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ECON 011

03. May 2022

Pharmaceutical Market Processes

Pharmaceutical companies produce treatments with the aim to cure, alleviate symptoms, or vaccinate patients. Pharmaceutical companies like Pfizer or biotech companies like Novazyme will allocate resources to achieve these goals. Allocating resources is considered to be stringent on a expected return on investments. A return on investment is defined by the needs, wants, and demands of targeted consumers. A lack of consumer demand is unattractive for businesses, so the FDA created incentives to increase R&D for small patient populations. Research, development, and commercialization is the primary goal of pharmaceutical companies, whether it be for moralistic or capitalistic gains because they will fund cash flow.

The pharmaceutical market entices business efforts because demand is apparent. The U.S. pharmaceutical market, in 2021, was $560 billion and is projected to grow to $861.67 billion by 2028.[1] The global pharmaceutical market was $1.27 trillion in 2020.[2] With positive growth, U.S. biotech startups raised $29.66 billion in venture capital for 2021, the U.S. health care venture capitalists secured $28.3 billion in 2021, and private-equity firms signed a total of $151 billion worth of healthcare deals globally in 2021.[3] [4] Right now, private capital is readily available to

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[1]"U.S. Pharmacy Market Size." *Business Fortune Insights*, https://www.fortunebusinessinsights.com/u-s-pharmacy-market-106306.
[2]Mikulic, Matej. "Global Pharmaceutical Market Size 2001-2019." *Statista*, 4 May 2021, https://www.statista.com/statistics/263102/pharmaceutical-market-worldwide-revenue-since-2001/#:~:text=The%20global%20pharmaceutical%20market%20has,about%201.27%20trillion%20U.S.%20dollars.
[3]Gormley, Brian. "Biotech Ipos Slow after Record-Breaking 2021." *The Wall Street Journal*, Dow Jones & Company, 24 Feb. 2022, https://www.wsj.com/articles/biotech-ipos-slow-after-record-breaking-2021-11645700402#:~:text=U.S.%20biotech%20startups%20raised%20%2429.66,year%20before%2C%20according%20to%20SVB.
[4]Kreutzer, Laura. "OrbiMed Seeks $4.75 Billion for Fresh Slate of Healthcare-Focused Funds." *The Wall Street Journal*, Dow Jones & Company, 29 Apr. 2022, https://www.wsj.com/articles/orbimed-seeks-4-75-billion-for-fresh-slate-of-healthcare-focused-funds-11651248801?mod=business_minor_pos1.

pharmaceutical companies and the industry's fundamentals remain strong to investors and analysts.

Within the pharmaceutical and biotech industry there is a market for orphan drugs. It became relevant after congress passed the Orphan Drug Act to increase the development of drugs to treat small populations of fewer than 200,000 patients.[5] An orphan drug is designated as such, within 90 days, by the FDA after a company submits an application. Novazyme achieved orphan drug status through their enzyme rehabilitation treatment for Pompe disease.[6] An approved application must designate a drug or biological product that has scientific rationale establishing a medically plausible basis to prevent, diagnose, or treat a rare disease or condition. The scientific rationale, for an orphan drug, may be sufficient with non-clinical proof of concept, un-extensive clinical data, or inconclusive results that demonstrate medical plausible use of the drug.[7] However, the orphan drug undergoing review must be proprietary information in which it is different or superior to drugs already on the market.

The orphan drug approval processes are different from regular drugs because the Orphan Drug Act offers incentives for orphan drug developers. First and foremost, the reduction in scientific rationale will decrease costs and increase the incentive to pursue the development of an orphan drug. For any other new molecular entities, pharmaceutical companies must open an investigational new drug application with the FDA.[8] The NME application must include molecular information, animal test results, and a detailed prospectus of future human clinical

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[5]Bohmer, Richard, and Bradley Campbell. "A Father's Love: Novazyme Pharmaceuticals, Inc." *Harvard Business Publishing Education*, 22 Oct. 2022, https://hbsp.harvard.edu/product/603048-HCB-ENG.
[6]Bohmer, Richard, and Bradley Campbell. "A Father's Love: Novazyme Pharmaceuticals, Inc." *Harvard Business Publishing Education*, 22 Oct. 2022, https://hbsp.harvard.edu/product/603048-HCB-ENG.
[7]Berry, Marissa. "FDA Designations for Rare Disease Products, Part 2: Orphan Drug Designation." *Premier Consulting*, 1 Apr. 2022, https://premierconsulting.com/resources/blog/fda-designations-for-rare-disease-products-part-2-orphan-drug-designation/.
[8]Spar, Debora, and Adam Day. "Drug Testing in Nigeria (A)." *Drug Testing in Nigeria (A) - Case - Faculty & Research - Harvard Business School*, 11 July 2006, https://www.hbs.edu/faculty/Pages/item.aspx?num=32953.

