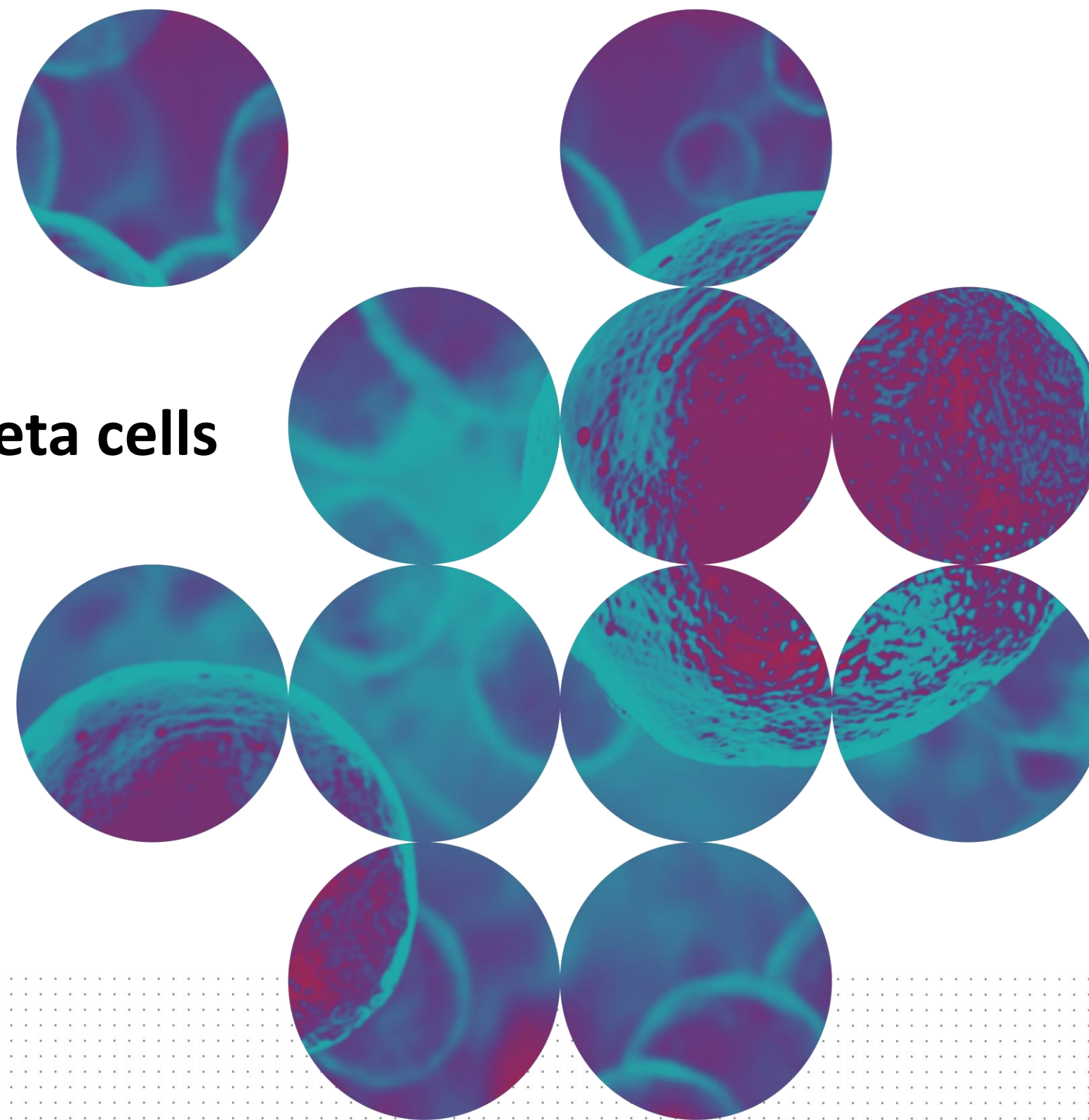


# EndoC- $\beta$ H5

Unlimited quantity of ready-to-use functional human beta cells



**Bruno BLANCHI, PhD**  
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**Hamza OLLEIK, PharmD, PhD**  
[h.olleik@humancelldesign.com](mailto:h.olleik@humancelldesign.com)

## Glucose dose response similar to native beta cells

Glucose stimulated insulin secretion (GSIS) response :

