

Developing treatment options for patients  
with rare gastrointestinal and endocrine  
disorders and unmet medical needs...

nps

pharmaceuticals

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*Senior Vice President and Chief Medical Officer*

*Treating rare diseases...  
Transforming lives...*

## Safe Harbor Statement



*This presentation contains forward-looking statements. These statements are based on management's current expectations and beliefs. Actual results could differ materially from those described. Please refer to company documents filed with the SEC for a more detailed discussion of risks. NPS is under no obligation (and expressly disclaims any such obligation) to update or alter its forward-looking statements, whether as a result of new information, future events, or otherwise.*

*September 2010*

Why investing in the orphan drug marketplace makes sense...

# Orphan and niche indications offer a number of favorable dynamics



- Market exclusivity
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- Favorable pricing and reimbursement potential
  - High unmet need, relatively small patient prevalence, and fewer reimbursement hurdles
- Lower clinical trial costs
  - Smaller studies
  - Potential for 'repurposing' already-approved therapies
- R&D costs of orphan drugs are typically much lower than that of standard drugs
  - Potential for conditional approvals
- Lower marketing costs
  - Focus groups mainly include specialist physicians and patient advocacy groups
- Priority review and/or fast track potential

# Healthcare reform may benefit orphan drug developers...



Fee exemption for branded prescription drugs

- Orphan drugs are *exempt* from the annual fees imposed on manufacturers of branded prescription drugs for federally funded programs

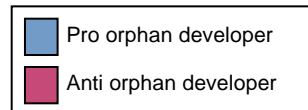
Discount exemption for 340B patients

- Orphan drugs are *exempt* from most required discounts for new entities covered by the 340B Drug Discount Program

*....but discounts to fill the Medicare “donut hole” may impact profits*

Filling Medicare “donut hole”

- Companies will be required to offer discounts for branded drugs to fill in the “donut hole” for Medicare Part D enrollees



Source: L.E.K. Research

# Payors are unlikely to significantly influence orphan pricing - despite pressure in other disease states



## Relatively low prevalence

- Low impact of orphan drugs on overall reimbursement spending
  - “... Payors see [fewer] orphan candidates because if there are only a few thousand candidates in the U.S. with a certain need, these patients are even further spread out amongst payors ...”  
Medical Director at Blue Cross Blue Shield, MS
- Limited contracting with orphan drugs due to low patient prevalence

## Public relations

- Payors will cover orphan drugs to avoid negative publicity from denying treatment for rare and often serious conditions
  - “... You don't want to be on the cover of the *Boston Globe* saying that your company won't cover these rare diseases ...”  
Pharmacy Director at Harvard Pilgrim, MA

## Cost offsetting

- Incentive to reimburse these drugs due to potential offset of high medical care costs they aim to prevent
  - “... For orphans, these are sick patients, if you don't treat them, they can run a hospital bill equivalent to drug costs ...”  
Pharmacy Director at Harvard Pilgrim, MA

**Orphan drugs will likely not be affected by pricing and reimbursement pressures in the near-term**

Source: Patient Protection and Affordable Care Act, In Vivo, Mondaq Business Briefing, Medical Marketing & Media, Inside Health Reform, L.E.K. research

## NPS strategy for success...

## NPS has transformed itself for success



*After a regulatory setback for its lead product candidate, NPS executed an aggressive strategic transformation...*

- Discontinued investment in early-stage discovery research
- Implemented an outsourcing-based business model
  - Increase efficiencies and reduce overhead costs
- Shifted the therapeutic focus from large primary care markets to rare gastrointestinal and endocrine disorders with high unmet medical needs
  - Few, if any, therapeutic options
  - Limited competition
  - Treatment by physician specialists with well-defined medical markets
  - NPS could successfully launch both compounds independently
- Focus on North American markets only
- Utilize partnerships to participate in the commercial success of therapeutic areas and geographies outside of core focus

