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Estimating HIV Drug Development Costs from Publicly Disclosed Data

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OVERVIEW

The cost of bringing a new pharmaceutical agent to market has been estimated to range from $70 million to $800 million, depending on the source of the data. These widely varying figures have been quoted in political and public relations campaigns about the feasibility and affordability of offering antiretroviral (ARV) to people with HIV in developing nations.

The U.S. pharmaceutical industry's trade group, Pharmaceutical Research and Manufacturers of America (PhRMA) says that developing a single new drug and bringing it to market takes on average 10 –15 years and costs $802 million. This estimate relies on a study from Tufts University based on self-reported and unaudited industry surveys.

In contrast, Public Citizen, a consumer group founded by Ralph Nader, estimated the pre-tax cost of bringing a new drug to market during the 1990s was $107M. After taxes, they say, the outlay on research and development (R&D) for each successful drug could be as low as $71M.

The actual cash outlays expended for developing any single HIV drug are not transparent in the financial records of the large pharmaceutical makers. Costs for individual drugs are grouped together with multiple product lines, many other drugs at several stages of development, drugs already on the market, research performed in-house and research acquired by license.

Past estimates have depended on two basic approaches to gauge the outlay needed to bring a drug from laboratory to pharmacy. First, an estimate can be derived by analyzing several companies' drug development projects individually. A drawback to this method is a reliance on company-supplied figures for research that may not reflect actual expenses.

The cost of research has also been estimated by using industry-wide aggregate figures for R&D and apportioning costs among the number of drugs actually approved during the study period. Neither of these methods provides specific data about the cost of various phases of drug development or on the specific costs of developing HIV drugs.

A different approach to estimating the cost of developing a single pharmaceutical product in isolation would be to analyze the research expenses of a small, publicly-held, start-up drug developer. A case study of a company with one or two lead compounds can be made by accessing publicly disclosed information about the firm's financial status, business progress and risks. Using this data it becomes relatively simple to chart the company's research and development expenses over time and relate them to milestones in the drug's development.

METHODS

The study presented in this poster examined publicly disclosed research and development (R&D) costs as reported in reports to the U.S. Government's Securities and Exchange Commission (SEC). *Source: www.sec.gov*

Two publicly traded pharmaceutical companies specializing in developing ARV drugs were analyzed. Research and development expenditures were charted from the companies' inception in the early-1990s to May of 2002 and were correlated with development milestones of the companies' key drug candidates.

RESULTS

Two HIV drug development companies lend themselves to this kind of analysis and are presented here. Trimeris, Inc. and Triangle Pharmaceuticals, Inc. are each similar in size and capitalization; both were founded in 1993; and both are located in the same labor market in North Carolina.

These companies were organized under very different business models, however. Trimeris is developing a novel class of compounds based upon original work performed by its founder as a virologist at Duke University. Triangle, in contrast, was organized as a clinical phase development company to purchase or license promising drugs from third parties and then guide them to regulatory approval.

