

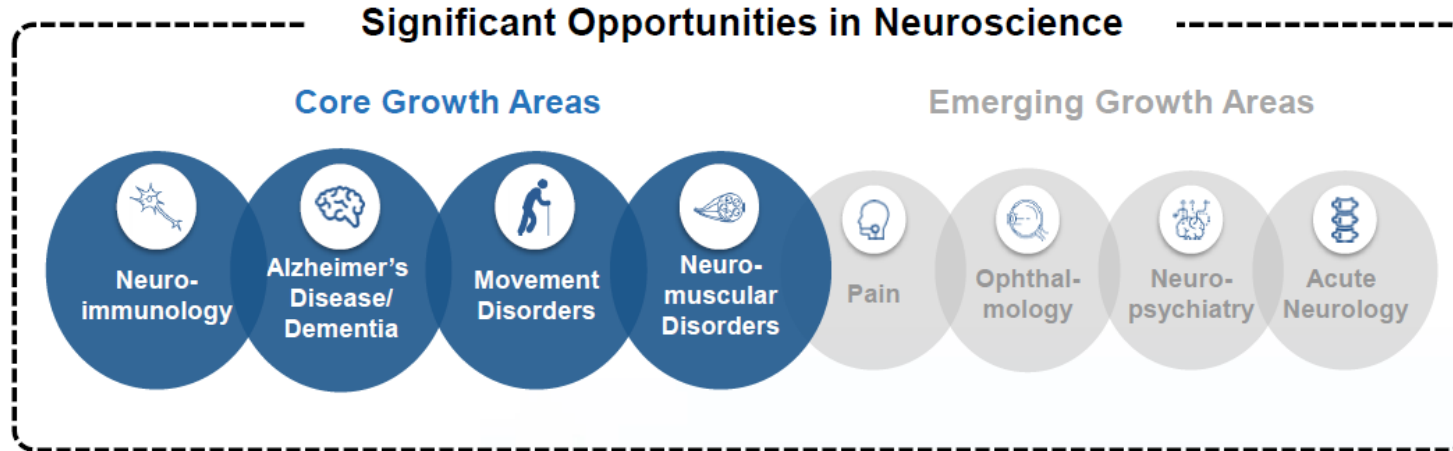
National Academy of Sciences  
Innovations in Pharmaceutical Manufacturing, October 28<sup>th</sup>

# Existing Mechanisms to Enable Innovation

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# Building an Industry Leading Neuroscience Company



**It is our belief that no other area of medicine holds as much promise with as much need as neuroscience.**

**#1** Cause of disability globally

**#2** Cause of deaths worldwide

**5<sup>th</sup>** Leading cause of death  
Stroke

**< 5 years** Average life expectancy for ALS

**~ 10M** Patients with Parkinson's disease

**~ 72M** Patients with dementia

**~ 2.5M** Multiple sclerosis patients

**SMA** is a leading genetic cause of infant mortality

# Building a Culture of Innovation

- Innovation is at the core of everything we do
- Every member of the staff is empowered to evaluate and drive new processes, initiatives and new ways of working
- Taking calculated risks and accepting the consequences
- Staying ahead of the business needs

# Enhanced Process Control for Next Gen Manufacturing of Drug Substance Biologics

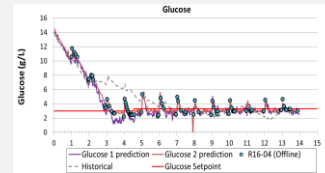
## Raw Material Screening, Rapid ID and Genealogy

- Critical material attributes identified and testing moved to supplier CoFA
- Real-time release of raw materials upon receipt using Raman Handheld and XRF technologies for >95% of raw materials
- Genealogy tools connect RM to MFG results



## Bioreactor Feed Control

- Nutrient feed controlled by inline capacitance probes.
- Glucose feed controlled by inline RAMAN



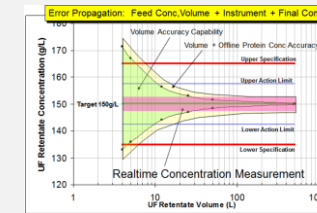
## Aggregation Feed Forward

- Feed-forward control of aggregate and process monitoring with Waters Patrol UPLC
- 10 min run time
- Result controls column loading decisions



## Inline RI Control of UF

- Historically ultrafiltration (UF) final concentration has a very low process Cpk
- The new process utilizes SPTFF technology with inline RI control for real-time protein concentration control



