

# **Challenges of Diabetes**

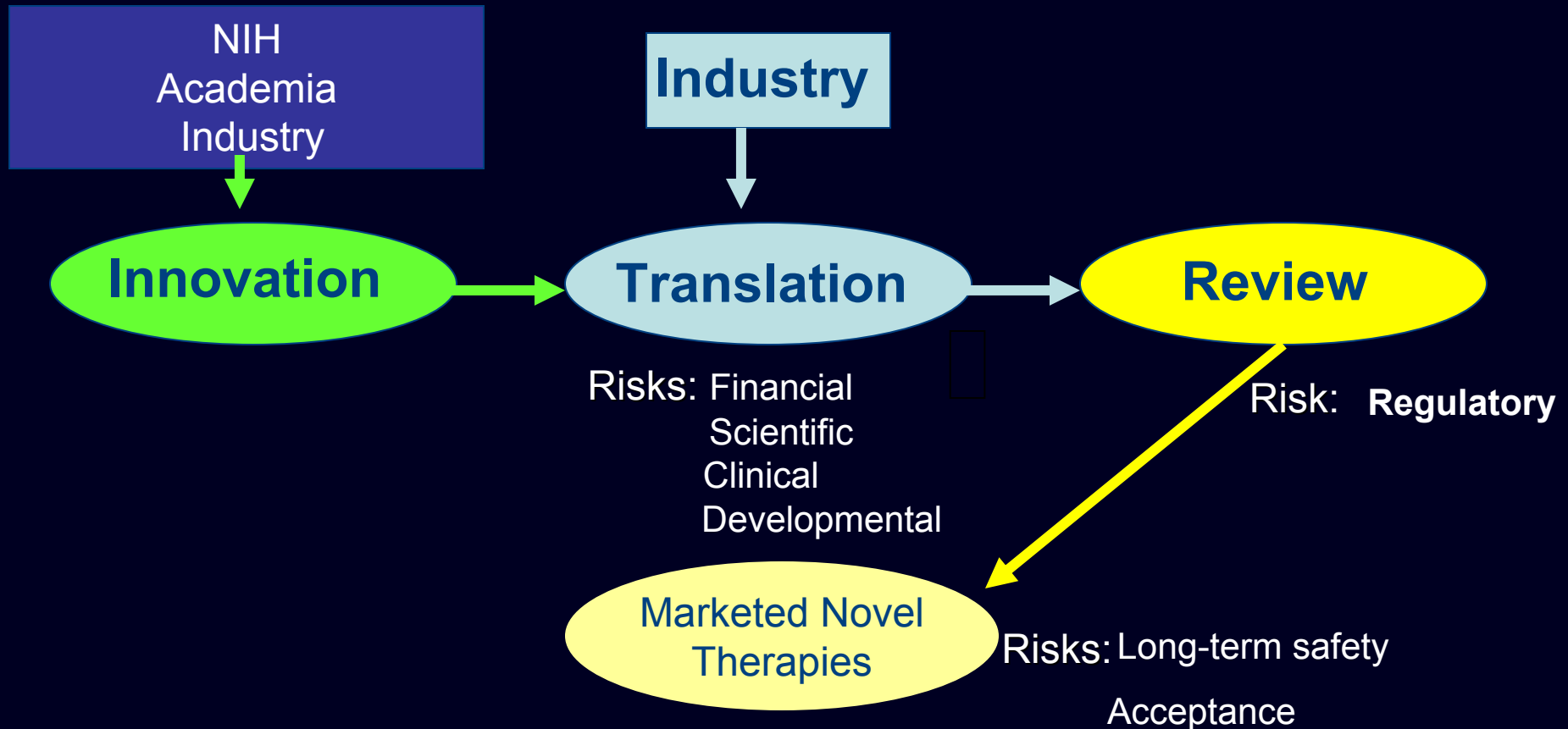
## **The Biotechnology/Biologics Perspective**

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# Biologics

- Often first-in-class and/or novel therapies
- Research and development largely in non-“big pharma” settings
- Peptides, proteins, cytokines, monoclonal antibodies, cell/gene based therapies
- Non-oral routes require targeting important unmet medical needs
- Science/technology often ahead of the regulatory guidelines
- Regulatory risk and uncertainties discourage novel R&D programs

