

2008 Report Summary

# development trends for peptide therapeutics

THE FIRST COMPREHENSIVE  
QUANTITATIVE ANALYSIS OF  
PEPTIDE THERAPEUTICS IN  
CLINICAL DEVELOPMENT



PEPTIDE  
THERAPEUTICS  
FOUNDATION

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## **ABOUT THE 2008 STUDY:**

The 2008 study of peptide development trends was conducted by the Tufts Center for the Study of Drug Development in cooperation with Ferring Research Institute (FRI), and was funded by FRI. The report resulting from the 2008 study has been donated by FRI to the Peptide Therapeutics Foundation. Please contact Dr. Janice Reichert by telephone at (617) 636-2182 or by e-mail at [janice.reichert@tufts.edu](mailto:janice.reichert@tufts.edu) with any 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](http://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](http://www.PeptideTherapeutics.org) for further information.



# introduction

With a total of 48 products now on the market, therapeutic peptides comprise an important class of drugs. Four products reached global sales over \$500 million each in 2007: Copaxane (\$3.33 billion), Lupron (\$1.88 billion), Byetta (\$967 million), and Forteo (\$709 million) [MedAdNews 2008 Jul:14(7)]. Although generally not as convenient to administer as traditional small molecules, peptides and protein-based therapeutics (e.g. monoclonal antibodies) are currently well-accepted by physicians and patients.

Commercial interest in therapeutic peptides has soared due in part to advances in synthetic, delivery and formulation technologies. The pharmaceutical industry is aggressively investing in therapeutic peptide R&D by initiating internal programs and by acquiring companies that focus on this area. This strategy has resulted in a notable increase in the number of peptide therapeutics that entered clinical study during 2000-2007.

In order to track clinical development and approval trends for this important therapeutic class Tufts Center for the Study of Drug Development, in cooperation with Ferring Research Institute, collected data on 419 peptide therapeutics, vaccines, and diagnostics that entered clinical study sponsored by commercial firms. The data set was analyzed in various ways, and results pertaining to the therapeutic peptides are presented in this 2008 report. Results include descriptive statistics, probabilities of success, and clinical and US approval phase lengths. Data for candidates in Phase 3, regulatory review, and recently approved products are also presented.



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# summary: trends in the clinical development and approval of peptides

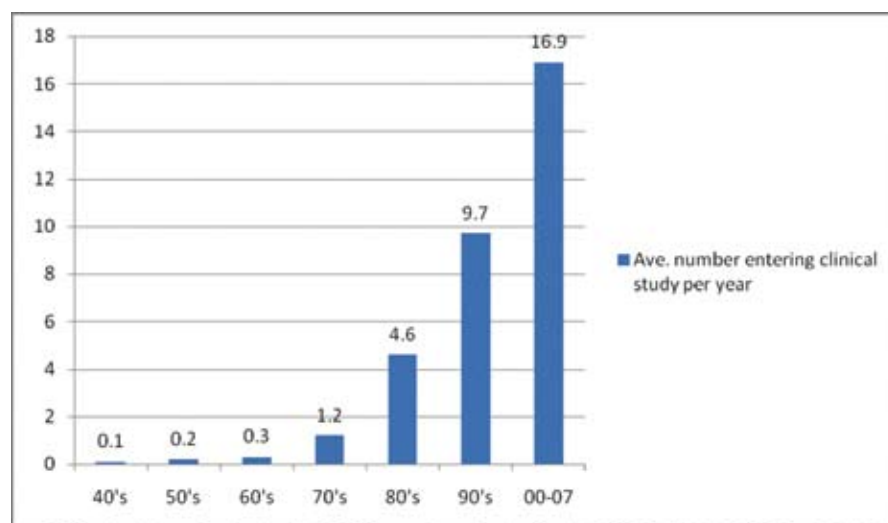
Janice Reichert, Ph.D., Senior Research Fellow  
Tufts Center for the Study of Drug Development, Tufts University

Although peptides have long been staples of research and development (R&D), the study of therapeutic peptides has recently attracted a great deal of attention from the pharmaceutical industry. Interest has been piqued in part because of advances in synthetic, delivery and formulation technologies, and acceptance of injectable therapeutics (e.g., monoclonal antibodies) in markets world-wide. Due to these factors, the pharmaceutical industry is aggressively investing in therapeutic peptide R&D by initiating internal programs and by acquiring companies that focus on this area.