# Lead indication for GATTEX is the treatment of parenteral nutrition dependent short bowel syndrome



- Short bowel syndrome (SBS) results from surgical resection, congenital defect or disease-associated loss of absorption
  - Characterized by the inability to maintain protein-energy, fluid, electrolyte or micronutrient balances on a conventional diet
  - Patients require intravenous feeding or parenteral nutrition (PN)
- Orphan indication
  - ~10,000 to 15,000<sup>1</sup> patients in the U.S.
- High unmet medical need
  - PN is current standard of palliative care

## Challenges of PN-dependence

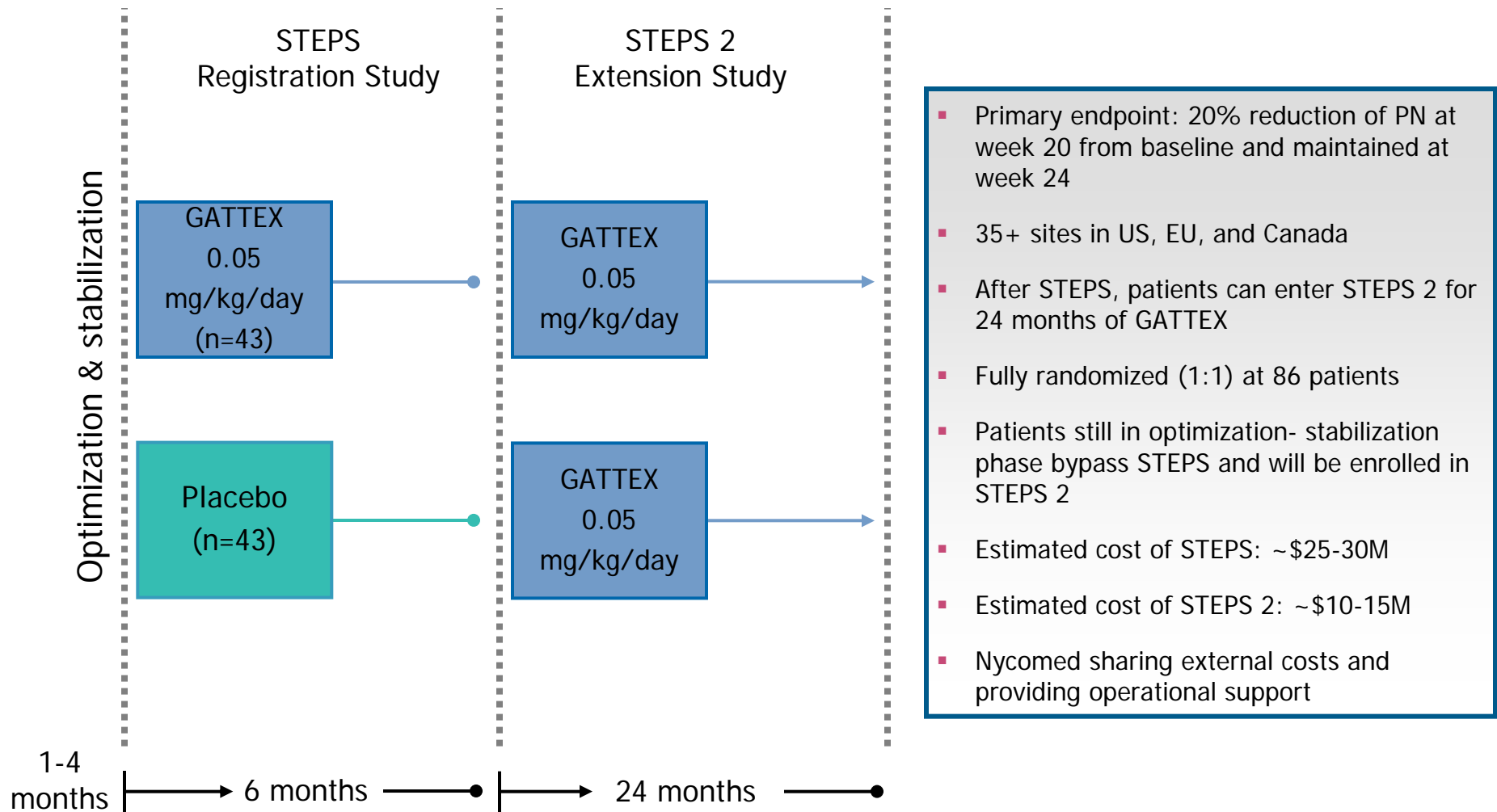
- IV drip up to 7 nights/week; 8-12 hrs/night
- Co-morbidities: liver damage, line sepsis, central venous thrombosis
- Low quality-of-life
- Direct cost \$100,000+ per patient per year