trials, which will give provisional authorization to conduct human clinical trials.[9] This is due to the Kefauver-Harris Drug Act that initiated more stringent drug-review procedures and required pharmaceutical companies to prove the safety and efficacy of a drug.[10]

Decreasing costs for orphan drug developers is important because orphan drugs are developed for small patient populations that "generate relatively small sales in comparison to the cost of developing the drug and consequently incur a financial loss."[11] Therefore, the FDA created further incentives for drugs that were designated as orphan drugs. Companies that met orphan drug requirements gained four major economic incentives including research grants from the FDA and NIH ranging from $100,000 to $200,000 per year, waived user fees of up to $290,000 per application, tax credits that can be carried forward 15 years or back 3 years, and seven years of market exclusivity. These incentives offset as much as half of the clinical development costs and made the capital markets less risky for biotechnology investors.[12]

The strongest of the four incentives was the seven-year market exclusivity because it raised barriers to entry and created monopoly status in the marketplace.[13] The exclusivity is so effective that "orphan drugs, on average, generate more sales than their nonorphan counterparts. In 2000, only 123 of the 10,000 products in the U.S. prescription drug market were orphan drugs, yet average sales for orphan drugs were $50 million versus only $14.5 million for the rest of the market."[14] The global orphan drug market is projected to reach $248.2 billion by 2026 from

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[9]Spar, Debora, and Adam Day. "Drug Testing in Nigeria (A)." *Drug Testing in Nigeria (A) - Case - Faculty & Research - Harvard Business School*, 11 July 2006, https://www.hbs.edu/faculty/Pages/item.aspx?num=32953.
[10]Spar, Debora, and Adam Day. "Drug Testing in Nigeria (A)." *Drug Testing in Nigeria (A) - Case - Faculty & Research - Harvard Business School*, 11 July 2006, https://www.hbs.edu/faculty/Pages/item.aspx?num=32953.
[11]Bohmer, Richard, and Bradley Campbell. "A Father's Love: Novazyme Pharmaceuticals, Inc." *Harvard Business Publishing Education*, 22 Oct. 2022, https://hbsp.harvard.edu/product/603048-HCB-ENG.
[12] Bohmer, Richard, and Bradley Campbell. "A Father's Love: Novazyme Pharmaceuticals, Inc." *Harvard Business Publishing Education*, 22 Oct. 2022, https://hbsp.harvard.edu/product/603048-HCB-ENG.
[13] Bohmer, Richard, and Bradley Campbell. "A Father's Love: Novazyme Pharmaceuticals, Inc." *Harvard Business Publishing Education*, 22 Oct. 2022, https://hbsp.harvard.edu/product/603048-HCB-ENG.
[14] Bohmer, Richard, and Bradley Campbell. "A Father's Love: Novazyme Pharmaceuticals, Inc." *Harvard Business Publishing Education*, 22 Oct. 2022, https://hbsp.harvard.edu/product/603048-HCB-ENG.

$190.8 billion in 2021.[15] The projected growth for orphan drugs, the biotechnology market, and the pharmaceutical market continue to reinforce their strong access to private capital and lucrative fundamentals for investors and analysts.

Private equity and venture capital are loosely understood as alternative investment classes to aid new or expanding businesses. Investments in pharmaceutical companies are important because developing a new drug is very expensive and risky. This was the case for the biotechnology startup Novazyme. The first CEO, John Crowley, raised $8 million in its angel round and it was still not enough to fund the whole development process."[16] In the United States, the development process of a new treatment consists of research in a laboratory or university, obtaining a breakthrough for effective treatment, multiple test phases, and manufacturing. Each stage in the process has its financial costs.

