - 2005, 2014
Liraglutide - 2010, 2014 (LEADER)
Dulaglutide - 2014, 2020 (REWIND, AWARD-11)
Albiglutide - 2014
Lixisenatide - 2016

Exenatide - 2005, 2014
Liraglutide - 2010, 2014 (LEADER)
Dulaglutide - 2014, 2020 (REWIND, AWARD-11)
Albiglutide - 2014
Lixisenatide - 2016
Semaglutide - 2017, 2020 (SUSTAIN-6), 2021 (STEP 1)

# Semaglutide

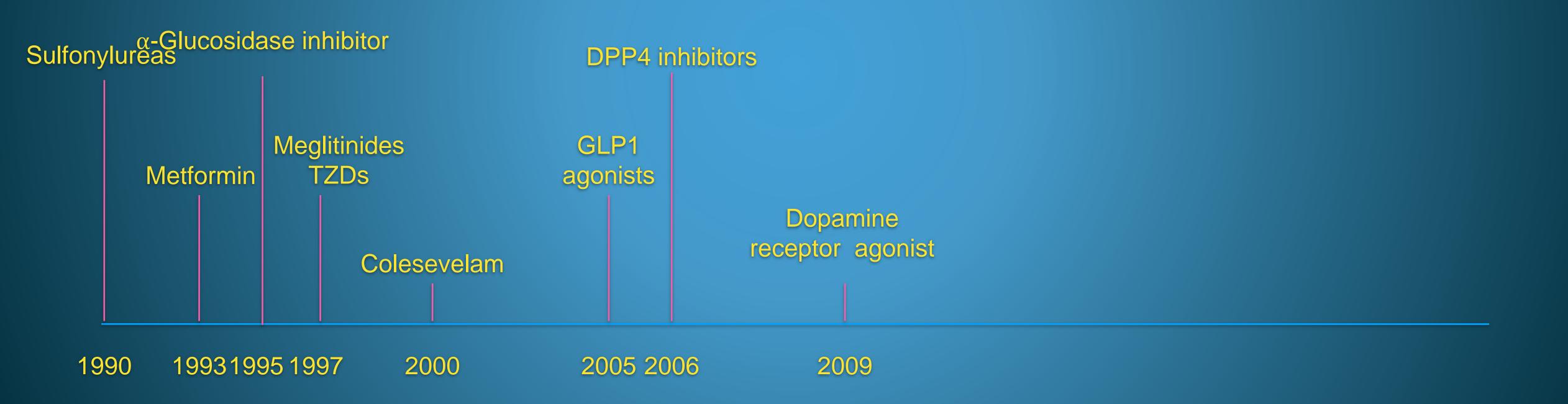
- As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
- To reduce the risk of MACE in adults with type 2 diabetes mellitus and established cardiovascular disease
- For weight loss in adults with BMI ≥ 30 alone or ≥ 27 with at least 1 weight-related comorbidity (HTN, high cholesterol)



# DPP4 Inhibitors

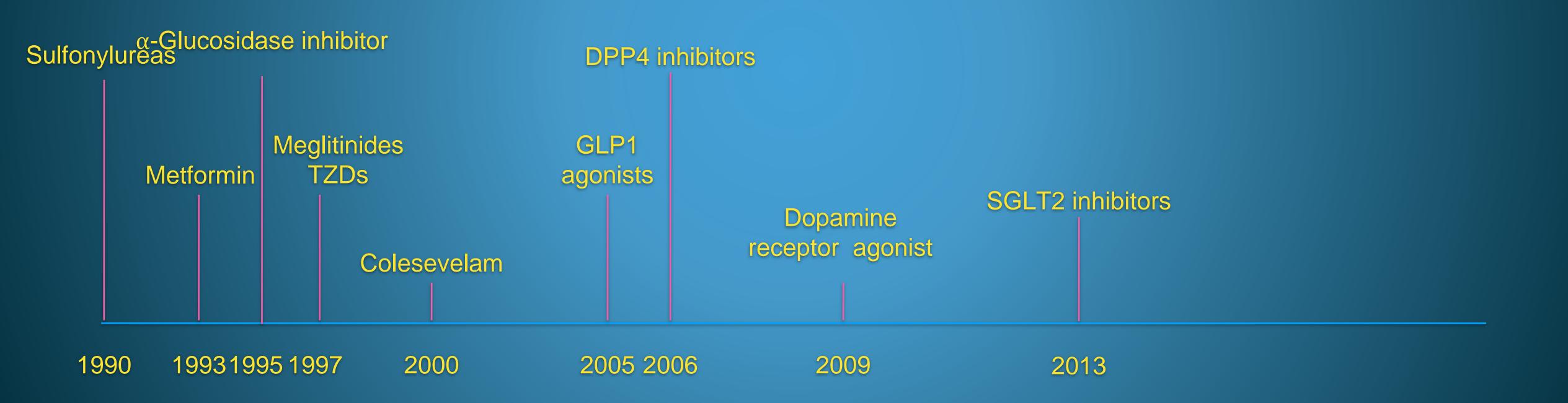
Sitagliptin - 2006

Saxagliptin - 2009 Linagliptin - 2011 Alogliptin - 2013



# Dopamine Receptor Agonist

Bromocriptine - 1978
Bromocriptine QR - 2009



# SGLT-2 Inhibitors

Canagliflozin - 2013, 2017 (CANVAS), 2019 (CREDENCE)

