Development Trends for Peptide Therapeutics: Status in 2016

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FERRING PHARMACEUTICALS

Abstract

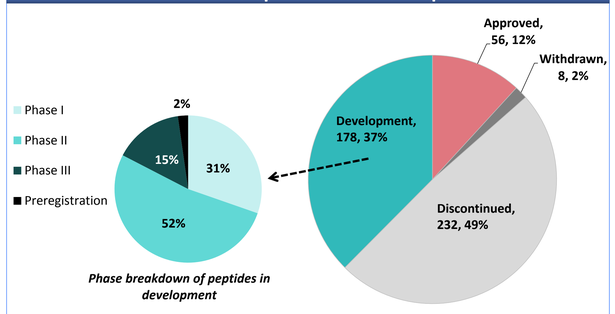
Peptides are an important class of therapeutics, with over 60 peptide drugs now approved in the US and other major markets. Peptides continue to enter clinical development at a steady pace. We have compiled and maintain a comprehensive dataset on >500 peptides that have entered human clinical studies (~250 currently approved or in active development by pharmaceutical companies).

Definitions and Introduction

- Key inclusion criteria for the peptide therapeutics database:
  - Each molecular entity was included only once in the database
  - Recombinant peptides <50aa in length; no length limit on synthetic peptides; thus, insulin products are not included
  - Peptide vaccines are not included
  - Peptide made through synthetic or recombinant methods rather than (non-ribosomal) bacterial fermentation
  - Potential regulatory/development path forward (i.e. not purely academic-sponsored)
- Only peptides with activity in major pharmaceutical markets (US, Europe, Japan) were included in the figures shown here.
- Other definitions: *"Development" refers to peptides being tested in clinical trials; "withdrawn" refers to previously approved products no longer on the market; "discontinued" refers to programs that were terminated prior to approval.*

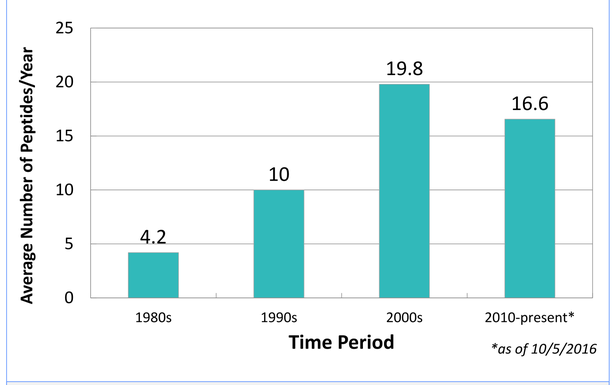
An analysis of peptide therapeutics development trends was previously published 2010 Janice Reichert, et al. with funding from the Peptide Therapeutics Foundation.

Current Development Status of Peptides



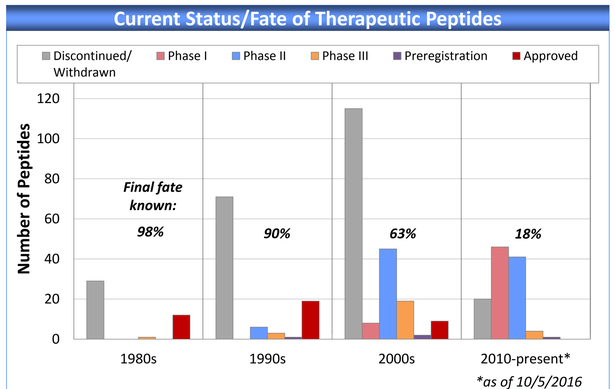
Of the 474 therapeutic peptides in the core data set, just under half are approved or in clinical development.

Average Number of Peptides Entering Clinical Trials



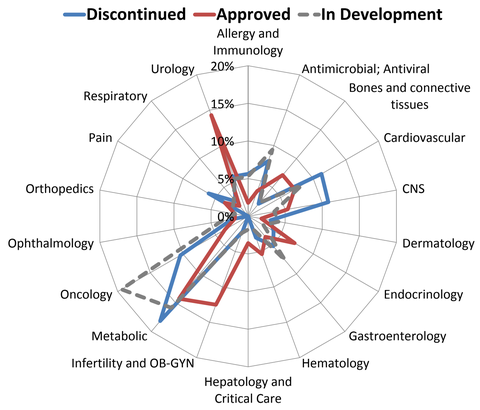
Although the average number of peptides entering clinical trials increased in the 1990's and 2000's, this pace has slowed in the 2010–present timeframe. Note that these numbers are *per-year* averages.