## Benefits of intestinal rehabilitation

- Reduction or elimination of PN dependence
- Improved nutrition and hydration
- Improved quality-of-life
- Reduction of direct and indirect costs

<sup>1</sup> AGA Technical Review on SBS & Intestinal Transplantation; Gastroenterology 2003;124:1111 – 1134 and NPS market research

# Second Phase 3 registration study of GATTEX (STEPS) fully randomized; results on track for early 2011



# Short bowel syndrome is a rare disorder that could represent a significant commercial opportunity



Rare & chronic disorder	<ul style="list-style-type: none"><li>▪ 10 to 15 thousand PN-dependent SBS patients in the U.S.</li><li>▪ Orphan drug status with 7 years exclusivity</li></ul>
Significant unmet need	<ul style="list-style-type: none"><li>▪ Parenteral nutrition (PN) is palliative</li><li>▪ Direct cost of PN exceeds \$100K per year</li><li>▪ PN-related complications increase burden</li><li>▪ PN significantly hinders quality-of-life</li></ul>
Favorable market dynamics	<ul style="list-style-type: none"><li>▪ Limited competition</li><li>▪ KOL-driven market</li><li>▪ Motivated patients desperately seeking solutions</li><li>▪ Positive reimbursement outlook; pricing inelasticity</li></ul>
Unique mechanism of action	<ul style="list-style-type: none"><li>▪ GI-specific mechanism of action</li><li>▪ Clinical benefits for SBS</li><li>▪ Potential to expand in additional intestinal rehabilitation related conditions</li></ul>

# Teduglutide's broad therapeutic spectrum could offer multiple opportunities in orphan indications



Intestinal failure is characterized by the inability to maintain protein, energy, fluid, electrolyte or micronutrient balance	
<i>Indication</i>	<i>Status</i>
Chemotherapy-induced GI mucositis	<ul style="list-style-type: none"> <li>▪ Pre-IND meeting held with FDA</li> <li>▪ Defining a clinical development strategy</li> </ul>
Pediatric SBS	<ul style="list-style-type: none"> <li>▪ Preclinical studies substantially complete</li> <li>▪ Potential synergies with Nycomed's pediatric investigation plan</li> </ul>
Malabsorption disorders Febrile neutropenia Radiation-induced GI mucositis Ulcerative colitis Additional pediatric indications: <ul style="list-style-type: none"> <li>▪ Necrotizing enterocolitis, acceleration of intestinal maturation, and congenital villous</li> </ul>	<ul style="list-style-type: none"> <li>▪ Under evaluation</li> </ul>

<sup>1</sup>Teduglutide, a novel mucosally active analog of glucagon-like peptide-2 (GLP-2) for the treatment of moderate to severe Crohn's disease. *Inflammatory Bowel Diseases*, 2010; 16(6):962-73

# NPS is preparing to file a US marketing application for its lead product candidate in 2011



- Two Phase 3 registration programs for specialty orphan indications
  - **GATTEX**<sup>®</sup> (teduglutide) for short bowel syndrome (SBS)
  - **NPSP558** (parathyroid hormone 1-84) for hypoparathyroidism
- Flexible outsourcing business model optimizes resources and limits financial exposure
- Internal programs complemented by valuable royalty-based portfolio for areas outside of core focus