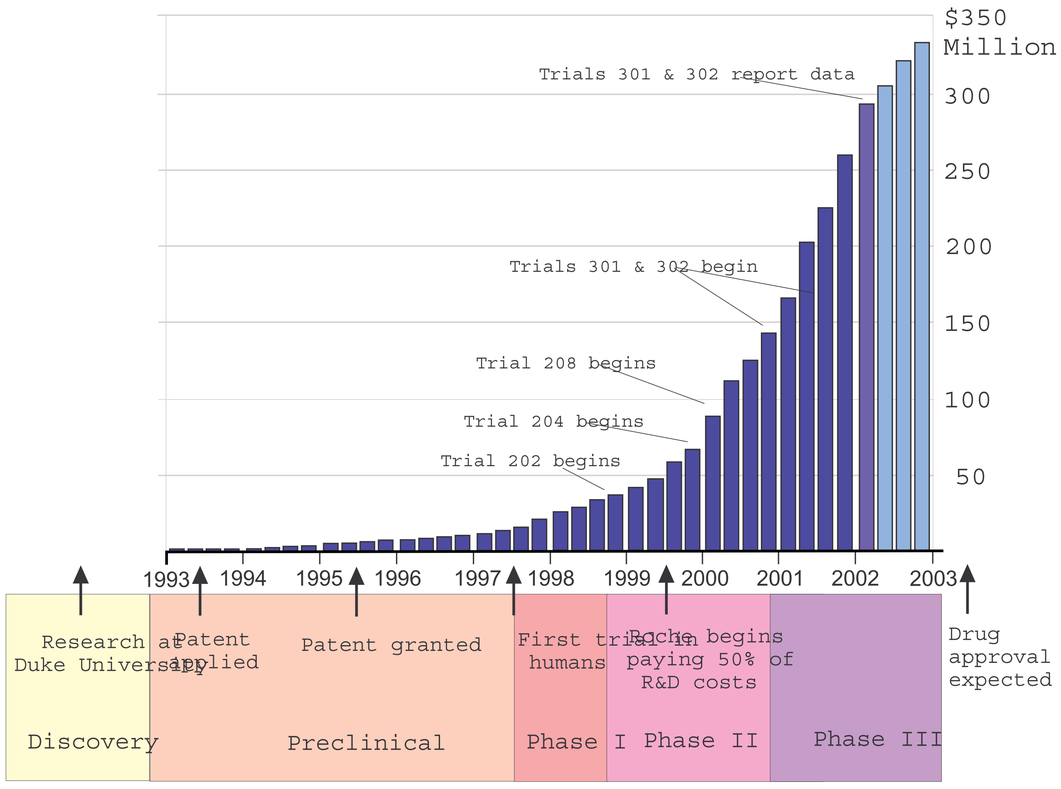
Both companies initiated public stock sales after meeting significant early milestones for their most promising drug candidates. Both companies entered into distribution agreements with major pharmaceutical partners as Phase III trials were begun. The initiation of later phase trials contributed to the greatest increases in cash expenditures for R&D.

Trimeris, Inc.

Trimeris, Inc. is a development-phase company involved with the discovery and development of peptide-based fusion inhibitors. Trimeris performs original research and actively seeks patents to protect its discoveries and processes. Trimeris has a royalty-free patent from Duke University for the underlying concept of fusion inhibition with peptides. The company depends on collaboration with partners for manufacturing and marketing.

Trimeris was founded in 1993 and commenced expenses for development that year. The company has never made money and does not anticipate sales of T-20 to commence until early 2003. Trimeris' research and development expenses include drug discovery research, drug synthesis and manufacturing costs, patent-associated costs, pre-clinical toxicology tests, clinical research, and employee compensation. From inception to March 2002, Trimeris has spent about $225 million on administration and R&D.

Trimeris, Inc.
Cumulative Research and Development Expenses



In July 1999, Trimeris announced an agreement with Roche to develop and market their HIV drug candidates, T-20 and T-1249, worldwide. Beginning in mid-1999, Roche and Trimeris have shared U.S. development expenses for T-20 and T-1249 equally. Under the agreement the two companies will split revenues on sales within the U.S. and Canada. In the rest of the world, Roche will bear all development costs and pay Trimeris royalties on sales. Trimeris is dependent on Roche to deploy the capacity to produce commercial quantities of their drug candidates.

The agreement with Roche to share development costs was signed at a point when Trimeris had invested approximately $45M in research. After the Roche agreement, R&D expenses increased rapidly as costly Phase III trials began. By the end of March 2002, Trimeris' cumulative R&D expenses had reached $170M. Some of Roche's investment was received as payments to Trimeris, but most will be carried on Roche's books. Any international expenses are Roche's exclusively. This results in some uncertainty about total cumulative investment toward launching T-20.

During the first quarter of 2002, Trimeris reported spending almost $15M on R&D. Because this amount is matched by Roche, total R&D for the quarter ran $30M. At this rate, with modest increases, about $350M will have been invested in T-20 by the first part of 2003 when approval is anticipated. A second, similar fusion inhibitor, T-1249, is said to be about two years behind T-20 in the development pipeline.

If opportunity cost, calculated at a rate of 10% compounded quarterly is considered, the investment figure could ultimately be closer to $450M. That said, Trimeris officials have told the investment community that worldwide sales of T-20 may reach $500M per year.

An unusual amount of R&D expense for T-20 may be due to an extraordinary investment in the manufacturing process. Because T-20 is not a "me-too" drug, its synthesis on a commercial scale has required a significant amount of research, engineering and capital investment not part of a more conventional compound's development.

Triangle Pharmaceuticals, Inc.