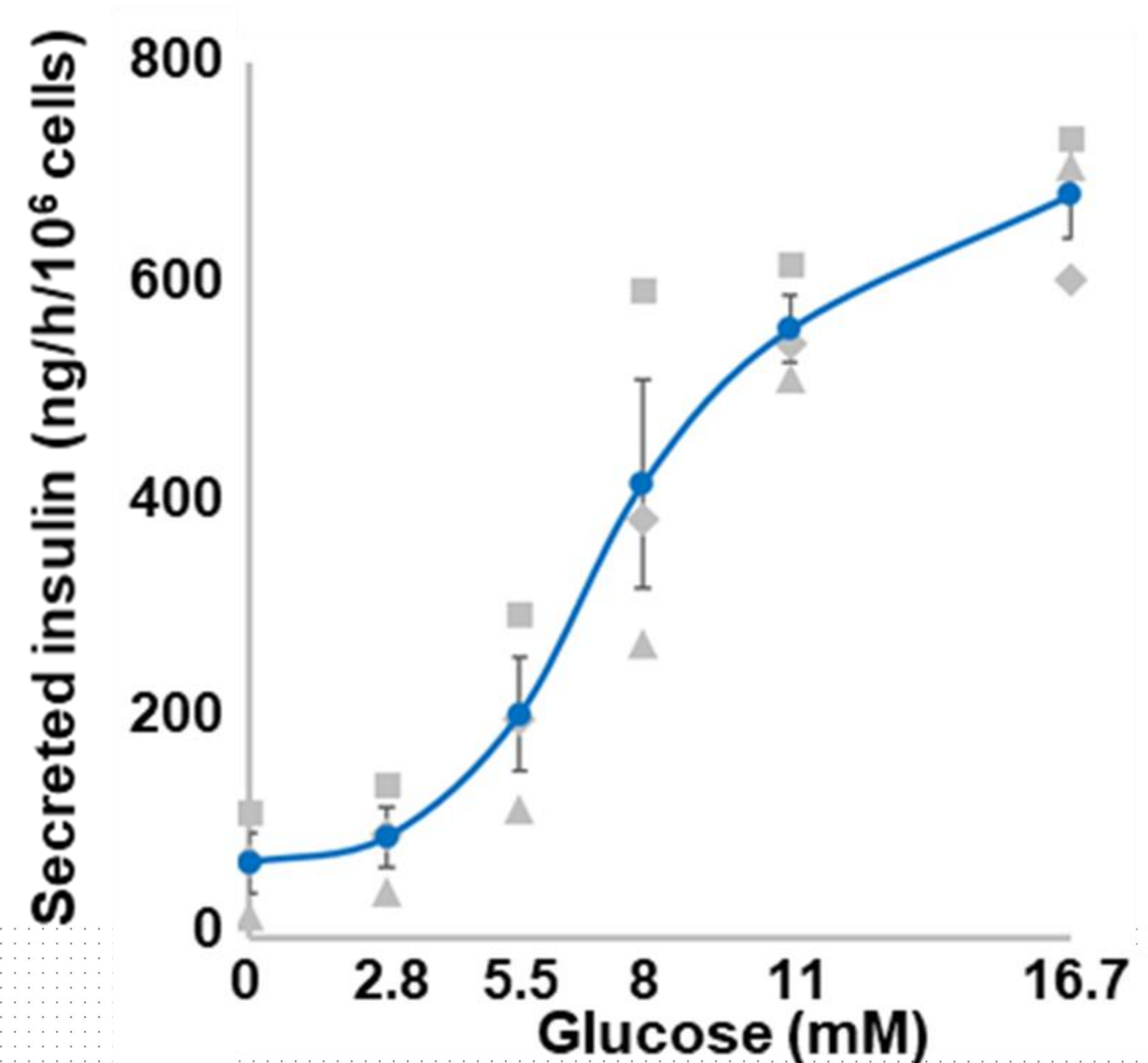
- Dose dependent

Highest potentiation between **5.5 and 8 mM** Glucose

- Highly sensitive

> **10 fold** increase in insulin secretion

- ✓ **A real physiological human beta cell model**



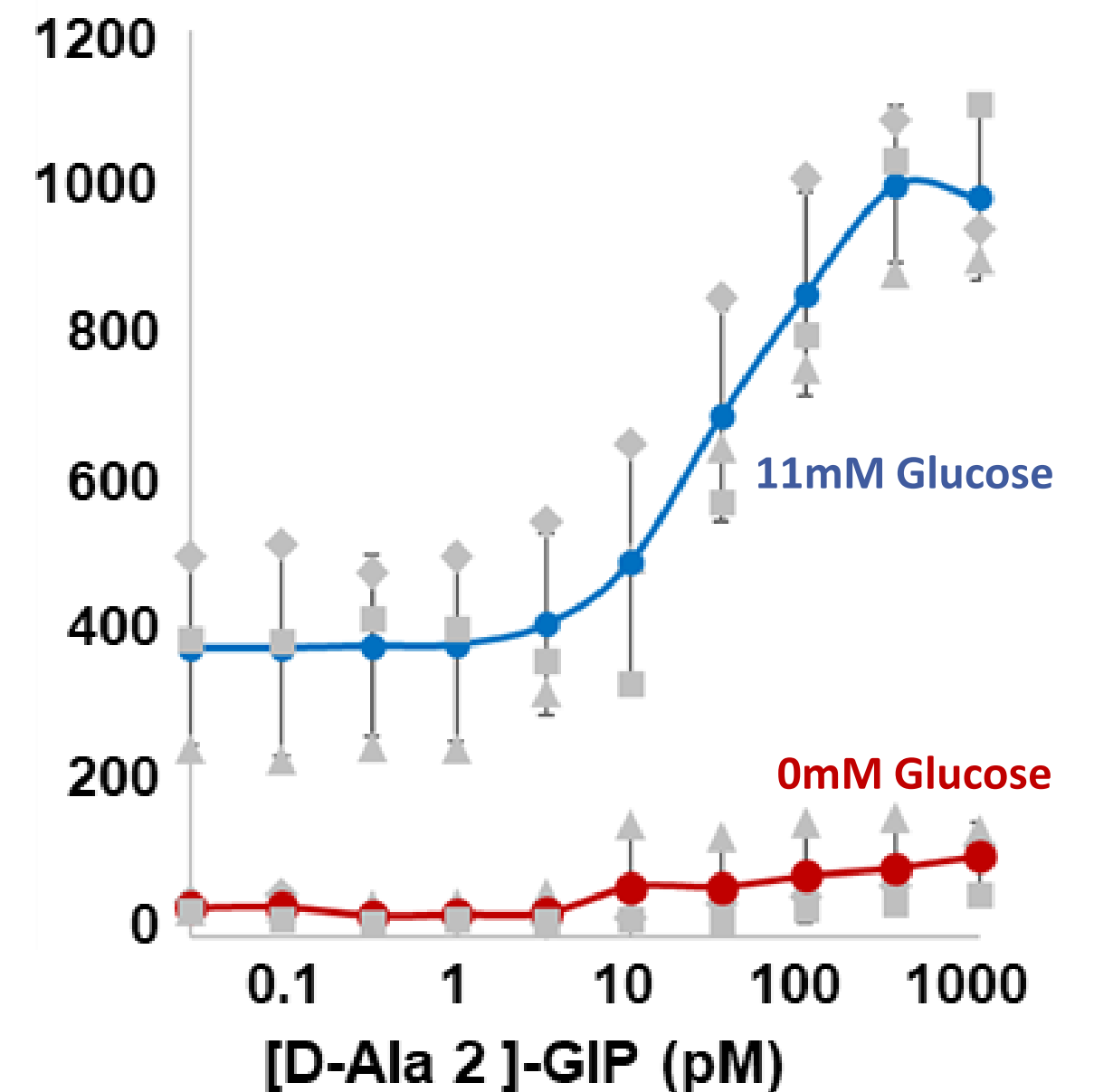
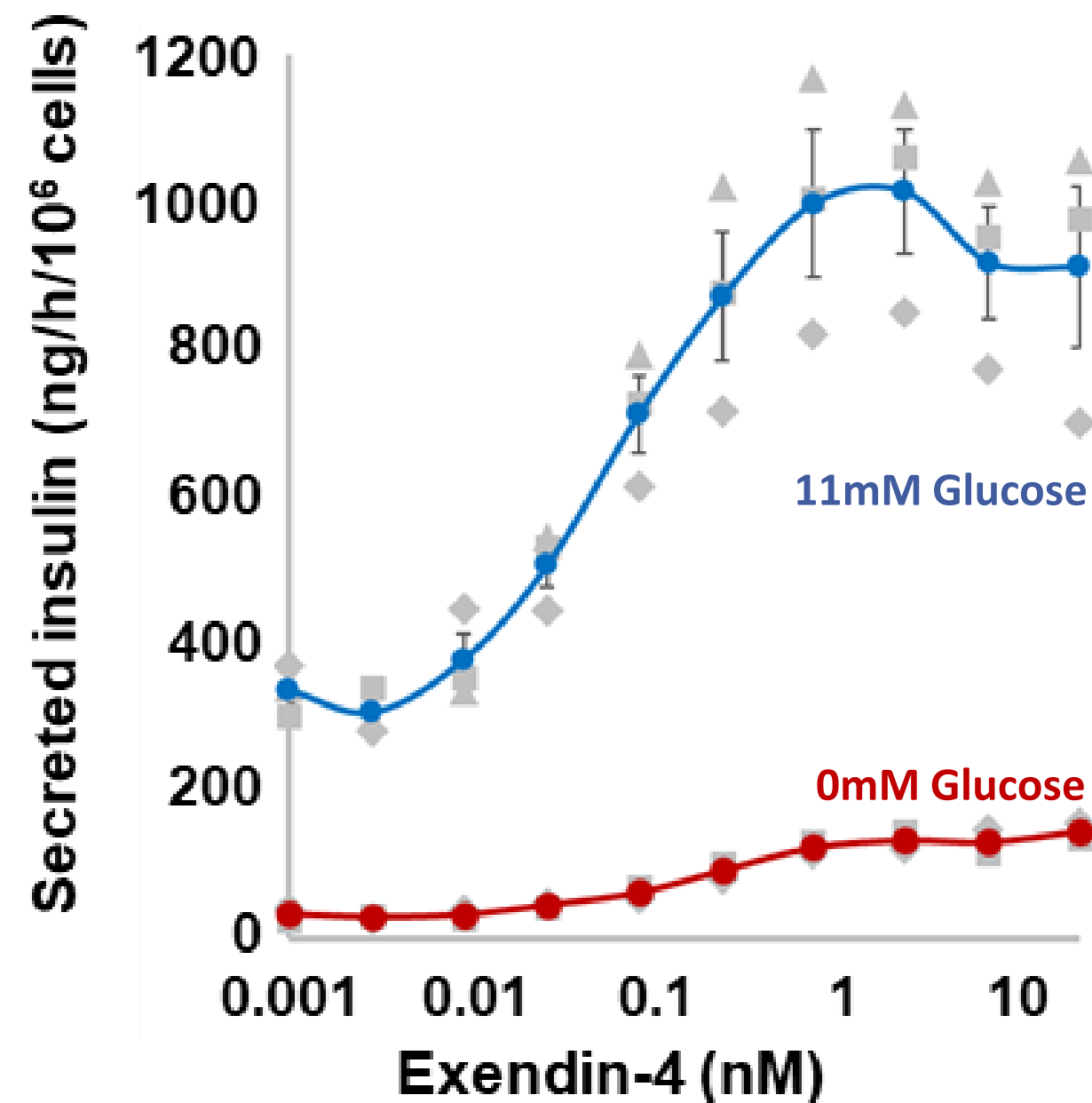