**AMGEN**



**Sensipar**<sup>™</sup>  
(cinacalcet HCl) Tablets  
30mg-60mg-90mg

**KYOWA KIRIN**  
Kyowa Hakkō Kirin Co., Ltd.



**REGPARA**<sup>®</sup>

**NYCOMED**



**PREOTACT**  
parathyroid hormone (1-84) origin or reconstituted

**ORTHO-McNEIL**  
PHARMACEUTICAL, INC.



**NUCYNTA**<sup>®</sup>  
tapentadol

Partially monetized

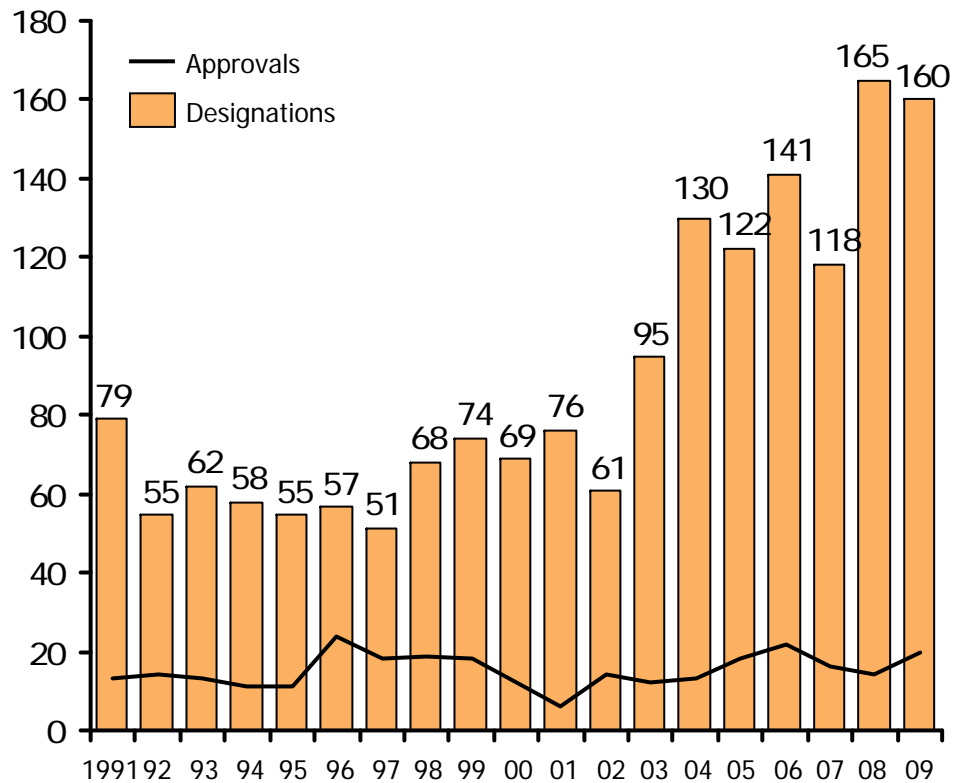
Unencumbered

Looking ahead at the rare disease market...

# Orphan and niche indications are attractive, but the regulatory path is challenging

## Annual U.S. orphan drug approvals and designations 1991-2009

Number of drugs



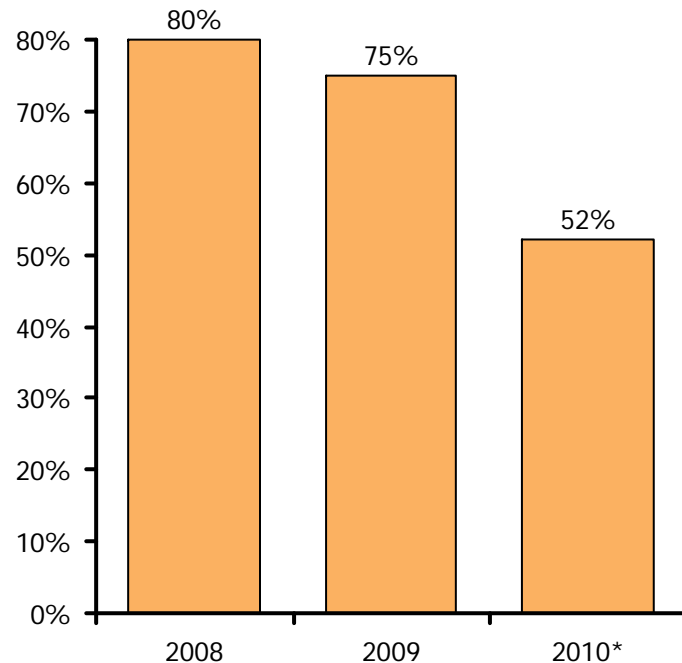
Note: \* 2010 estimated based on approvals and designations up through 2009

