Ongoing developments reflect the explosion in the number of kinase inhibitors that have entered and are moving through clinical development:

• A series of 6 bi-monthly updates will provide an up-to-date assessment of the kinase pipeline outlook.

• Their collective sales exceeded $4 billion.

• Three more kinase inhibitors have been approved in 2007 and others have moved into Phase III in 2008.

Continued on next page
Overview

- In addition to ongoing studies of approved kinase inhibitors seeking line extensions, a further 11 are in Phase III studies.
- More than 130 kinase inhibitors are reported to be in either Phase I or Phase II clinical development, with 47 reported to be in Phase II studies.

Protein kinases constitute a large family of proteins that is now firmly established as a major class of drug targets for the pharmaceutical industry. The sequencing of the human genome has led to the identification of 518 protein kinases encoded within it—the human kinome. This constitutes one of the largest and most druggable classes of targets for the pharmaceutical industry, with the number of kinases exceeding the number of G protein—coupled receptors in the human genome.

An essential report for industry professionals working in R&D, portfolio management, and kinase product management, Kinase Therapeutic Pipelines: An Assessment of Targets and Agents in Development and updated to October 2008 by the second of 6 bi-monthly supplements, reviews the considerable array of drug development efforts directed at kinases and:

- Provides profiles of the activities of the major companies as well as the kinase inhibitors in development, and some of the specialist companies active in the field
- Assesses the potential impact of the more advanced kinase inhibitors, which offer significant market potential
- Discusses some of the technical challenges faced in developing such inhibitors
- Concludes with commentaries from leading experts in the field

With so many inhibitors reported to be in clinical development and many more in preclinical development, kinase inhibitors now make up a significant fraction of most major pharmaceutical companies’ pipelines, as well as an area of focus for many biotechnology companies. The increased interest in this class of targets reflects both advances in identifying selective protein kinase inhibitors and a growing perception that these drugs offer a novel, well-tolerated oral therapy in some of the most untreatable cancers.

Although direct kinase inhibitors accounted for only 7% of the value of the oncology market in 2006, their increasing availability and use is likely to be one of the major drivers of growth in this market.

The number of kinase inhibitors in clinical development ensures that during the next 10 years a significant number of such agents will reach the market. The majority of these will be for oncology indications, reflecting the more acute nature of the disease, and thus greater tolerability of potential side effects, and the current emphasis on developing kinase inhibitors for cancer indications.

About the Authors:
Peter Norman, PhD, MBA, is a pharmaceutical consultant and analyst based in Burnham Beeches, near Windsor, England. He has written and presented widely on various aspects of respiratory disease, drug development, and on the analysis of diverse therapeutic markets. Dr. Norman has more than 20 years of experience in the pharmaceutical industry in both R&D and competitive intelligence. His publications include many reviews.
Mark C. Via, an editor at CTB International Publishing, has more than 14 years of experience writing and editing for pharmaceutical trade publications. He holds a BA in history from Williams College. Mr. Via has authored previous Cambridge Healthtech reports, including Monoclonal Antibodies: Pipeline Analysis and Competitive Assessment (www.insightpharmareports.com/reports/2007/88_Monoclonal_Antibodies/overview.asp).

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Professor Sir Philip Cohen, FRS, FRSE, Medical Research Council Protein Phosphorylation Unit, University of Dundee
Jeffrey Settleman, PhD, Department of Medicine, Harvard Medical School

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GPCRs: Dawn of a New Era?

Despite their popularity as drug targets, one can easily argue that the pharmacologic potential of G protein-coupled receptors (GPCRs) is far from exhausted. This report explores current and likely consequences of recent advances concerning GPCR x-ray structures, allosteric interactions, multimerization, and functional selectivity; extensively tabulates marketed drugs and compounds in development (arranged by receptor type and subtype); presents in-depth interviews with recognized experts in the field.

This report also spotlights numerous small pharmaceutical companies, which tend to push the limits of GPCR pharmacology by attacking more targets and by attempting to apply cutting-edge concepts derived from basic research.

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