## Reproducible dose dependent responses to GLP-1 and GIP receptor agonists

### Exendin-4 and [D-Ala 2]-GIP dose responses :

- Reproducible responses
- Dose dependent
- Robust (> 3.5) fold increase
- Reproducible EC50

✓ Robust pharmacological responses

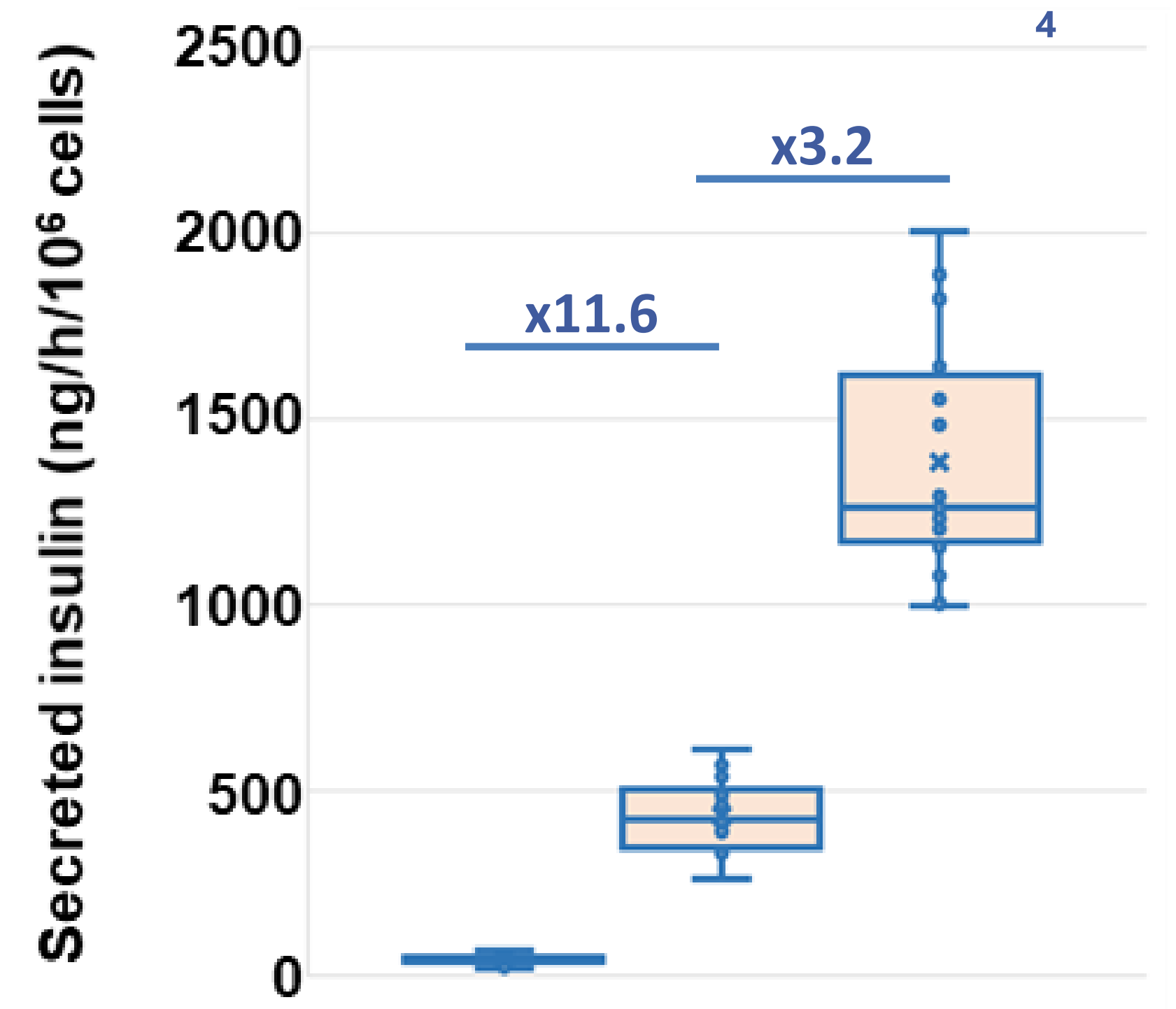


### GSIS reproducibility between batches :

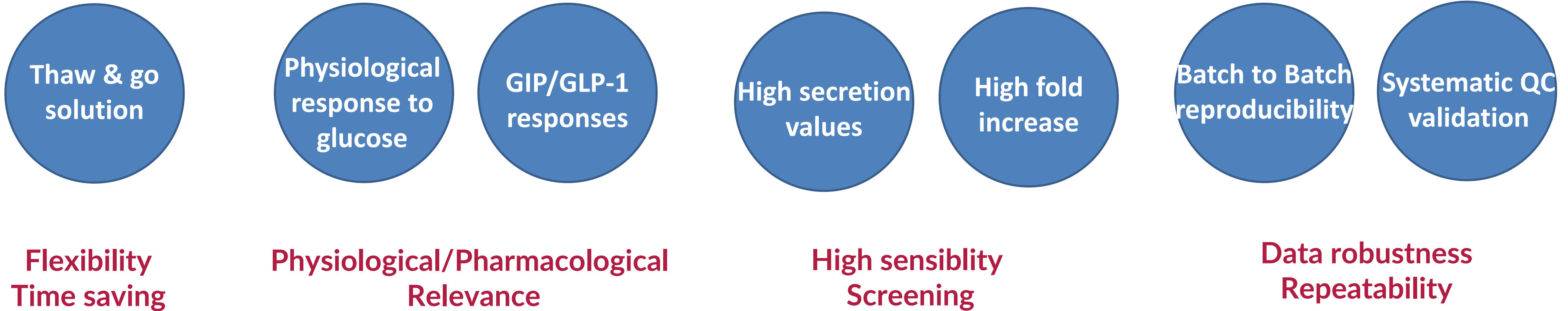
- Reproducible response to glucose
- Reproducible response to GLP-1 receptor agonist (Exendin-4)
- High absolute values of insulin secretion