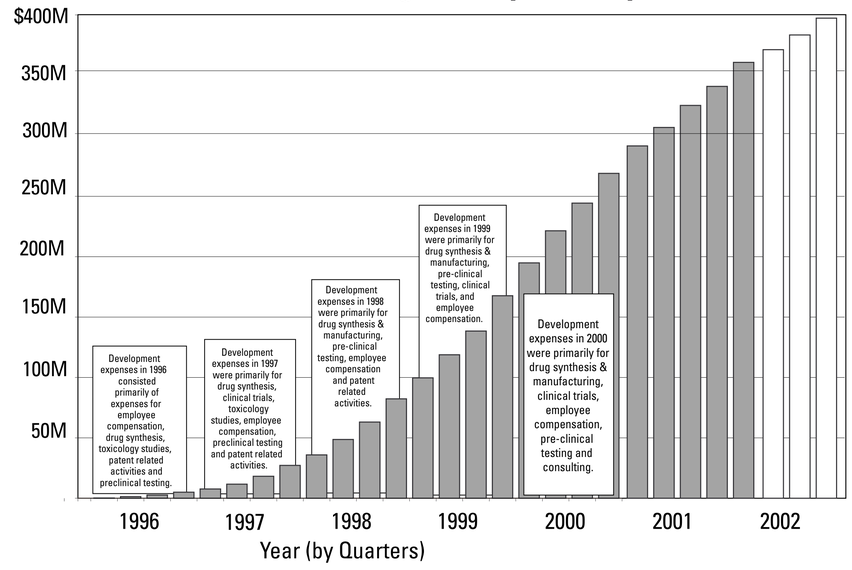
Triangle Pharmaceuticals, Inc. is a development-phase company that is grooming several antiviral drug candidates for market approval. Triangle's strategy is to focus on drug development rather than drug discovery. The company purchases or licenses drugs that have shown favorable pre-clinical or early phase clinical data. Triangle concentrates on designing clinical trials and optimizing drug synthesis for production, while the actual manufacturing and conduct of the trials are performed by third parties. The firm has relied on clinical trials in countries other than the U.S. for much of its later phase research. Developing a patent portfolio is not a significant part of Triangle's strategy.

Triangle was founded in 1993 and commenced development expenses in January 1994. No products have been approved and the company has not yet made money. Currently, only two HIV drugs are in clinical development. Payments of license fees secure the company's right to develop and market its drug candidates. If the fees are not met, these rights can be lost. The HIV drug DMP-450 was acquired in an outright purchase.

This strategy has risks. Recently, Triangle abandoned development of emivirine and DMP-450, two compounds that had advanced to relatively large and expensive clinical studies. Trials of another of Triangle's candidate drugs, FTC, were temporarily suspended by the FDA due to safety concerns. The development of FTC is now continuing. Finally, third parties other than the licensors have made patent claims involving FTC and DAPD, placing Triangle's rights to those drugs in jeopardy.

Since inception, Triangle has spent nearly $400 million on development, license fees and purchased research. Over 2100 patients have been enrolled in all phases of clinical trials for all of their drug candidates. During 2001, clinical trials, drug synthesis and manufacturing comprised the largest part of Triangle's development expenses. Expenses for employee compensation, consultation and pre-clinical testing followed as the next largest categories.

Triangle Pharmaceuticals
Cumulative Drug Development Expenses



CONCLUSIONS

Using U.S. Government Securities and Exchange Commission records of audited financial statements to examine the R&D expenditures of companies with dedicated HIV drug programs allows an unusual degree of transparency for examining the costs of preclinical and clinical drug development.

Based on trends in R&D spending by these two companies, an estimate for the total cost of bringing a single HIV drug to market can be plausibly set at a figure in excess of $300 million. Large, phase III clinical trials are associated with the largest increases in R&D expenditures.

As case studies, these observations may not be generalizable to large pharmaceutical manufacturers for a number of reasons:
* Overhead may be lower for a small company
* Economies of scale may benefit a large company
* The cost of capital for a biotech startup may be considerably higher than for a large corporation
* Tax considerations that may influence a large company's spending do not impact a small startup with no revenue

Although the cases of Trimeris, Inc. and Triangle Pharmaceuticals suggest that drug development expenses are not trivial, they do not support PhRMA's estimate of $800M average per drug.

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