development trends for peptide therapeutics

A COMPREHENSIVE QUANTITATIVE ANALYSIS OF PEPTIDE THERAPEUTICS IN CLINICAL DEVELOPMENT
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ABOUT THE 2010 STUDY:
The 2010 study of peptide development trends updates the first report of these trends, which was issued in early 2009. Both studies were conducted by the Tufts Center for the Study of Drug Development (CSDD) in cooperation with Ferring Research Institute (FRI). The 2010 report was funded by the Peptide Therapeutics Foundation. Please contact Dr. Janice Reichert by telephone at (617) 636-2182 or by e-mail at janice.reichert@tufts.edu with questions or comments regarding the study.

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ABOUT THE TUFTS CENTER FOR THE STUDY OF DRUG DEVELOPMENT:
Founded in 1976, Tufts Center for the Study of Drug Development (CSDD) is an independent, academic, non-profit research group at Tufts University. The mission of Tufts CSDD is to develop strategic information to help drug developers, regulators, and policy makers improve the quality and efficiency of pharmaceutical development, review, and utilization. Please visit Tufts CSDD’s website at csdd.tufts.edu for further information.

ABOUT THE PEPTIDE THERAPEUTICS FOUNDATION:
The Peptide Therapeutics Foundation is a non-profit organization founded in 2008. The mission of the Foundation is to promote the research and development of peptides. Please visit the Foundation’s website at www.PeptideTherapeutics.org for further information.

SPONSORS:
This Report and the update of the underlying data set was underwritten by an unrestricted guaranteed grant from the AMYLIN, Ferring Research Institute, IPSEN and The PolyPeptide Group.
Peptides are attracting increasing attention as therapeutics. To date, four of these products have reached global sales over US$1 billion: glatiramer acetate (Copaxone; $3.18 billion), leuprolide acetate (Lupron; $2.12 billion), goserelin acetate (Zoladex; $1.14 billion), and octreotide acetate (Sandostatin; $1.12 billion). In addition, exenatide (Byetta) and the recombinant peptide teriparatide (Forteo) are nearing the $1 billion benchmark, with global sales of $751 and $780 million, respectively, in 2008. The increasing interest by the pharmaceutical industry in developing peptides as drugs is at least partially a consequence of the now widespread acceptance of protein therapeutics by physicians and patients, and development of solutions to problems such as short half life and delivery of the molecules.

To track trends in the clinical development and marketing approval of peptides, Tufts Center for the Study of Drug Development and Ferring Research Institute compiled publicly-available data for a total of 435 peptides that entered clinical study sponsored by commercial firms. We focused our analysis primarily on therapeutics, which comprised 77% of the data set, although peptide vaccines and diagnostics were also included. Our results provide a historical overview of peptide therapeutics development, and may inform strategic planning in this area.
# Table of Contents

**Executive Summary** .................................................................................................................. 07

**Chapter 1: Data Set**
- Sources and type of data collected ......................................................................................... 08
- Inclusion/exclusion criteria ........................................................................................................... 09
- Analysis criteria .......................................................................................................................... 10

**Chapter 2: Peptide Therapeutics**
- Development Status .................................................................................................................. 11
- Number entering clinical study per year during seven periods ................................................. 12
- Development status per period .................................................................................................. 13
- Categories of peptide candidates ............................................................................................... 14
- Number of amino acids .............................................................................................................. 15
- Peptide candidates with attachments or extensions ................................................................. 16
- Manufacturing method ............................................................................................................... 17

**Chapter 3: Molecular Targets**
- By location ................................................................................................................................ 18
- Extracellular ............................................................................................................................... 19
- Background on structure and function of G-protein coupled receptors ................................. 20
- G-protein coupled receptors as targets ..................................................................................... 21
- Therapeutic peptides targeting GPCR-A and GPCR-B family members .............................. 22
- Modes of action vs. G-protein coupled receptor A ..................................................................... 24
- Modes of action vs. G-protein coupled receptor B ..................................................................... 25
- Innovation - First-in-class vs. follow-up targeting of peptides ................................................. 26

**Chapter 4: Approved Products**
- World-wide and US approvals by year ...................................................................................... 27
- Global sales of selected therapeutic peptides ............................................................................ 28
- Therapeutic categories .............................................................................................................. 29
- New peptide therapeutics approved in the US or EU since 1995 ........................................... 30
- New peptide therapeutics approved in the US or EU 2008-09 ................................................ 31
  - Romiplostim (NPLATE) ........................................................................................................... 31
  - Icatibant (FIRAZYR) ............................................................................................................... 32
  - Degarelix (FIRMAGON) ......................................................................................................... 33
  - Mifamurtide (MEPACT) .......................................................................................................... 34
  - Liraglutide (VICTOZA) .......................................................................................................... 35
- Clinical phase and US approval phase lengths ........................................................................... 36