✓ Batch to batch reproducibility

✓ Systematic QC validation



## A unique storable and functionally validated human beta cell source



✓ **Improve diabetes research**



# Acknowledgement



**Bruno BLANCHI, PhD**  
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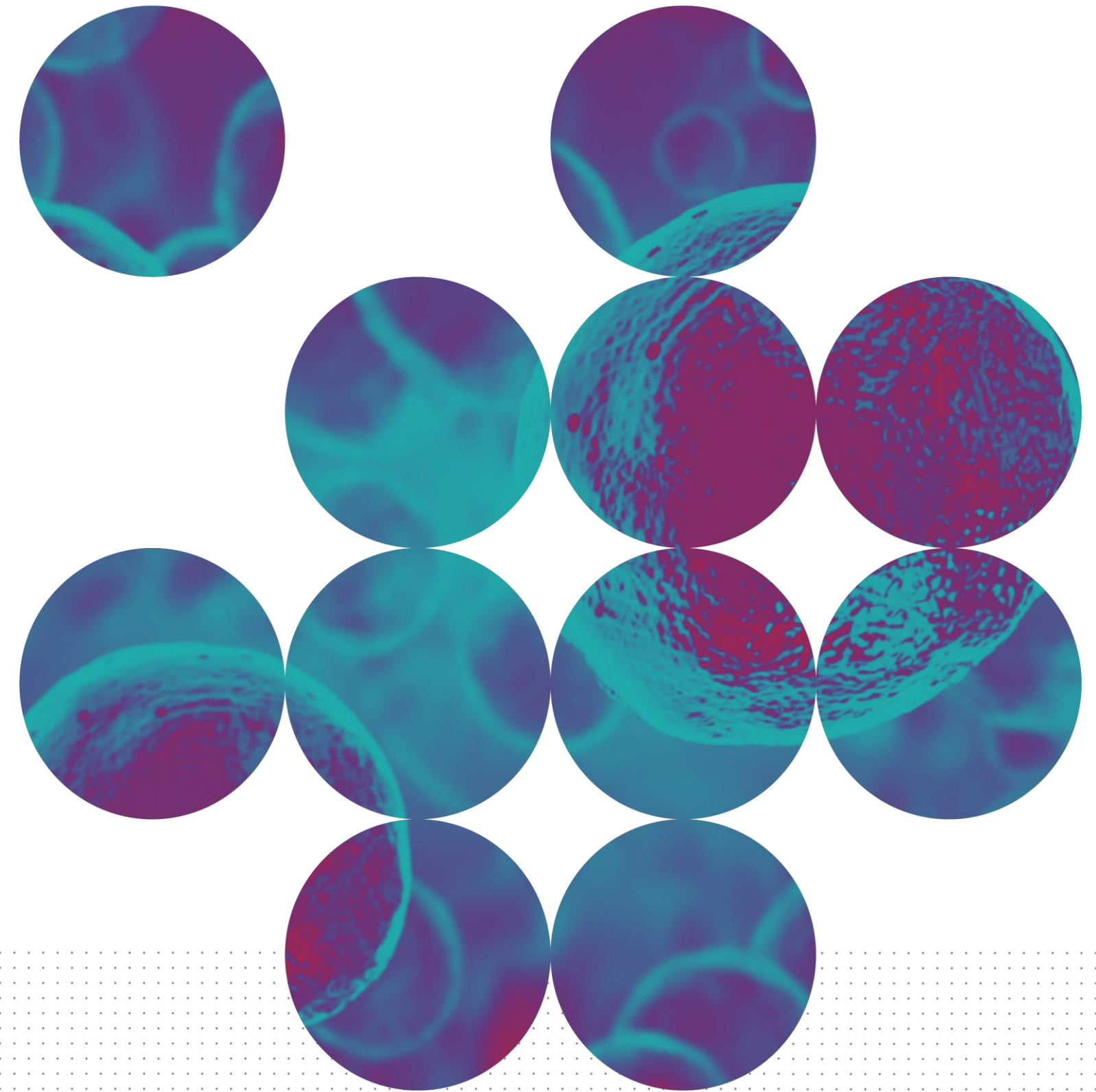


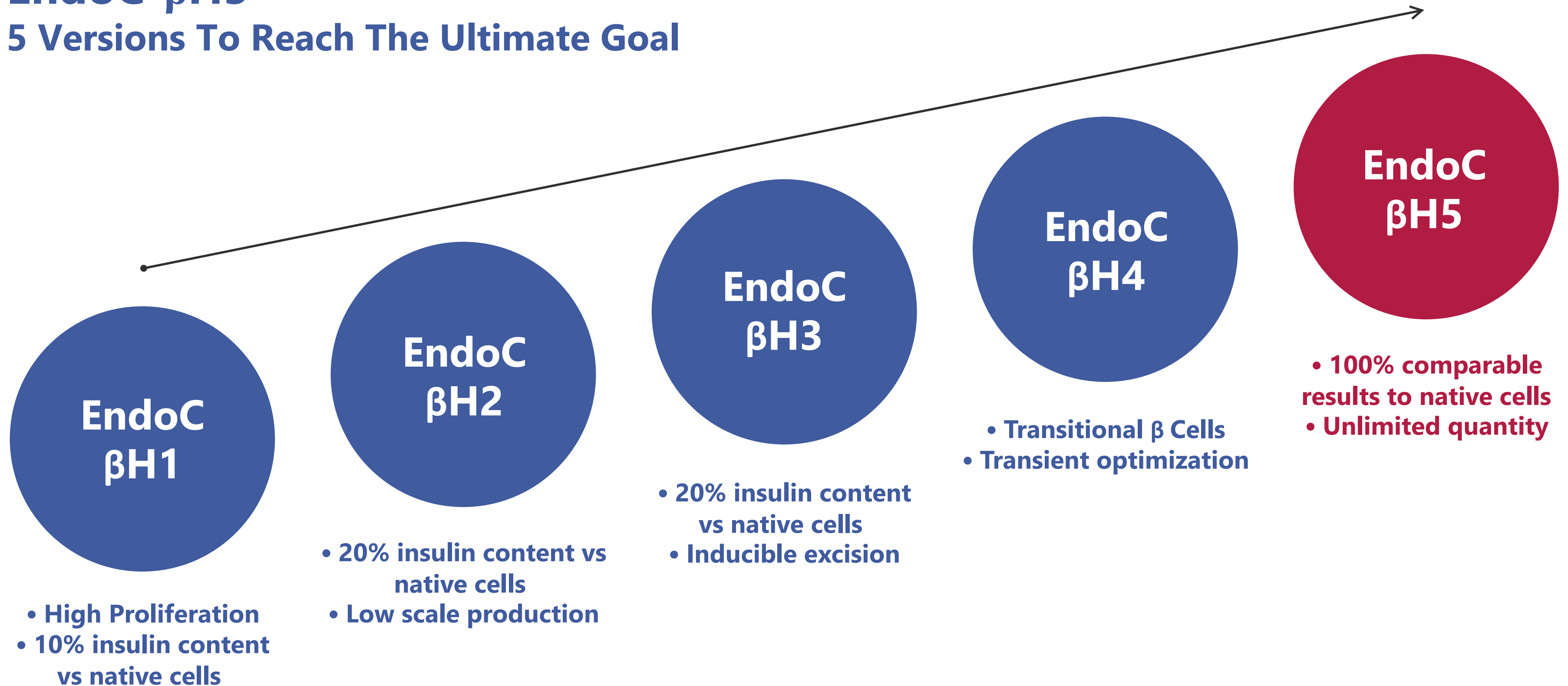


# HUMAN CELL DESIGN

**Experts On Complex Cell Line  
Management & Human Cell Line  
Development**