Raw Materials



Cell Culture



Harvest



Purification and UF/DF

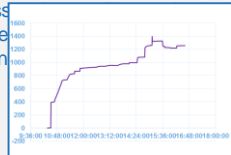


Filling

DS Release

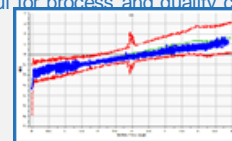
## Buffer and Media Control

- Real-time testing of media/buffer dissolution rate on con



## Multivariate modeling: Process Condition Monitoring

- Process Condition monitoring to provide real time data to manufacturing operations.
- Evolve models to fault detection that are useful for process and quality control.



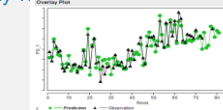
## Protein Concentration

- On the floor real-time testing for protein concentration with SoloVPE

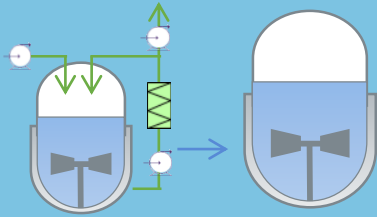


## Multivariate Modeling: Softsensors

- Models for determining if processes are in control and what variables are impacting performance.
- Predictive models aim to compliment and possibly replace laboratory testing for CQAs



# The New Way of Working



## “3X” MANUFACTURING TECHNOLOGIES

- Cell lines and media optimized for productivity
- Perfusion steps increase efficiency
- High capacity Protein A chromatography



## ENHANCED PROCESS CONTROL

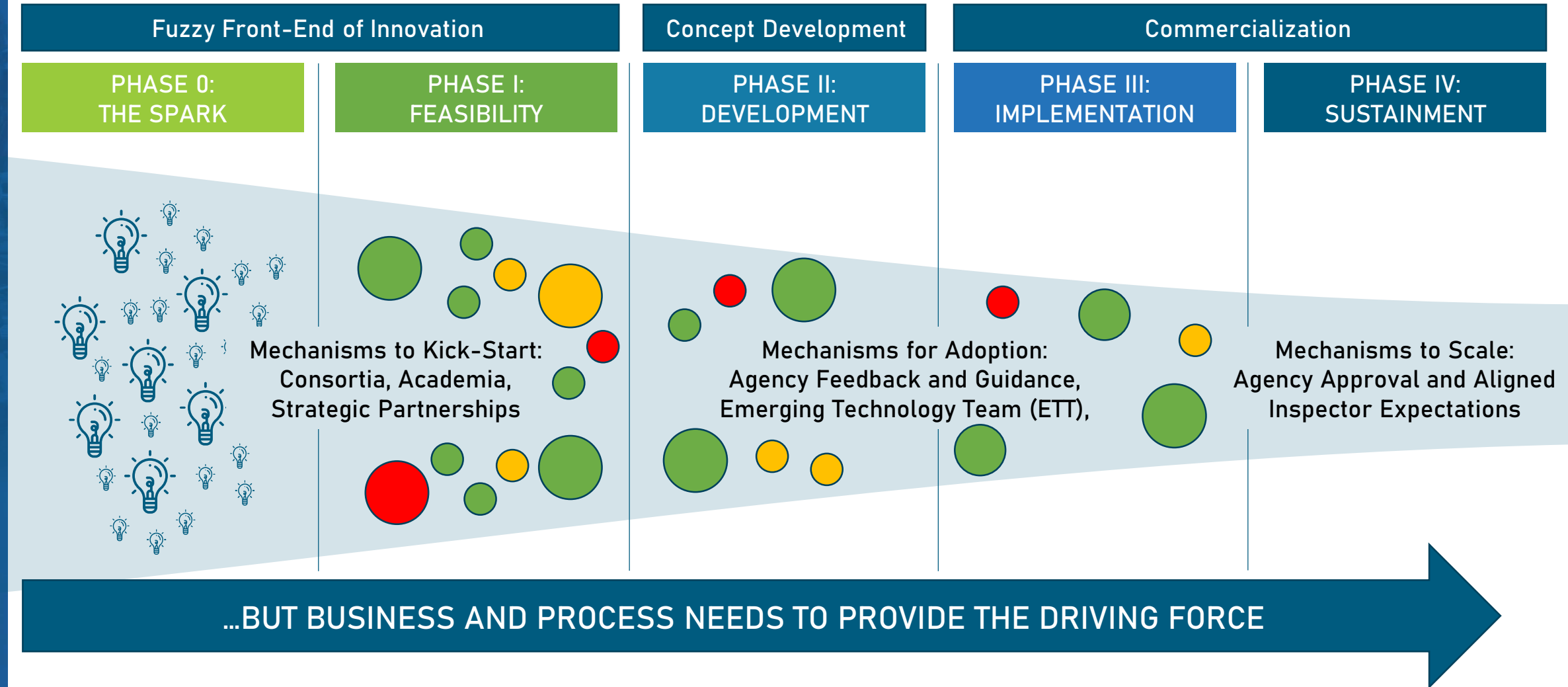
- State-of-the-art analytical technology
- Real-time control builds in quality
- Multivariate predictive modeling