Current Status/Fate of Therapeutic Peptides



Most of the peptides that entered the clinic in the 1980s and 1990s have either been discontinued or approved in one or more countries. However, 37% and 82% of peptides that entered clinical trials in the 2000s or 2010s are still in development.

Peptide Approvals and Discontinuations, by TA



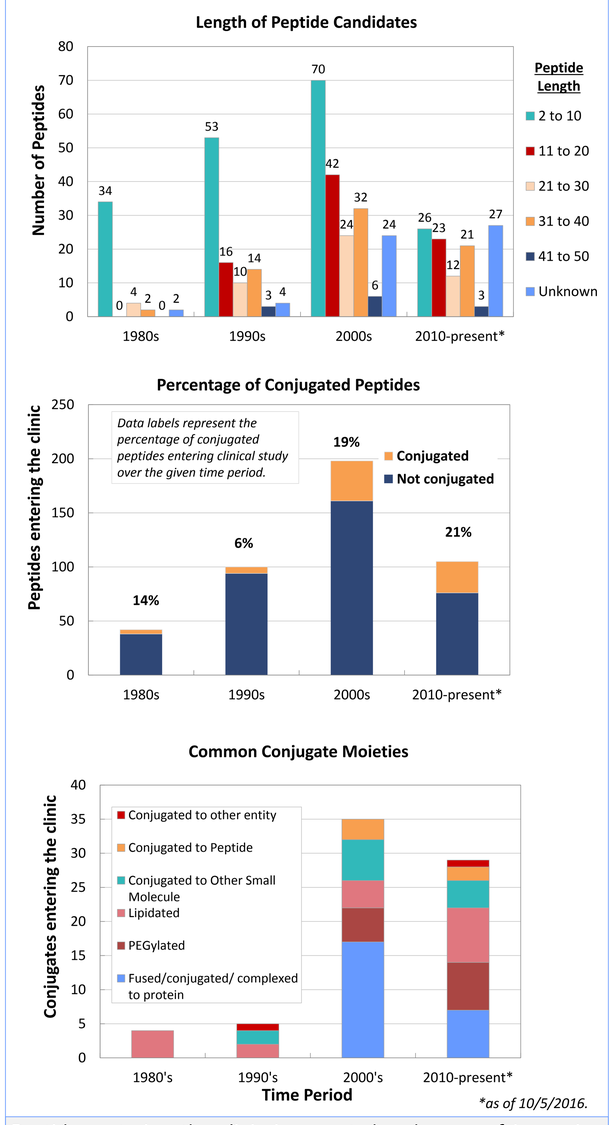
Values are given as a percentage of all peptides within the group. Each peptide was assigned to a primary TA.

Primary TA of Peptides Entering the Clinic, by Time Period

Primary Therapeutic Area (TA)	1980s	1990s	2000s	2010-present
Metabolic	1 (2%)	12 (12%)	30 (15%)	40 (35%)
Oncology	5 (11%)	8 (8%)	32 (16%)	15 (13%)
Gastroenterology	3 (7%)	6 (6%)	9 (4%)	8 (7%)
Cardiovascular	8 (19%)	9 (9%)	19 (9%)	8 (7%)
Allergy and Immunology	2 (4%)	6 (6%)	9 (4%)	6 (5%)
Antimicrobial & antiviral	2 (4%)	11 (11%)	18 (9%)	5 (4%)
Respiratory	1 (2%)	4 (4%)	2 (1%)	6 (5%)
Urology	3 (7%)	9 (9%)	11 (5%)	4 (3%)
CNS	3 (7%)	12 (12%)	14 (7%)	3 (2%)
Endocrinology	3 (7%)	3 (3%)	7 (3%)	3 (2%)
Ophthalmology	0 (0%)	1 (1%)	7 (3%)	3 (2%)
Hematology	1 (2%)	3 (3%)	7 (3%)	2 (1%)
Pain	0 (0%)	6 (6%)	10 (5%)	2 (1%)
Dermatology	1 (2%)	2 (2%)	10 (5%)	2 (1%)
Hepatology & critical care	0 (0%)	0 (0%)	1 (0%)	2 (1%)
Infertility and OB-GYN	8 (19%)	3 (3%)	4 (2%)	1 (0%)
Orthopedics	0 (0%)	1 (1%)	2 (1%)	1 (0%)
Dental	0 (0%)	0 (0%)	0 (0%)	1 (0%)
Bones and connective tissues	1 (2%)	4 (4%)	6 (3%)	0 (0%)
Total number of candidates entering clinical trials:	**42**	**100**	**198**	**112**