# Appendices

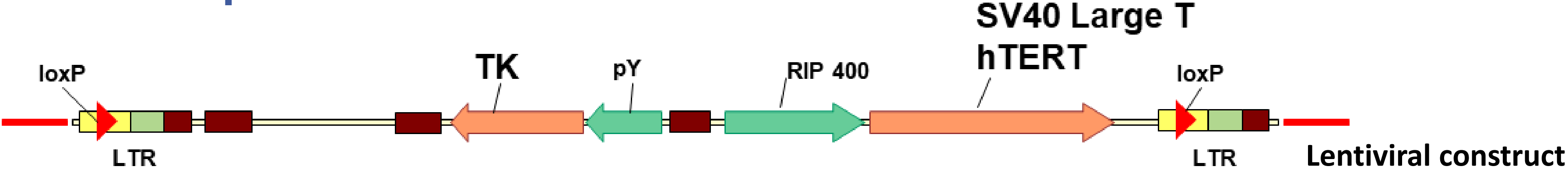




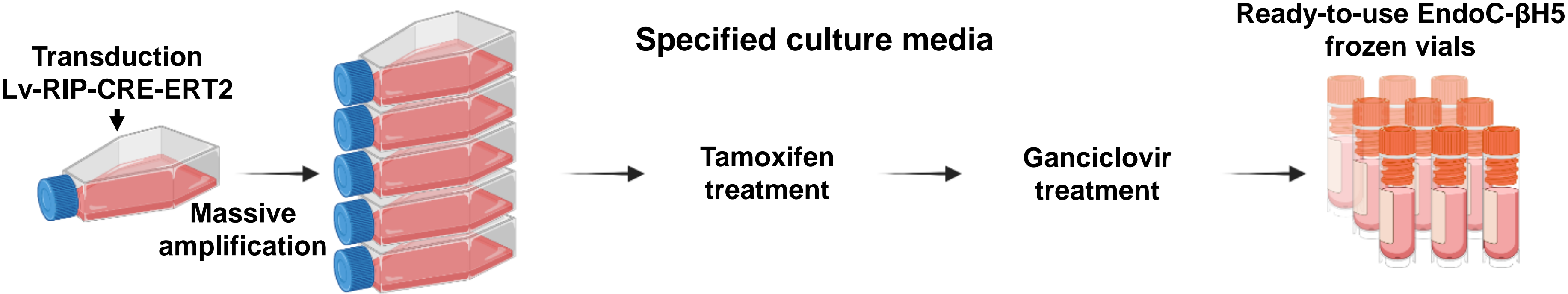


# EndoC-βH5<sup>®</sup>

## Generation and production



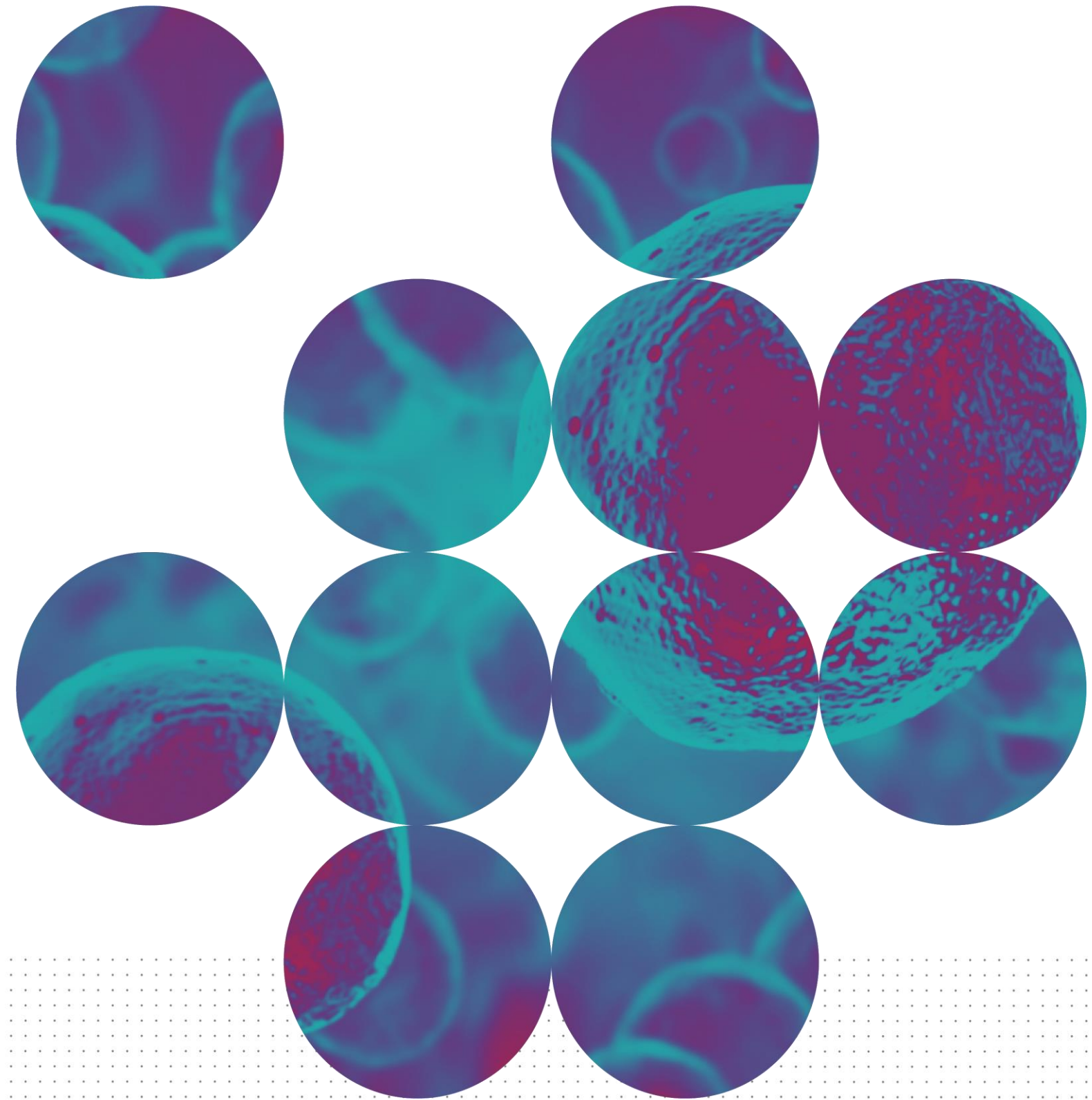
### SV40 Large T / hTERT mediated immortalization



### Frozen and ready-to-use EndoC-βH5 production

## EndoC- $\beta$ H5 human beta cells

- **Frozen vials**
- **Long term storage**
- **Large batches**
- **>3.5 million live cells per vial guaranteed**
- **QC validated glucose and Ex-4 responses**