Source: FDA, BCC Research, Business Insights, L.E.K. analysis

# Changing regulatory requirements makes approval decisions on orphan drugs unpredictable

## FDA advisory committee positive recommendations for new drugs

Percent



- Fewer positive recommendations for NCEs in 2010
  - More products are being reviewed by advisory committees given new requirements under FDAAA 2007\*\*
  - Conflict of interest rules limit the available pool of experienced panel members for AC participation
- If this trend holds, orphan drug developers may face an increasingly challenging approval landscape
  - Given the rarity and complexity of some niche diseases, there may be a scarcity of experts

Notes: \* As of August 2010; \*\* Food and Drug Administration Amendments Act of 2007  
Source: Concept Capital, thestreet.com, L.E.K. analysis

## Leveraging existing treatments for common diseases into rare diseases may offer favorable advantages



- FDA database launched in June 2010 aims to encourage orphan drug development through database of FDA-approved compounds and products that also show promise in rare diseases
  - Advantages to 'repurposing' already-approved products
- Orphan-designated products with at least one marketing approval for a common disease indication: ~**180\***
- Orphan-designated products with at least one marketing approval for a rare disease indication: ~**170\***
- Orphan-designated products with marketing approvals for both common and rare disease indication: ~**100\***

### Large Unmet Need for New Treatments:

Despite the incentives in the Orphan Drug Act, there are only about 350 such drugs that have been approved — and there are some 7,000 rare diseases.<sup>\*\*</sup>

\* U.S. Food and Drug Administration Rare Disease Repurposing Database (RDRD) data

\*\*<http://blogs.wsj.com/health/2010/06/18/fda-database-aims-to-spark-orphan-disease-drug-development/>