**Chapter 5: Clinical Development Success Rates**
- Clinical and review phase transition probabilities ................................................................. 37
- Transition probabilities of by phase of development ............................................................... 38
- Probabilities of approval success ............................................................................................. 39
- Predicted number of candidates per approval ......................................................................... 41
- Phase transition probabilities for therapeutic categories ....................................................... 42
- Reasons for attrition .................................................................................................................. 44

**Chapter 6: Late Stage Pipeline**
- Candidates in Phase 3 .............................................................................................................. 45
- Candidates in regulatory review ............................................................................................... 46

**Chapter 7: Conclusion**
- Conclusion ................................................................................................................................. 47
list of figures and tables

CHAPTER 2
Figure 1 Development status of 334 therapeutic peptides ..........................................................11
Figure 2 Average annual number of peptide therapeutics entering study during seven periods ......................12
Figure 3 Development status for therapeutic peptides entering Phase 1 studies during 3 periods .................13
Figure 4 Therapeutic categories for peptide candidates entering study in three periods ........................14
Figure 5 Length of therapeutic peptides that entered clinical study in three periods .................................15
Figure 6 Types of extensions or attachments to peptides studied in the clinic .......................................16
Figure 7 Manufacturing method for therapeutic peptides entering study in three periods ......................17

CHAPTER 3
Figure 8 Location of target for therapeutic peptides entering clinical study in three periods ....................18
Figure 9 Extracellular target type for therapeutic peptides entering clinical study in three periods ............19
Figure 10 GPCR type targeted by therapeutic peptides entering clinical study in three periods ...............21
Table 1 Therapeutic peptides targeting GPCR-A family members .......................................................22
Table 2 Therapeutic peptides targeting GPCR-B family members .......................................................23
Figure 11 Activity of GPCR-A targeting therapeutic peptides entering clinical study in three periods ........24
Figure 12 Activity of GPCR-B targeting therapeutic peptides entering clinical study in three periods ........25
Figure 13 Novelty of targets for therapeutic peptides entering clinical study in three periods .................26

CHAPTER 4
Figure 14 Cumulative number of therapeutic peptides approved during 1980-2008 .................................27
Figure 15 Global sales for 13 peptide therapeutics .............................................................................28
Figure 16 Therapeutic categories for 51 peptides approved for marketing ...........................................29
Table 3 Peptide therapeutics approved in the US or EU since 1995 ......................................................30
Figure 17 Mean clinical and US approval phases for peptide NCEs approved by FDA during 2000-08 .........36

CHAPTER 5
Figure 18a Phase transition rates for therapeutic peptides entering study 1984-2005 ............................37
Figure 18b Phase transition rates for therapeutic peptides entering study 1994-2007 ............................37
Figure 19 Overlapping periods 1984-2005 .....................................................................................38
Table 4 Success rates for therapeutic peptides entering clinical study in four periods ............................39
Figure 20a Approval probabilities for therapeutic peptides at four stages, 1984-2005 ..........................40
Figure 20b Approval probabilities for therapeutic peptides at four stages, 1994-2007 ..........................40
Figure 21a Predicted ratio of therapeutic candidates in pipeline per one approval, 1984-2005 ...............41
Figure 21b Predicted ratio of therapeutic candidates in pipeline per one approval, 1994-2007 ...............41
Figure 22a Clinical phase transition probabilities for peptides in six therapeutic categories .................42
Figure 22b Approval probabilities for therapeutic peptides in six therapeutic categories .....................42
Figure 23 Reason for attrition of therapeutic peptides that entered study during 1989-2000 .................44

CHAPTER 6
Table 5 Therapeutic peptides in Phase 3 studies ...............................................................................45
Table 6 Therapeutic peptides in regulatory review ...........................................................................46
OVERVIEW OF THERAPEUTIC PEPTIDE DEVELOPMENT:
A total of 334 therapeutic peptides were included in the data set. Of these, approximately equal numbers were in development (131 candidates) or had been terminated (149 candidates), while a total of 54 had been approved for marketing. The candidates in development included 41 at Phase 1, 72 at Phase 2, 16 at Phase 3 and two in regulatory review. Although peptides have been studied as drugs for decades, the rate of entry into clinical study was low prior to the 1980s. The average number of new candidates entering study per year has steadily increased; this number was 1.2 per year in the 1970s, 4.6 per year in the 1980s, 9.7 per year in the 1990s, and 16.8 per year so far in the 2000s (Figure 1).