Tufts Center for the Study of Drug Development continuously collects data for both new candidates entering clinical study and those recently acquired by companies from non-commercial sources. In cooperation with Ferring Research Institute, we have established a data set of over 400 peptide therapeutics, vaccines and diagnostics based on information available in the public domain. As of October 2008, the data set included a total of 419 peptides that were either developed in-house or in-licensed by commercial firms, and had been studied in a clinical setting. The majority (76%) of the candidates were therapeutics, with the remainder studied as vaccines (21%) or diagnostics (3%). This data set was used

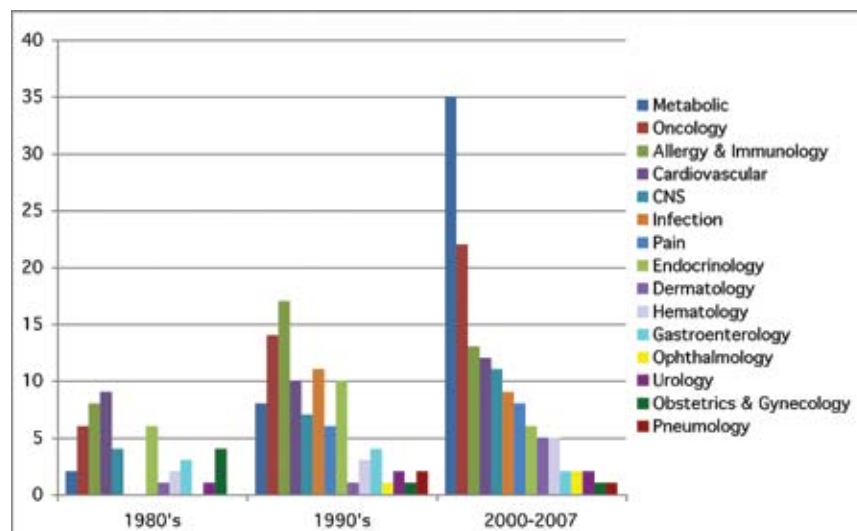
## figure 1

Average annual number of peptide therapeutics entering study during seven time periods



## figure 2

Therapeutic categories for peptide candidates entering study in three time periods



to determine trends in the development and approval of peptide therapeutics reported here.

The combined efforts of biotechnology and pharmaceutical firms have led to a notable increase in the average number of molecules entering clinical study each year (Figure 1). This number nearly doubled between the 1990s and the 2000-2007 periods. Final fates (approval in any country or discontinuation of all clinical development) are known for most (87%) of the therapeutic peptide candidates that first entered clinical study in the 1980s and 1990s, but the majority of candidates that entered the clinic recently are still being evaluated in early-stage studies.

Therapeutic peptides were studied in a total of 15 therapeutic categories during the 1990s and 2000-2007 periods, which was an increase from the 11 categories investigated in the 1980s (Figure 2). During 2000-2007, new therapeutic peptides entering study were most frequently treatments for metabolic indications (26%), whereas only 4% and 8% of peptides entering study in the 1980s and 1990, respectively, were studied for these disorders. Decreases were observed in the study of peptides as treatments for cardiovascular (20%, 10% and 9% for the 1980s, 1990s and 2000-07 periods, respectively) and allergy & immunological diseases (17%, 18% and 10% for the 1980s, 1990s and 2000-07 periods, respectively).