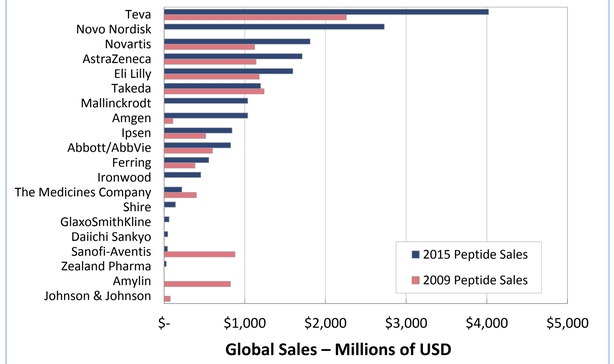
The cardiovascular and infertility TAs were the most popular for peptide development in the 1980s, but over a third of peptides that entered clinical trials since 2010 address metabolic diseases.

Length and Physical Properties of Peptides Entering Clinical Study, by Time Period

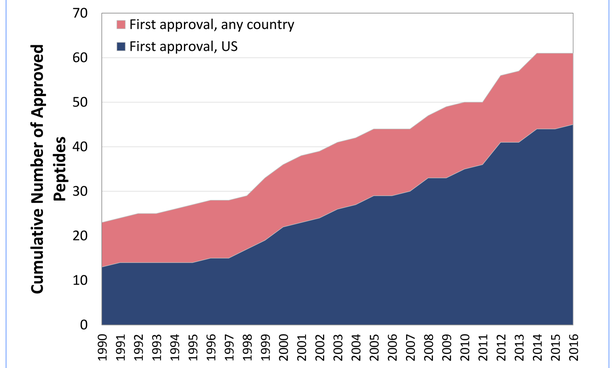


Peptides entering the clinic in recent decades are of increasing complexity with respect to length and conjugation.

The Peptide Sales Landscape

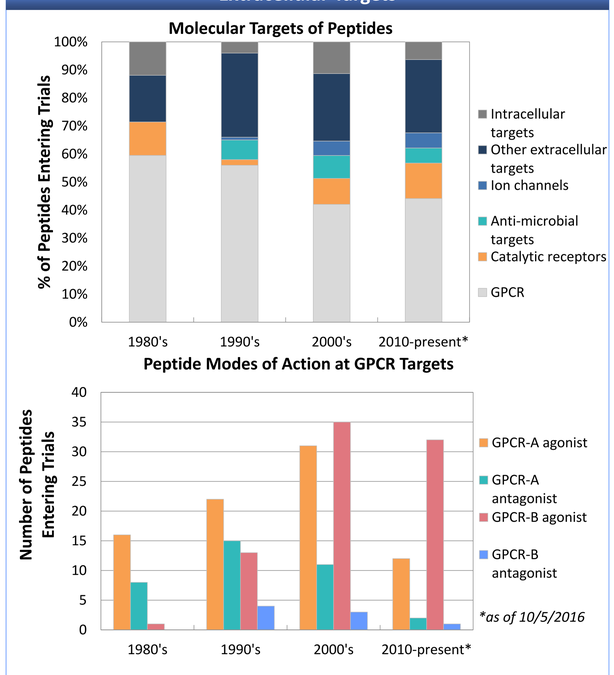


Cumulative Number of Peptide Regulatory Approvals



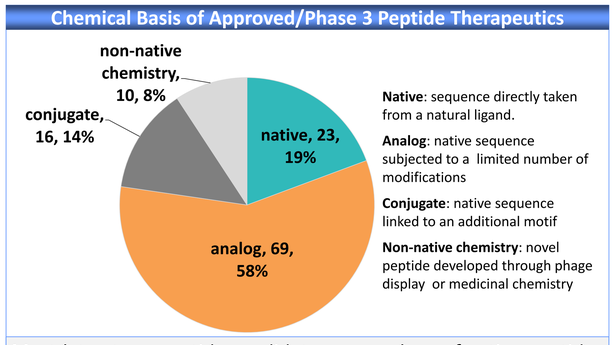
Over 60 peptides were approved in major markets worldwide, as of 2016. This figure includes peptides that were initially approved but later withdrawn from the market. No new peptides have been approved in 2015 and 2016 (as of 10/20/2016), aside from the US approval of a peptide previously approved in Europe.