Dapagliflozin - 2014, 2021 (DECLARE, DAPA-HF)

Empagliflozin - 2014, 2021 (EMPA-REG)

Ertugliflozin - 2017

# Canagliflozin

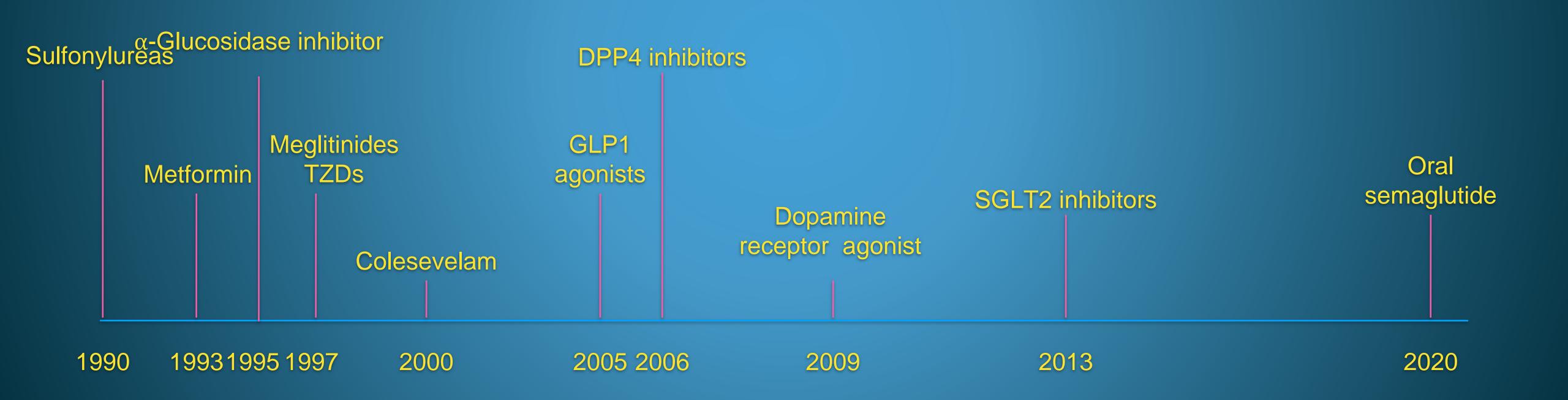
- Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
- To reduce the risk of MACE in adults with type 2 diabetes mellitus and established CV disease
- To reduce the risk of end-stage kidney disease, doubling of serum creatinine, CV death, and hospitalization for heart failure in adults with type 2 diabetes mellitus and diabetic nephropathy with albuminuria

# Dapagliflozin

- Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
- To reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and established cardiovascular disease or multiple cardiovascular risk factors (45% RRR in DECLARE-TIMI 58 trial)
- To reduce the risk of cardiovascular death and hospitalization for heart failure in adults with NYHA Class II-IV heart failure with reduced EF (26% RRR in DAPA-HF trial with NNT=21)

# Empagliflozin

- Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
- To reduce the risk of CV death in adults with type 2 diabetes mellitus and established CV disease (EMPA-REG)



# New Delivery Systems for Existing Drugs

Glucagon Insulin

# Glucagon nasal powder

### Indication

 Hypoglycemic emergencies (unable to eat, having seizure, or unconscious) in adult and pediatric patients with diabetes ages 4 years and above

### Dosing

- 3 mg intranasal (does not need to be inhaled)
- May be repeated if no response after 15 minutes

# Hybrid Closed Loop Insulin Pump

### Medtronic/Minimed 670 G

- Auto Mode automatically adjusts basal insulin delivery every 5 minutes based upon CGM to keep glucose within target range
- Manual Mode with Suspend before low option proactively addresses hypoglycemia and rebound hyperglycemia by automatically suspending insulin delivery before reaching a preselected low glucose limit and resuming delivery when sensor glucose levels recover.

# Advanced Hybrid Closed Loop Insulin Pump

Tandem T-Slim X2 Pump + Dexcom G6 CGM

- Basal-IQ predicts glucose levels 30 minutes ahead and helps prevent frequency and duration of hypoglycemic events by turning insulin on and off as often as every 5 minutes
- Control-IQ adjusts basal insulin delivery every 5
  minutes + delivers correction bolus once per hour to
  prevent high and low blood glucose levels

## InPen

Calculates personalized doses Tracks active insulin and logs doses Reminds to dose and check BG Synchs with CGMs and glucose meters Bluetooth-compatible with iPhone and Android Creates shareable reports x email, print, share, fax 12-month battery life and warrantee Up to 30 units/dose

# WHAT'S NEXT