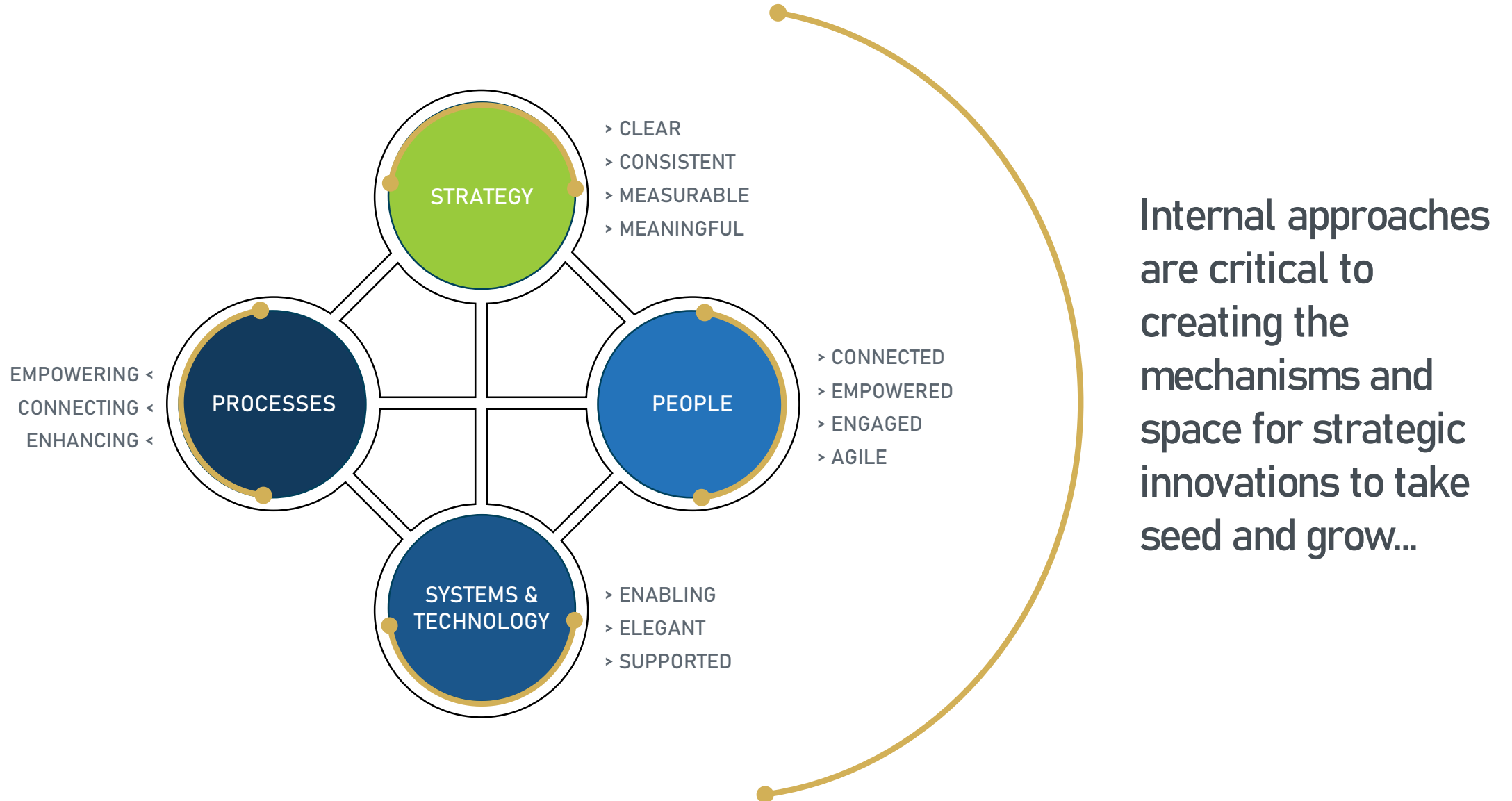
## HIGH PERFORMANCE OPERATIONS

- Localized testing, samples never rest
- Technology puts information at our fingertips
- Empowered to make timely decisions