Most Therapeutic Peptides Are Directed at GPCRs and other Extracellular Targets



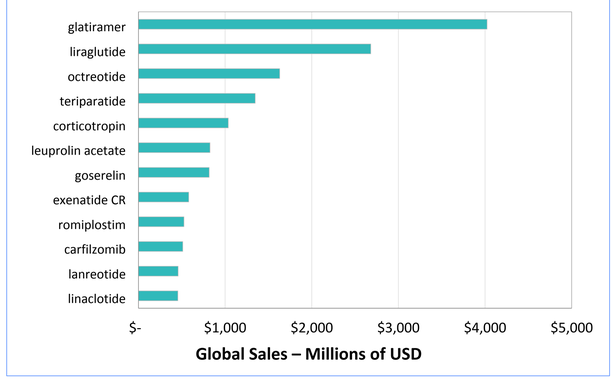
GPCRs are popular peptide targets, but other extracellular targets, such as receptor tyrosine kinases and ion channels have increased in popularity in recent years. Few peptides with intracellular targets enter the clinic.

Chemical Basis of Approved/Phase 3 Peptide Therapeutics

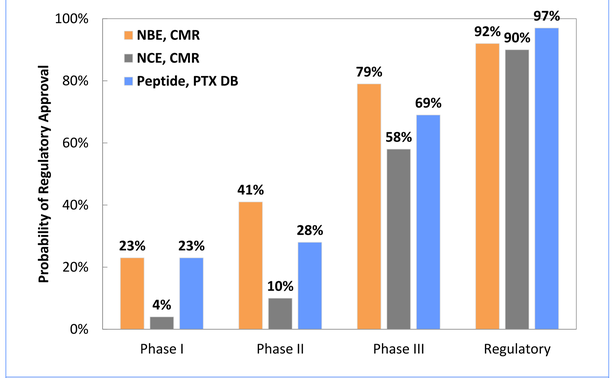


Most late-stage peptide candidates are analogs of native peptides that have been modified to improve activity or pharmacokinetics.

Peptide Top Sellers, 2015

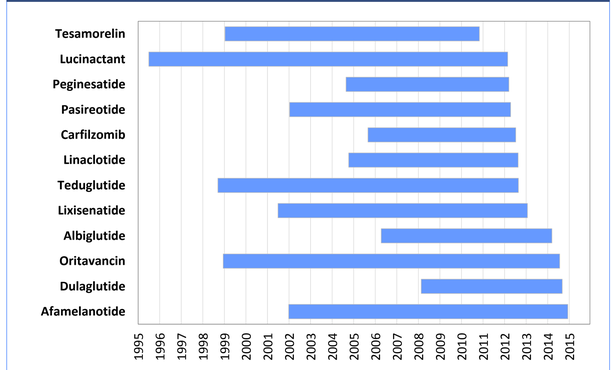


Probability of Regulatory Success by Molecule Type



Peptide regulatory success rates are intermediate between NBE and NCE rates. Most peptides are considered chemical entities by regulatory agencies. NBE=new biological entity; NCE=new chemical entity. *Sources: CMR 2015 Factbook; FRI Peptide Therapeutics Database 2015*

Development Time for Peptides Approved 2010–2016



The bars indicate the time period from start of clinical trials to first regulatory approval. This graph includes all peptides approved in the US and/or EU in 2010–2016.

Upcoming Peptide Regulatory Decisions

FDA PDUFA Dates

- Abaloparatide for osteoporosis (Radius Health): Q1 2017
- Plecanatide for CIC and IBS-C (Synergy Pharma): January 2017
- Etelcalcetide for secondary hyperparathyroidism (Amgen): unknown pending re-submission

EMA submissions

- Plitidepsin for multiple myeloma: 2H 2017

Conclusions

The peptide therapeutics space is one of active research and development. New methodologies have enabled the production of longer peptides and peptides conjugated to more complex chemical moieties, and companies are testing peptides in a wide range of disease indications.

Acknowledgments

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