

## Infographic

# GLP-1 Development Programs: One Size Does Not Fit All

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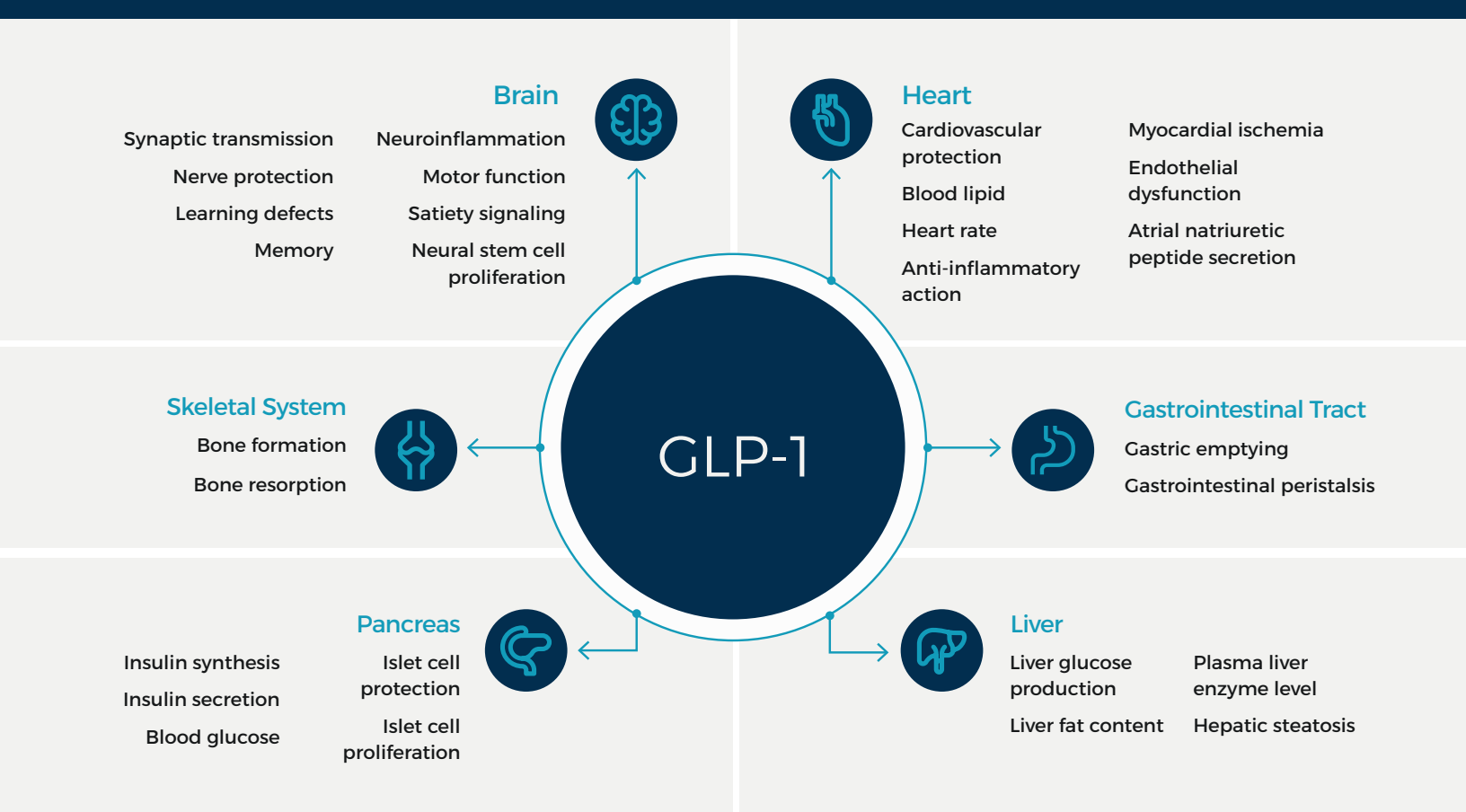
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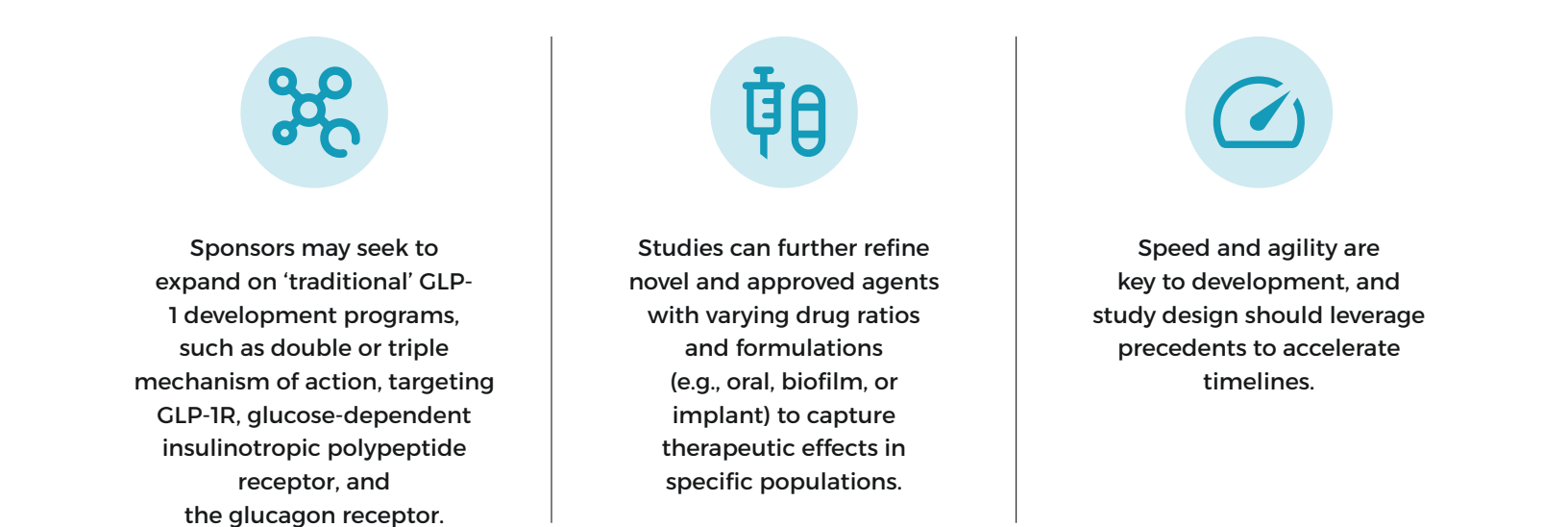
Glucagon-like peptide-1 (GLP-1) receptor agonists have completely changed the field of type 2 diabetes (T2D) and obesity. Three main development strategies are apparent in this constantly shifting area: traditional, enhancement, and exploration. Despite overlapping mechanisms of action, these approaches vary considerably in development strategy and trial design.