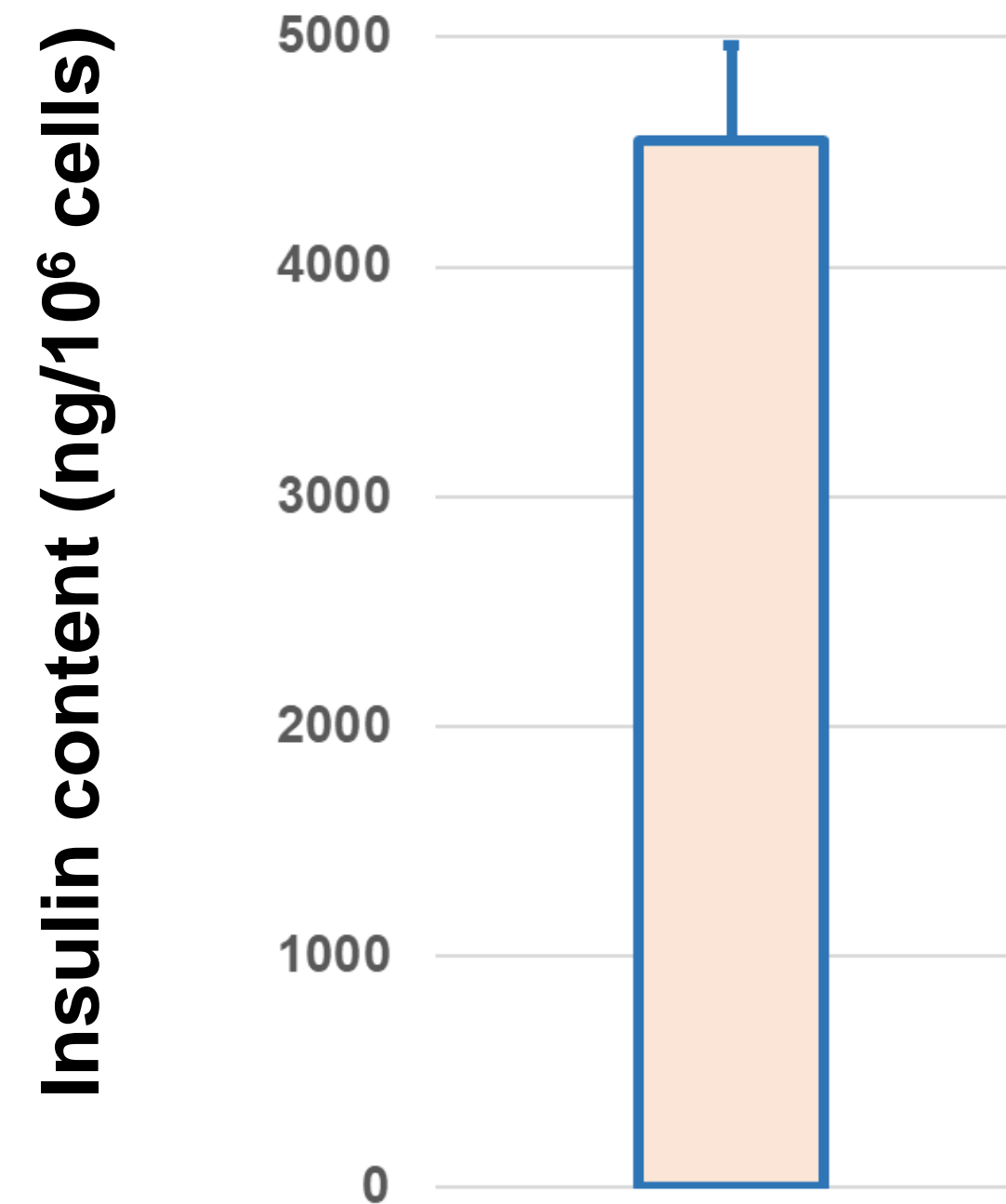


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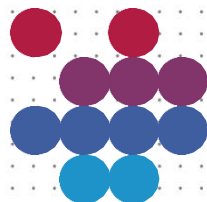
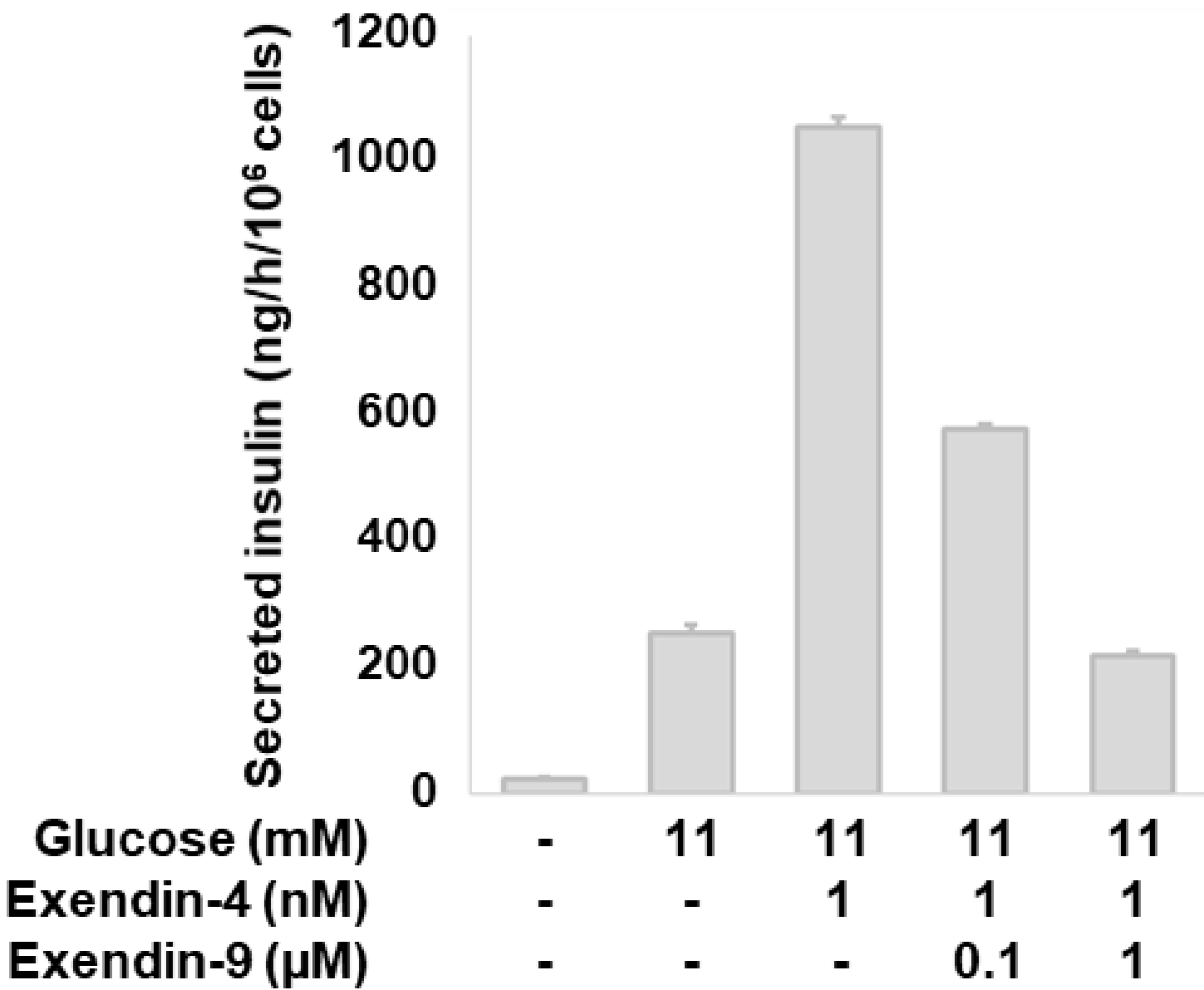
**Hamza OLLEIK, PharmD, PhD**  
[h.olleik@humancelldesign.com](mailto:h.olleik@humancelldesign.com)