# BIOTECHNOLOGY: The Development Value Chain

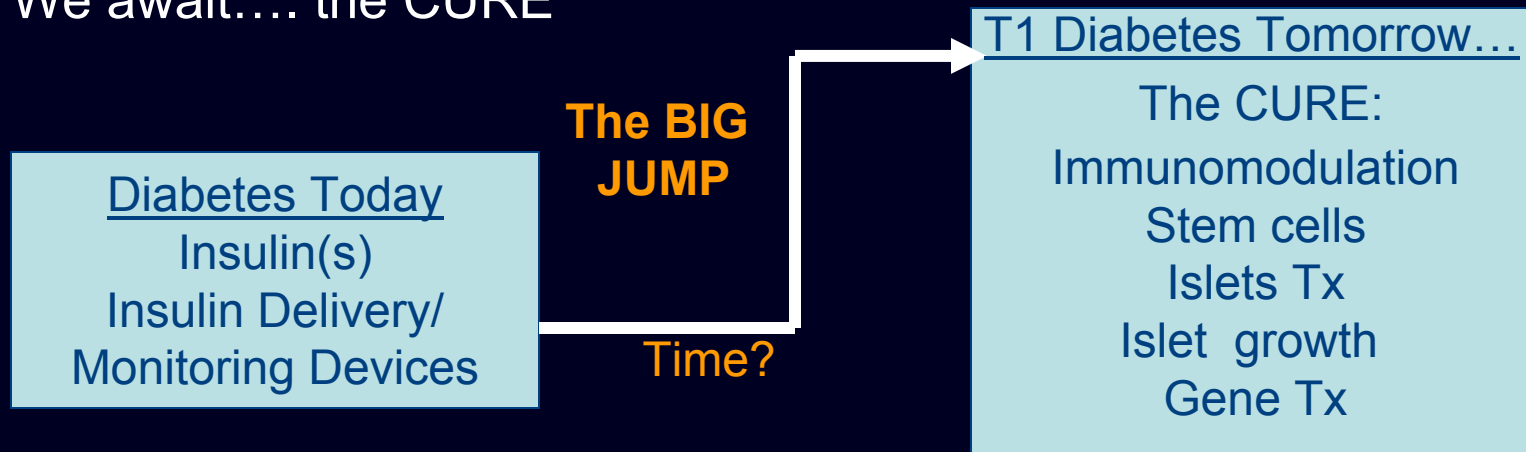


# **Diabetes and Biotechnology**

## **Is there an Unmet Need?**

# Greatest Unmet Need in Diabetes: Type 1 and Insulin Requiring Type 2

- In today's "mindset" a single control variable **insulin** is necessary and sufficient for the treatment of insulin-treated diabetes
- Barriers to control are thought to be simply technical and patient related
- We await.... the CURE



**While waiting for the CURE what remain unmet needs?**

# Despite Important Advances In Insulin Therapy Glycemic Control Is Not Optimal

## Challenges:

- Failure to attain and sustain optimal long-term glycemic control
- Inadequate postprandial glucose control
- Unpredictable glucose fluctuations
- Weight gain
- Hypoglycemia risk
- Poor Quality of Life- **Diabetes is a serious life altering disease requiring serious therapies**

# Regulatory Challenges

While waiting for the CURE....

- If insulin is considered “sufficient” for glycemic control, is there a role for other glucose lowering therapies (other control variables)?

The majority of insulin using patients do NOT achieve glycemic goals.....**Other control variables are desirable**