# THE EXTERNAL PATHWAYS TO INNOVATION EXIST AND CONTINUE TO IMPROVE

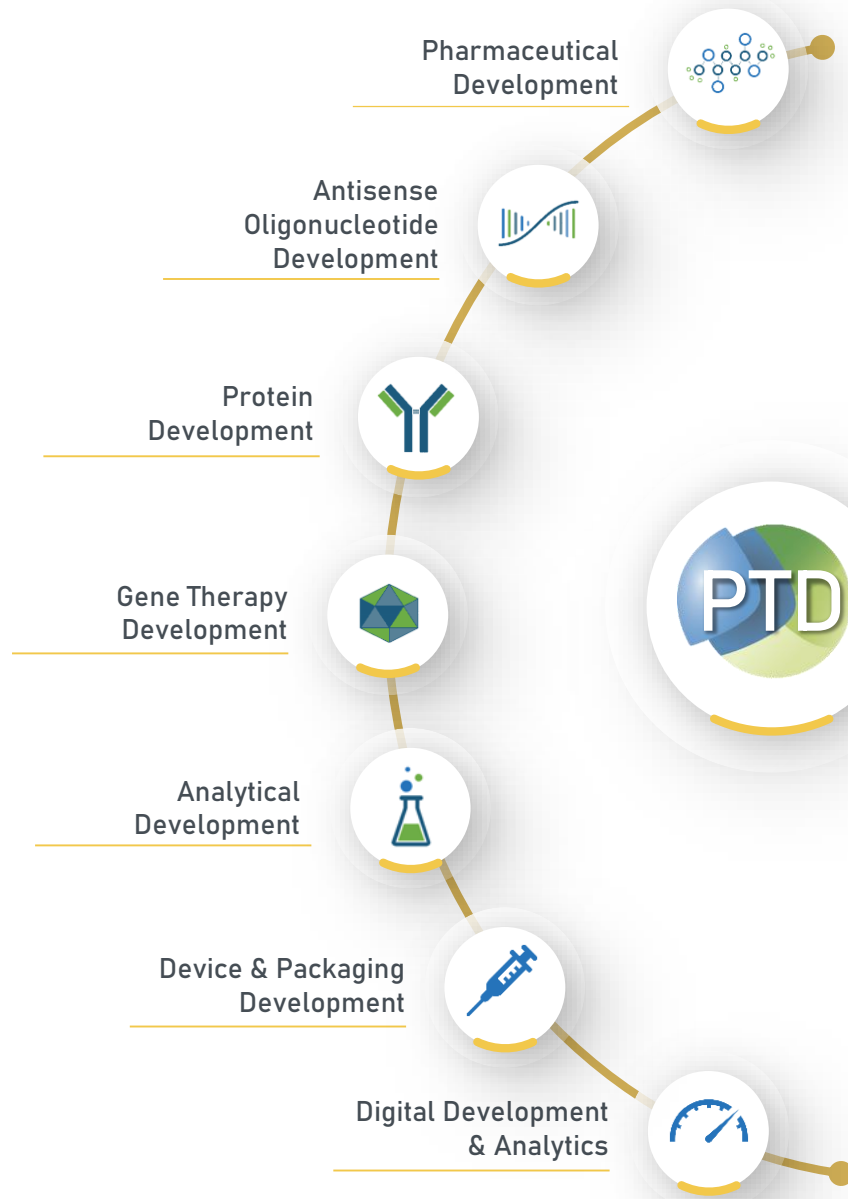


# A MAJOR ENABLER: INTERNAL INNOVATION SYSTEMS





# TECHNOLOGY THAT SUPPORTS THE INNOVATION PROCESS



Innovation Hub enables strategic prioritization, a central idea and knowledge repository, and unified visibility for innovation spanning all Development areas

## PTD INNOVATION HUB

On-ramp To:

+ Innovation Accelerator

+ CI Program

+ Program/Platform Improvements





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