Total insulin content expressed as ng insulin per million cells



GLP-1 receptor specificity of Exendin-4 potentiation of GSIS

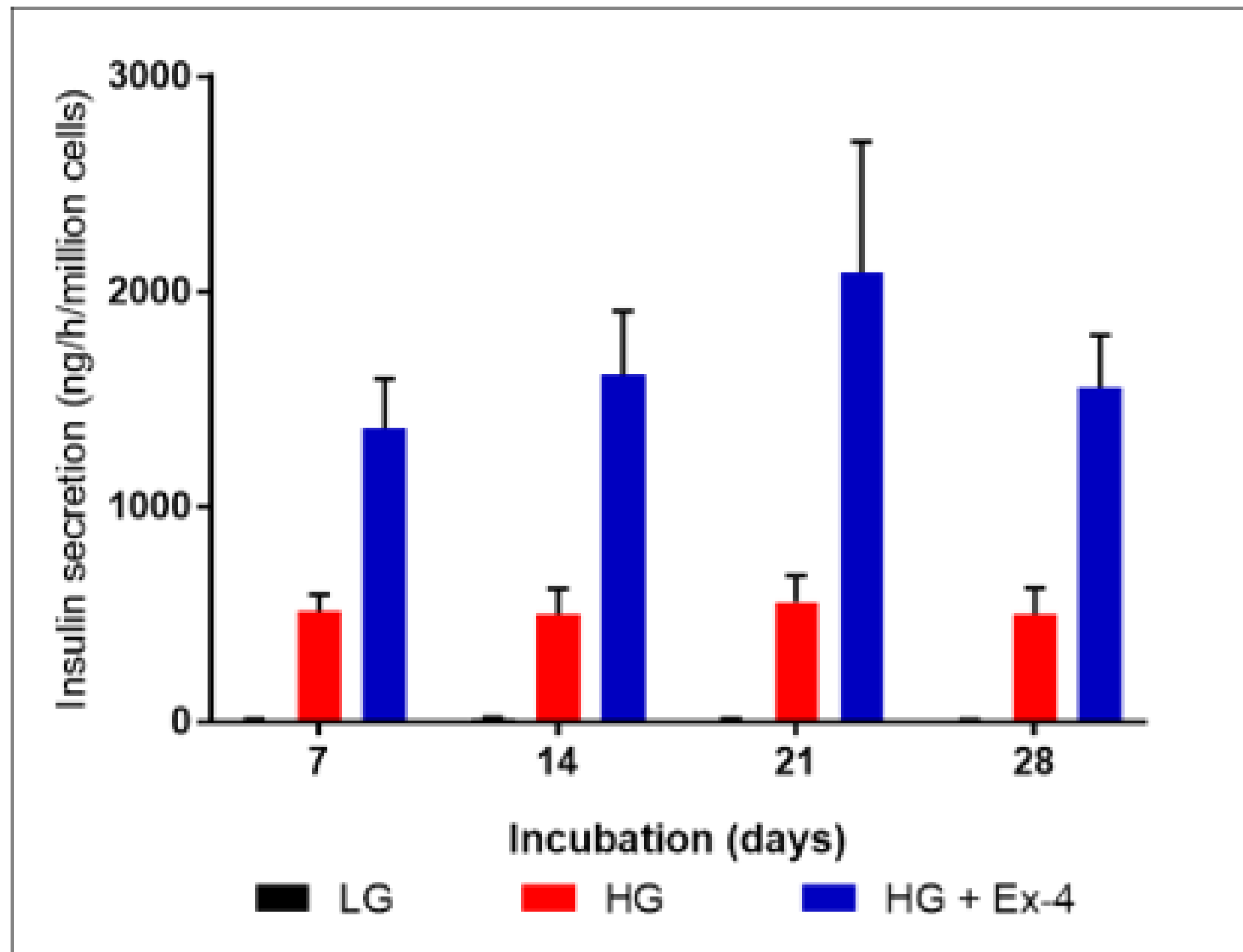




# EndoC-βH5<sup>®</sup>

## Compatible with chronic treatment studies

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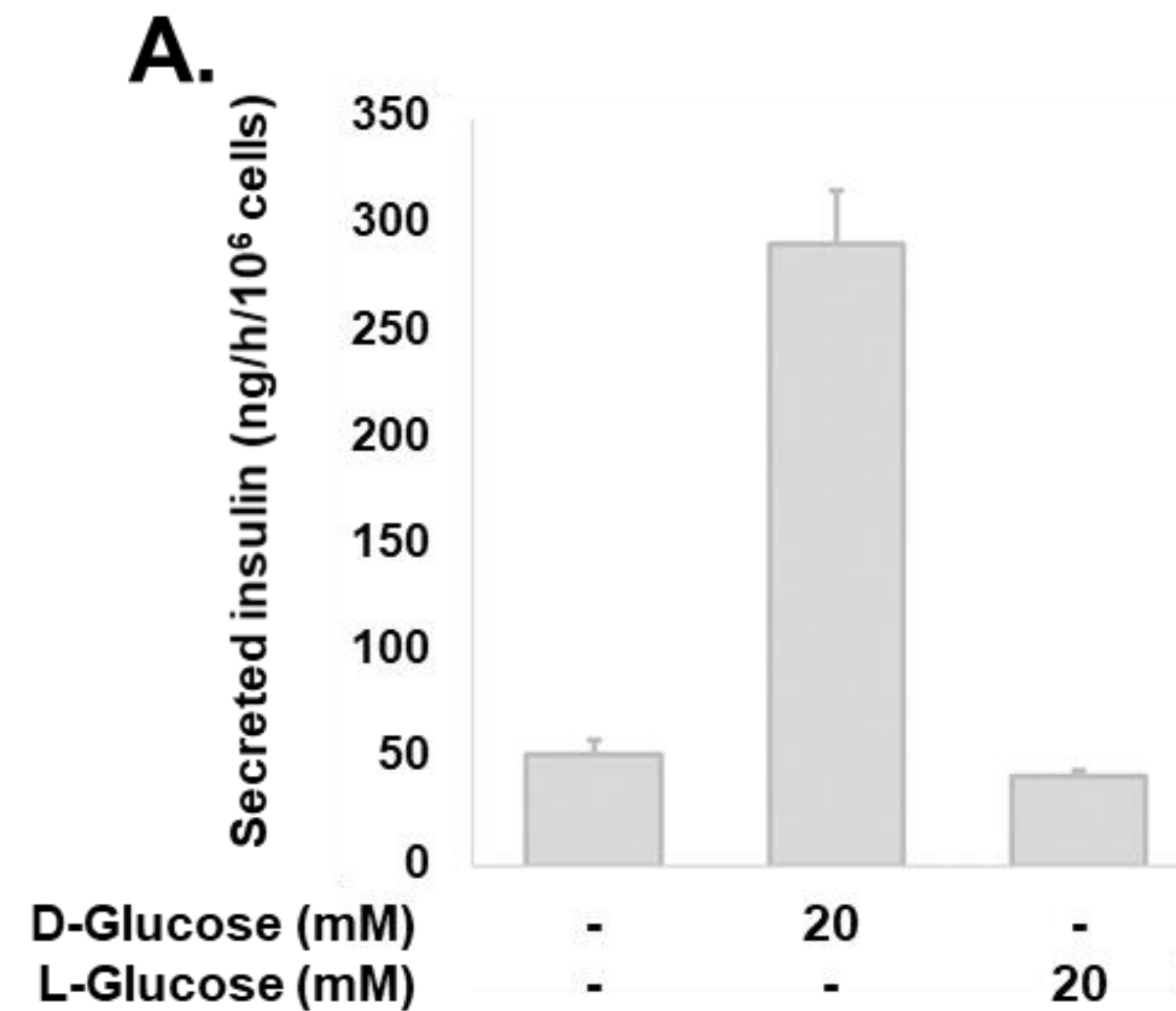
GSIS experiments were performed 7 days to 28 days after thawing and seeding of EndoC-βH5<sup>®</sup> cells:

- Stable responses for **4 weeks** post thawing and seeding
- Glucose
- GLP1R agonist Exendin-4