# Orphan Drug designation can be leveraged to extend runway on blockbusters



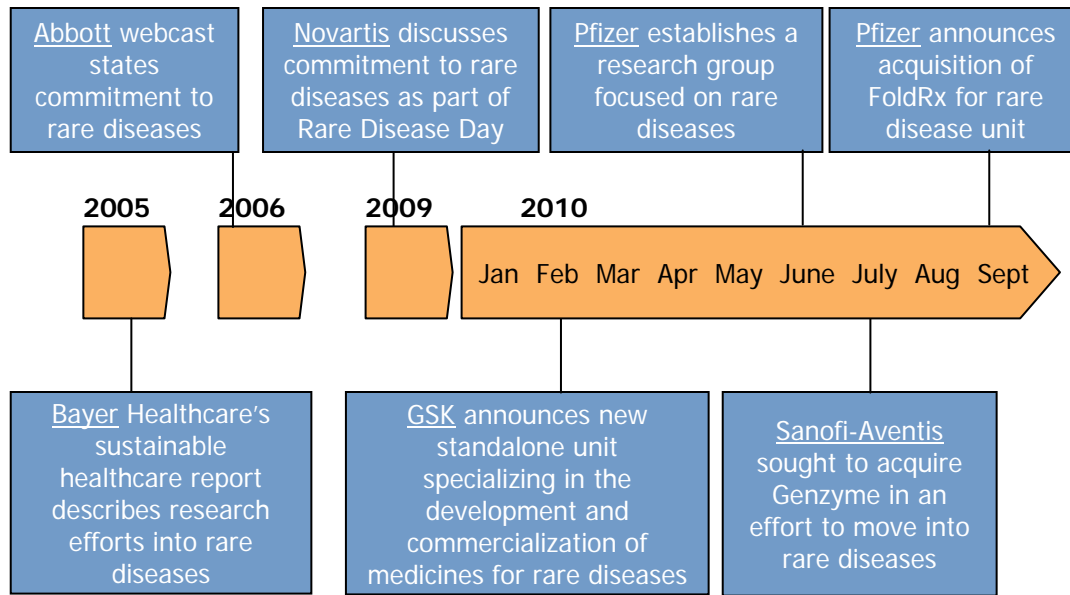
Manufacturer	Drug	Approved Common-Disease Indications**	Approved Orphan-Designated Indications**	Orphan Designated Indications Pending Approval**
		<ul style="list-style-type: none"> <li>Temporary improvement in the appearance of moderate to severe frown lines in adult patients <math>\leq 65</math> years of age.</li> <li>Upper limb spasticity in adult patients.</li> <li>Severe underarm sweating in adult patients.</li> </ul>	<ul style="list-style-type: none"> <li>Eyelid twitching associated with dystonia in adults (patients <math>\geq 12</math>)</li> <li>Cross-eyes or lazy eye associated with dystonia in adults (patients <math>\geq 12</math>)</li> <li>Cervical dystonia in adults</li> </ul>	<ul style="list-style-type: none"> <li>Dynamic muscle contracture in pediatric cerebral palsy patients</li> <li>Synkinetic closure of the eyelid associated with VII cranial nerve aberrant regeneration</li> </ul>
		<ul style="list-style-type: none"> <li>Rheumatoid Arthritis</li> <li>Psoriatic Arthritis</li> <li>Ankylosing Spondylitis</li> <li>Crohn's Disease</li> <li>Plaque Psoriasis</li> </ul>	<ul style="list-style-type: none"> <li>Moderately to severely active polyarticular juvenile idiopathic arthritis (patients <math>\geq 4</math> yrs)</li> </ul>	<ul style="list-style-type: none"> <li>Pediatric Crohn's disease</li> </ul>
 		<ul style="list-style-type: none"> <li>Refractory EGFR-expressing metastatic colorectal cancer</li> </ul>	<ul style="list-style-type: none"> <li>Squamous cell carcinoma of the head and neck in combo with radiation therapy</li> <li>Recurrent or metastatic squamous cell carcinoma of the head and neck</li> </ul>	<ul style="list-style-type: none"> <li>Pancreatic cancer</li> </ul>

\* U.S. Food and Drug Administration Rare Disease Repurposing Database (RDRD) data    \*\* Full label information truncated for length

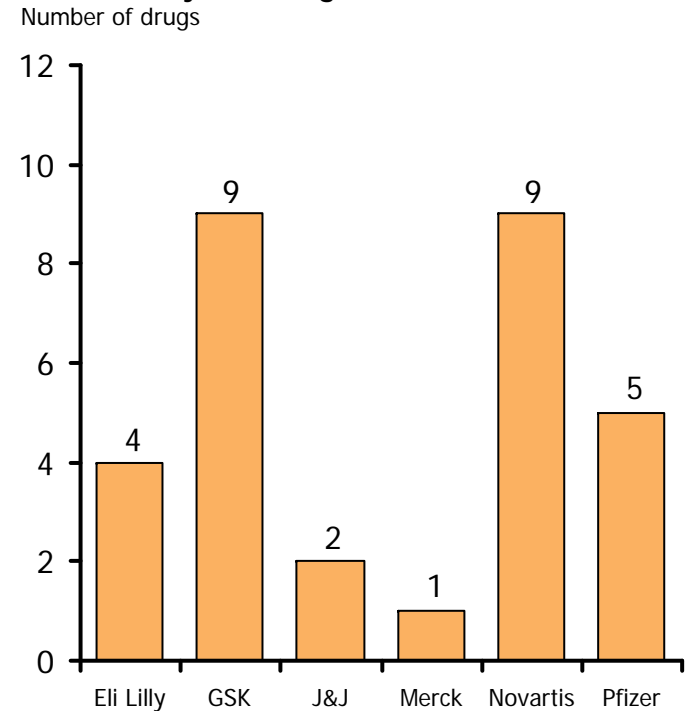
# Future of orphan drug development will continue to evolve the space



*Increased focus from big Pharma will heighten interest*



**Currently marketed orphan drugs in the U.S. by select Big Pharma\***



*Note: \* Non-comprehensive list  
Source: NPS Strategic Research*

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Thank you and questions

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