## GLP-1 Receptors & Target Organs

GLP-1 receptors (GLP-1R) are located throughout the body within key endocrine organs, as well as the central nervous system and heart, and GLP-1 activity at each target site has different impacts on bodily function.



## Traditional GLP-1 Development Programs

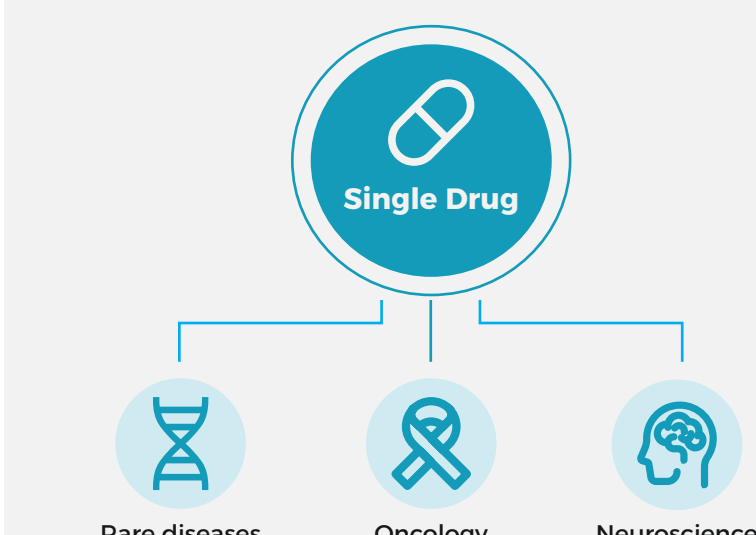


## Enhancement Hypotheses

- Sponsors pursuing an 'enhancement' hypothesis** aim to demonstrate an additive or synergistic effect with approved GLP-1 therapies.
- Enhancement hypotheses** commonly hinge on improved efficacy (e.g., weight loss and glycemic control) or improved tolerability (e.g., preservation of lean muscle mass and reduced gastrointestinal symptoms).
- Demonstrating value** above and beyond existing approved agents is paramount, demanding tailored populations and endpoints for rigorous differentiation.

## Exploratory Programs

- Given the success of GLP-1 agents across cardiometabolic indications, sponsors may set their sights on a seemingly unrelated indication within an 'exploration' program.
- GLP-1 receptors are found throughout the body and may play a key role in oncology, neuroscience (e.g., Alzheimer's or Parkinson's), and rare diseases.
- Familiarizing oneself with indication-specific guidance, study designs, populations, and assessments is key to designing a study that connects therapeutic benefits in the cardiometabolic space to an unexplored indication.



## Critical Role for Strategic Partnerships

- Sponsors developing GLP-1 products should seek a strategic partner with experience within and outside the cardiometabolic space.
- In a crowded and competitive environment, product differentiation must be embedded in Phase I clinical studies.
- Choose a partner with proven success both within and beyond the cardiometabolic space to investigate the wide-ranging therapeutic benefit of GLP-1 agents.

## Development Strategy Overview

Control	Traditional	Enhancement	Exploration
Mechanism of action	Direct overlap with GLP-1	Complimentary to GLP-1	Direct overlap with GLP-1
Differentiation	<ul style="list-style-type: none"> <li>Formulation</li> <li>Route/regimen</li> <li>Combination/agonist ratio</li> </ul>	<ul style="list-style-type: none"> <li>Improved efficacy (e.g., weight loss or HbA1c reduction)</li> <li>Improved tolerability (e.g., lean muscle mass preservation, or reduced GI side effects)</li> </ul>	<ul style="list-style-type: none"> <li>Novel indication</li> <li>Specific population</li> </ul>
Indication	Cardiometabolic (e.g., obesity, T2D, or MASH)	Cardiometabolic (e.g., obesity, T2D, or MASH)	Cardiometabolic, oncology, neuroscience, and rare disease
Objective	505b1/505b2 for streamlined approval	Demonstrate additive or synergistic effect	Safety and efficacy in special populations
Construct	Noninferiority or Superiority	Superiority	Superiority
Design considerations	Predictable clinical development plan that leverages precedent	Populations and endpoints that demonstrate added benefit	Indication-specific guidance on study designs, landscape, and special assessments

Contact us today to discuss your upcoming GLP-1 trial.

### References

- Zhao X, Wang M, Wen Z, Lu Z, Cui L, Fu C, Xue H, Liu Y, Zhang Y. GLP-1 Receptor Agonists: Beyond Their Pancreatic Effects. Front Endocrinol. 2021 Aug 23;12:721135. PMID: 34497589. PMCID: PMC8419463. doi: 10.3389/fendo.2021.721135.