# EndoC- $\beta$ H5<sup>®</sup>

## Specific response to D-Glucose

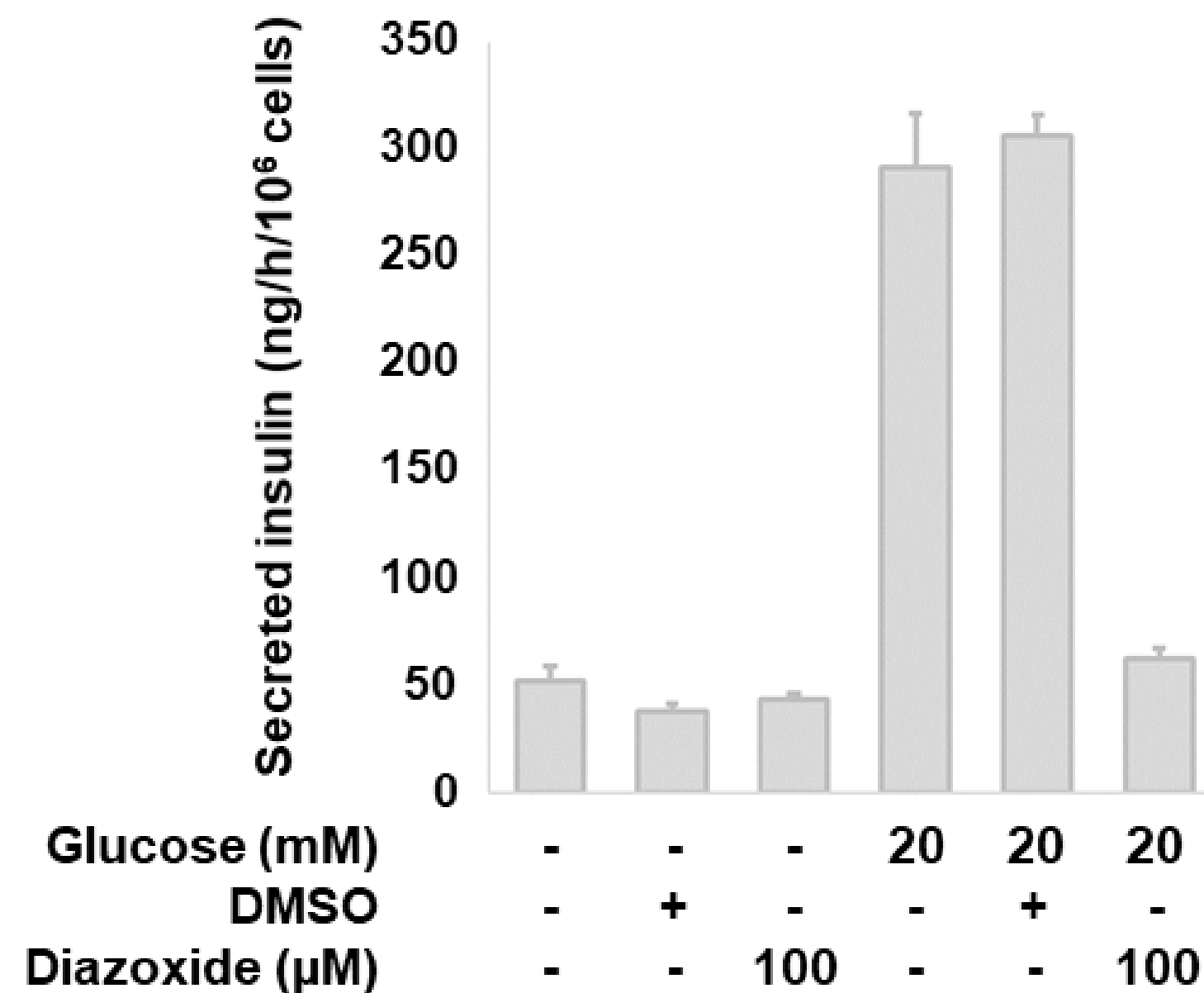
14





## Insulin secretion inhibition by Diazoxide

**B.**



# EndoC-βH5<sup>®</sup>

## Independant Validation

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Article

### Large-Scale Functional Genomics Screen to Identify Modulators of Human β-Cell Insulin Secretion

Iwona Szczerbinska <sup>1,\*</sup>, Annamaria Tessitore <sup>2</sup>, Lena Kristina Hansson <sup>3</sup>, Asmita Agrawal <sup>2</sup>, Alejandro Ragel Lopez <sup>2</sup>, Marianne Helenius <sup>3,4</sup>, Andrzej R. Malinowski <sup>1</sup>, Barak Gilboa <sup>2</sup>, Maxwell A. Ruby <sup>1</sup>, Ramneek Gupta <sup>3</sup> and Carina Ämmälä <sup>1</sup>

<sup>1</sup> Department of Discovery Biology and Pharmacology, Novo Nordisk Research Centre Oxford,

Using the EndoC-βH5<sup>®</sup> model, a new publication was published validating novel genes regulating human β-cell insulin secretion.

1. Established a **384-well** functional screen
2. Used **disease-relevant** insulin secretion **endpoints**
3. Successfully applied **siRNA**-mediated loss-of-function
4. Identified potential **T2D drug targets**



ENDOC-BH CELLS  
Hamza OLLEIK, PharmD, PhD  
All rights reserved © Human Cell Design



# HUMAN CELL DESIGN

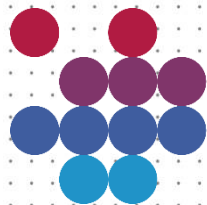
17

A leading biotech company focusing on functional human cell models and assay development

- ✓ Human cell model development and production experts
- ✓ Complex cell culture specialists
- ✓ Proprietary terminal maturation platform - Natline®
- ✓ High credibility:
  - > 200 labs worldwide
  - > 115 publications in peer reviewed journal

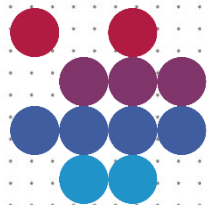
# Cell Comparison To Native $\beta$ Cells

		ENDOC- $\beta$ H1	ENDOC- $\beta$ H5	NATIVE $\beta$ CELLS
Functionality	Physiological glucose dose response	+	+++	+++
	GLP-1/GIP response	No	Yes	Yes
	Insulin content (µg/M $\text{C}$ )	0.5 – 1	Up to 10	Up to 10
Characteristics	Proliferation	Yes	No	No
	Fully mature	No	Yes	Yes
	Amplification	> 100 passage	Single use	Single use
	Purity	100% $\beta$ cells	100% $\beta$ cells	$\alpha$ / $\beta$ / $\gamma$ cells
Experimental	Time for doing your first GSIS	8 weeks	7 days	Islet preparation
	Chronic Treatment	Yes	> 4 weeks	Few days
	Handling	Culture and Preparation		Preparation
	Reproducibility and Robustness	+	+++	+
Logistics	Flexibility	+	+++	-
	Availability	Unlimited	Unlimited	Rare
Screening	96 well plate	No	Yes	Hard due to availability
	HTS	Conditional	Yes	Hard due to availability



# Cell Comparison To Native $\beta$ Cells

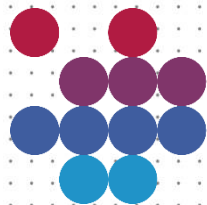
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Experimental	Time for doing your first GSIS	8 weeks	7 days	Islet preparation
	Chronic Treatment	Yes	> 4 weeks	Few days
	Handling	Culture and Preparation	Thaw-and-go / Ready to use	Preparation
	Reproducibility and Robustness	+	+++	+
Logistics	Flexibility	+	+++	-
	Availability	Unlimited	Unlimited	Rare
Screening	96 well plate	No	Yes	Hard due to availability
	HTS	Conditional	Yes	Hard due to availability





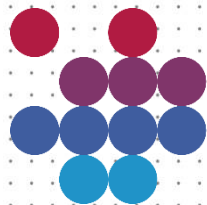
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Logistics	Flexibility	+	+++	-
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	Flexibility	+	+++	-
Logistics	Availability	Unlimited	Unlimited	Rare
Screening	96 well plate	No	Yes	Hard due to availability
	HTS	Conditional	Yes	Hard due to availability



## Take Home Messages: Added Values



EndoC-βH5

- ✓ **Batch to Batch Reproducibility**
- ✓ **Flexibility: Thaw cells when needed**
- ✓ **Availability: Unlimited**
- ✓ **HTS: 96 and 384 well plate compatibility**
- ✓ **Chronic Treatment: >4 weeks**
- ✓ **Time saving: Thaw-and-go - Results in few days**





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