peptide NCEs entering clinical study

Since the 1980s, peptides have been studied as treatments for a wide variety of indications. During 2000-2008, peptides entering study were most frequently treatments for cancer and metabolic disorders (18% and 17%, respectively). The percentage of candidates for metabolic disorders represents a notable increase from the 1980s and 1990s, when 2% and 11% of peptide therapeutics, respectively, were studied in this category. Indications such as diabetes, obesity, and osteoporosis are included in the metabolic category. Decreases were observed in the study of peptides as treatments for allergy and immunological disorders, as well as for cardiovascular disease.

Continued on next page
The majority of peptide candidates targeted extracellular molecules, with less than 10% known to bind intracellular targets. The most common extracellular targets during the 1980s, 1990s, as well as 2000-2008 were G-protein coupled receptors (GPCRs). This family of receptors includes nearly 1000 transmembrane proteins that activate cellular responses. GPCRs are the target of numerous marketed drugs, as well as clinical candidates that are intended as treatments for a variety of indications. Of novel peptide candidates that entered clinical study during the 1980s, 1990s and 2000-2008, GPCRs were targeted by 69%, 75% and 60%, respectively, and most of these had agonist activity.
A total of 54 therapeutic peptides in the data set were approved by at least one regulatory agency, although four were subsequently withdrawn from their markets. Of the products now approved, 26 are currently marketed in the US and other countries and 28 are marketed only outside the US. Many (61%) of the products were approved during the 1990s and 2000s. Products were approved in an array of therapeutic categories, with the largest number of approvals in the oncology (17%), obstetrics/gynecology (9%) and allergy and immunological categories (9%).

Of the US-marketed products, 10 were approved after 2001 (Table 1).

Probabilities of approval success are important for strategic planning of product pipelines. Based on the data currently available for candidates with known fates (approval or termination), the approval success rates for peptide candidates that entered clinical study during 1984-2000 were in the range of 23-26%. Many of the candidates that entered clinical study during the 2000s remain under investigation.

Clinical and approval phase lengths are also important benchmark measures. To determine phase lengths that would be useful for planning purposes, we examined data for 15 peptide new molecular entities that were approved by FDA after enactment of the Prescription Drug User Fee Act (PDUFA) of 1992. This legislation, and subsequent reauthorization acts, defined timeline goals for FDA's review of candidates based on a two-tier ranking system. Under the current guidelines, candidates are given either a priority or standard review, with performance goals of six and ten months, respectively, for the time to FDA's first action on an application.

* Withdrawn from US market in May 2005 due to poor sales
clinical and US approval phases

For all 15 products, the average clinical and approval phases were 103.0 and 24.8 months, respectively. The total time from the initiation of clinical studies to FDA approval was thus 127.8 months (Figure 2). The average clinical phase for the six priority reviewed products was 74.2 months, which was 28% shorter than the average for all 15 NME peptides. Standard-reviewed products had an average clinical phase of 122.3 months, which was 19% longer than the average for all products. Priority reviews are given to candidates that are treatments for serious or life-threatening diseases, or that might represent a significant improvement in the treatment of a disease. Candidates that fit this description are eligible for FDA programs such as Fast Track that may shorten the clinical phase. Indeed, three of the five products with the shortest clinical phases had either fast track designation or received an accelerated approval.

Note: The product clinical phase was defined as the time from the earliest of either the first investigational new drug application filing date or the date clinical study was initiated to the date the marketing application was submitted to the FDA. The approval phase was defined as the time from the marketing application submission date to the first approval date. The approval phase is therefore the sum of all FDA review time and all sponsor response time. P: priority review; S: standard review.
future directions

Peptide therapeutics research and development is dynamic, with increasing numbers of candidates entering clinical study in a wide variety of therapeutic categories. We anticipate that the pharmaceutical and biotechnology industries will continue to focus on these versatile molecules because of the increased acceptance of injected drugs on the market, the availability of new formulation and delivery technologies, and the relatively high approval success rates. In particular, peptide candidates for metabolic disorders such as diabetes, obesity, osteoporosis that are prevalent in a sedentary, aging population are likely to enter study in increasing numbers. More than 15 candidates are in Phase 3 clinical studies or regulatory review, which suggests that peptide therapeutic products will continue to be approved at a steady pace in the future. Our research results represent a baseline against which future growth will be measured.