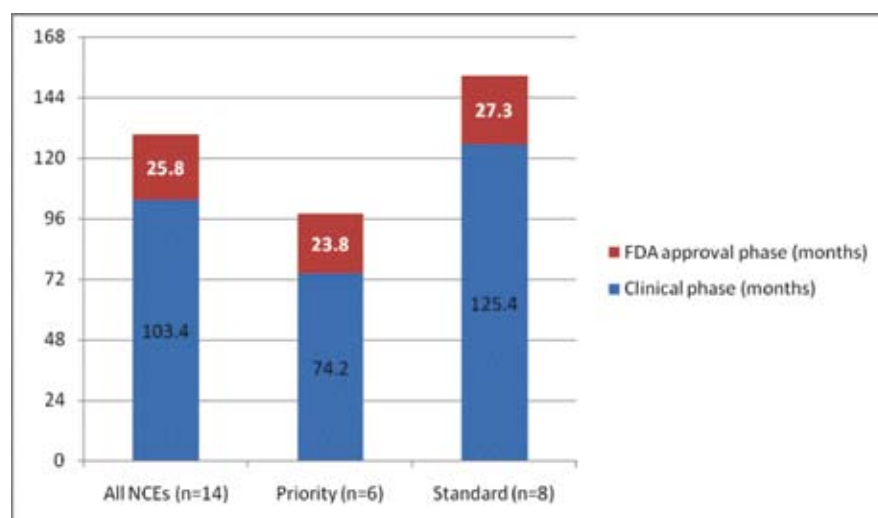
The majority of therapeutic peptide candidates were directed toward extracellular targets, with less than 10% known to bind intracellular molecules. The most common extracellular targets were G-protein coupled receptors (GPCRs). Other targets included the cytokine receptor superfamily, the natriuretic peptide receptor family, channel molecules, enzymes, cell adhesion molecules, viral proteins, cholesterol metabolism and transport, the insulin receptor family, glycoprotein IIb/IIIa, and gap junction molecules. Of the candidates targeting GPCRs, nearly all

therapeutic peptides studied in the 1980s were directed toward GPCR-A. During the 1990s, about two-thirds targeted GPCR-A and one-third targeted GPCR-B. The focus on GPCR-B has increased in the 2000s - nearly half of peptides known to target GPCRs that entered studies during 2000-2007 were directed toward GPCR-B.

Phase transition probabilities for therapeutic peptides have remained relatively steady over three overlapping periods encompassing 1984-2005. The results suggest that demonstration of efficacy is the primary bottleneck in the clinical

## figure 3

Mean clinical and US approval phases for peptide new chemical entities approved after 1992



development process (45% Phase 2 to 3 transition value). The cumulative success rates for peptides (20-30% overall) compare favorably to the values for antibody therapeutics while being approximately twice that for small molecules. Probabilities of success are important for strategic planning, but it is important to note that success rates will vary at least somewhat until fates of all candidates in the cohorts are known.

A total of 48 peptide therapeutics are now approved for marketing either in the US and other countries (24 products), or only outside the US (an additional 24 products). The near-term prospects for additional approvals are promising – four peptide candidates were undergoing US regulatory review as of October 2008. These are mifamurtide, sinapultide, liraglutide, and degarelix.

Average clinical and approval phase lengths were calculated for 14 peptide new chemical entities approved by FDA after enactment of the Prescription Drug User Fee Act of 1992. This legislation and subsequent reauthorization acts defined timeline goals for the review of candidates based on a two-tier ranking system. Under the current guidelines, candidates are given a priority or standard review,

with goals of six and ten month time to first action. Priority reviews are given to candidates that are intended as treatments for serious or life-threatening diseases or that might represent a significant improvement in the treatment of a disease. The average clinical phase for candidates ultimately given a priority review by FDA was notable shorter (41%) compared those given a standard review. The average FDA approval phase was also shorter for priority-reviewed products, but by 3.5 months (13%) only. On average, clinical evaluation and FDA review of new therapeutic peptides required 10.8 years, although the length of this period was notably different for candidates granted priority review (8.2 years) compared to those granted standard review (12.7 years).

Peptide therapeutic R&D is highly dynamic with increasing numbers of candidates entering clinical study in a wide array of therapeutic categories. We anticipate that the pharmaceutical and biotechnology industries will continue to focus on these versatile molecules because of the availability of new technologies aimed at improving synthesis, delivery and formulation and because of the relatively high approval success rates. In order to report on future trends, we will continue to collect data for these important therapeutic products.



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