# Regulatory Challenges

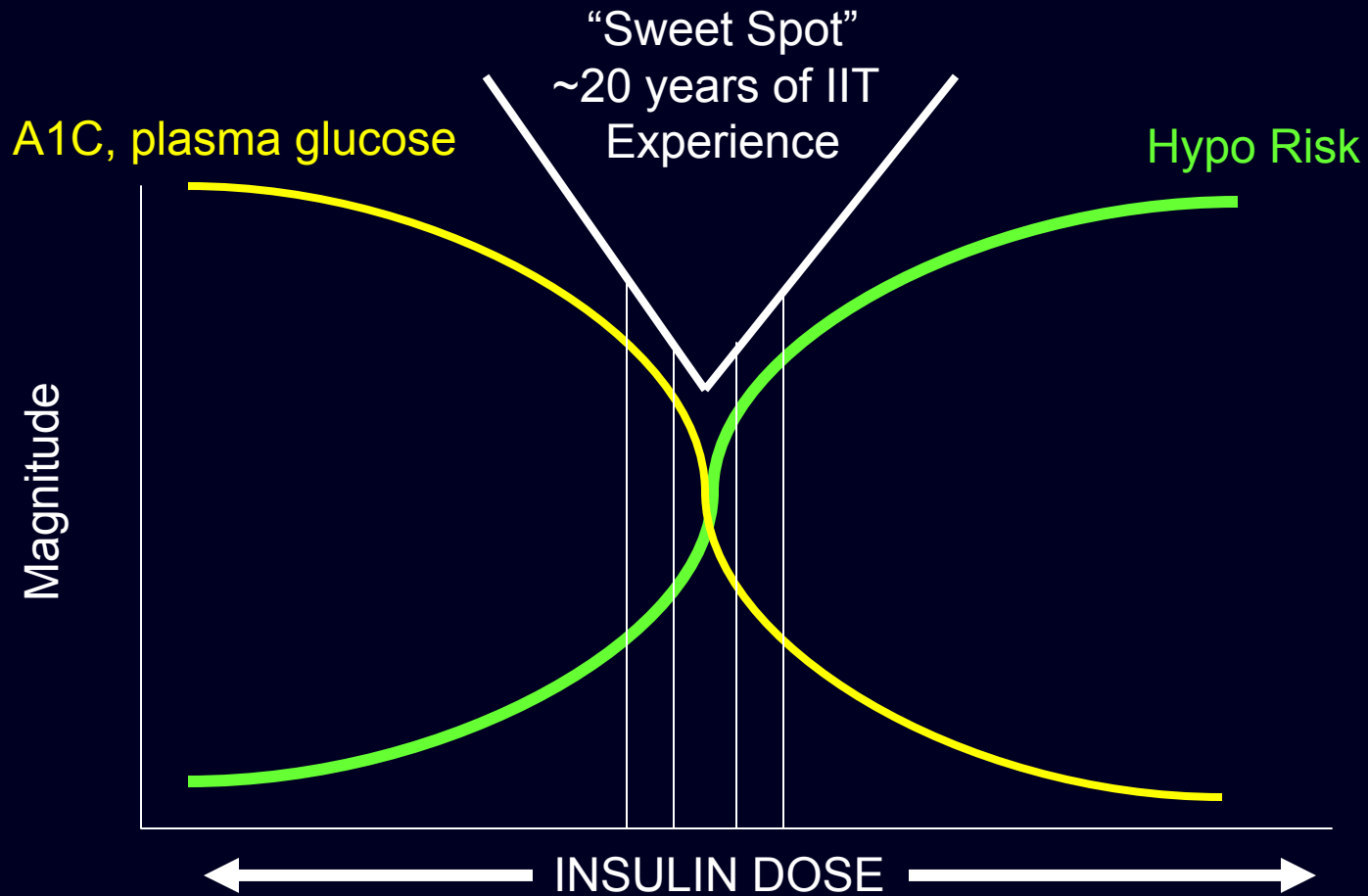
While waiting for the CURE....

- The unmet need for insulin treated diabetes is serious and deserves the same sense of urgency as cancer or AIDS
  - Patients are opting to undergo risky unproven therapies - pancreatic transplant, islet transplant, immunomodulation/suppression
- What is an acceptable Risk/Benefit for novel therapies?
  - Over 80 years of insulin experience



# The “Insulin Experience”

## The Single Control Variable Model



# Regulatory Challenges

## How to Evaluate Other Control Variables added to IIT?

- Are blinded studies appropriate?
  - The “insulin experience” is no longer valid and can potentially confound outcomes
- Is superiority (A1C) over IIT needed?
  - Other variables matter....

# Regulatory Challenges

## How to Evaluate Novel Therapies for patients on IIT?

- Variables other than HbA1c matter
  - Postprandial glycemc excursions?
  - What is the value of dampening amplitude and frequency of glucose excursions?
    - On QOL, complications, hypoglycemia
- Weight control
- What matters to patients?

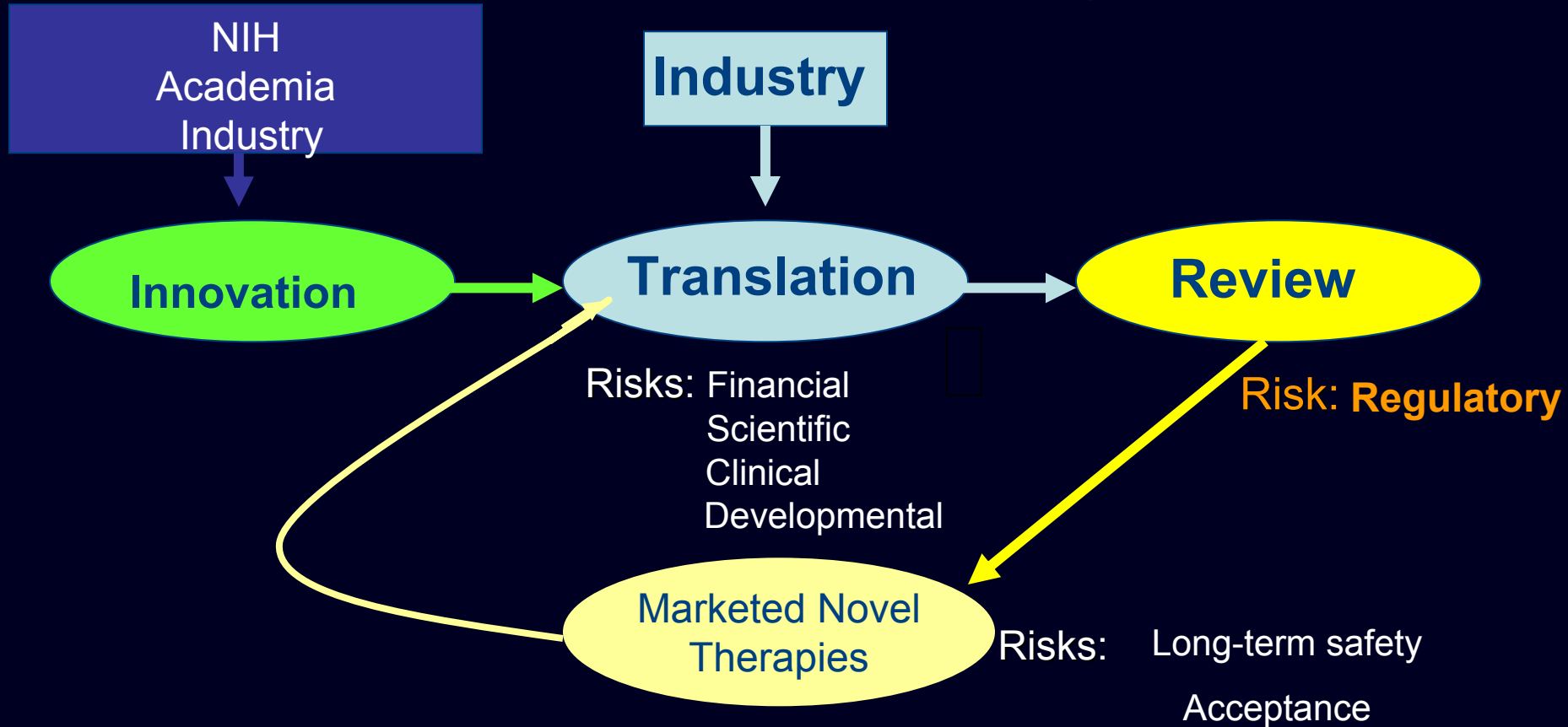
# Regulatory Challenges

## March towards the CURE....

### At what risk?

- A cure:
  - Insulin-independence is worthwhile at what cost?
  - What do the patients say?
- A “partial” cure:
  - Is improving insulin production but not sufficiently to achieve insulin-independence worthwhile to patients, to the FDA?

# BIOTECHNOLOGY: The Path to Novel Drugs



Reducing regulatory uncertainties spurs innovation