Beginning stage costs can be offset by doing research in a university setting because of access to lab space, equipment, and graduate students, but an up-front payment with additional royalty payments of 2%-6% is negotiated. Novazyme, in its biotech startup phase, pursued this route but negotiated an equity position instead.[17] Once promising treatment is developed, a company will then assume costs for manufacturing. It will have to evaluate its goals against manufacturing strategies for clinical trials and commercialization. The company can build a state-of-the-art manufacturing facility, within months or years, that requires tens or hundreds of millions of dollars, acquire a turn-key plant, outsource to several contract manufacturing organizations, or obtain a strategic partnership with another firm within the industry.[18] Beyond determining

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[15]Publishing, BCC. "Global Markets for Orphan Drugs." *Orphan Drugs Market Size, Share & Growth Analysis Report*, https://www.bccresearch.com/market-research/pharmaceuticals/orphan-drugs-market-report.html#:~:text=The%20global%20orphan%20drugs%20market,period%20of%202021%20to%202026.

[16] Bohmer, Richard, and Bradley Campbell. "A Father's Love: Novazyme Pharmaceuticals, Inc." *Harvard Business Publishing Education*, 22 Oct. 2022, https://hbsp.harvard.edu/product/603048-HCB-ENG.

[17]Bohmer, Richard, and Bradley Campbell. "A Father's Love: Novazyme Pharmaceuticals, Inc." *Harvard Business Publishing Education*, 22 Oct. 2022, https://hbsp.harvard.edu/product/603048-HCB-ENG.

[18]Bohmer, Richard, and Bradley Campbell. "A Father's Love: Novazyme Pharmaceuticals, Inc." *Harvard Business Publishing Education*, 22 Oct. 2022, https://hbsp.harvard.edu/product/603048-HCB-ENG.

manufacturing goals, pharmaceutical and biotech companies have to undergo animal testing and human testing trials in which a lot of investments, opportunity costs with time, and stringent FDA approval will be required. Ultimately, the probability of receiving additional funding increases as the development process advances, which is important because the costs of developing a drug are $2.6 billion according to Ed Silverman; Silverman is a special writer for the Wall Street Journal.[19]

Developing a new drug for approved use by the FDA requires stringent protocol. First and foremost, adherence to the Declaration of Helsinki or the laws and regulations of the host country, whichever offers greater protection of human subjects, is a vital component of the approval process. Generally, this meant informed consent meant subjects knew "1) they were part of a study using an unproven drug, 2) what alternative treatments, if any, were available, and 3) that their participation was voluntary."[20] In accordance with these principles, approval can be given through two channels. Go through the standard FDA approval process or attempt to get accelerated approval and priority review from the FDA. Pfizer's procedure for their meningitis treatment is an example of the standard process and Novazyme's Pompe disease treatment can be reviewed to examine the accelerated approval process.

Pfizer's Trovan, a promising new antibiotic for meningitis and a range of other devastating infections required the standard FDA approval process. This required a proper IND application and years of human clinical trials in which a 20-year patent protection, on a NCE, would have run half its course. The IND consisted of identifying the therapeutic target, animal testing, and potential safety issues of administering the drug. The IND will be filed with enough evidence of

[19]Silverman, Ed. "Developing a Drug Costs $2.6 Billion, but Not Everyone Believes This." *The Wall Street Journal*, Dow Jones & Company, 18 Nov. 2014, https://www.wsj.com/articles/BL-270B-1036.
[20]Spar, Debora, and Adam Day. "Drug Testing in Nigeria (A)." *Drug Testing in Nigeria (A) - Case - Faculty & Research - Harvard Business School*, 11 July 2006, https://www.hbs.edu/faculty/Pages/item.aspx?num=32953.

both efficacy and safety to the FDA. Clinical trials on human subjects would begin if the FDA approved the IND. The human clinical trials are

> **Phase I** was a safety test that gave small dosages of the proposed medication to 20–40 healthy patients. If the initial tests resulted in benign responses, the dosage size was increased to ensure safety at a higher dosage level.
>
> **Phase II,** the drug was administered to patients suffering from the targeted disease. This phase focused on drug effectiveness and involved more subjects and a longer testing period than Phase I. Phase I and II were often completed in close consultation with the FDA, which had the power to suspend IND testing at any time.
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> **Phase III** was the most comprehensive and rigorous phase of the drug-approval process, involving further assessments of the drug's safety, efficacy, and optimal dosage regimes. Phase III involved between several hundred and several thousand patients and often included randomized, double-blind tests with placebo controls.[21]

Additionally, companies can undergo FDA testing protocols outside of the United States. Companies can set up procedures themselves or rely on contract research organizations. CROs can manage clinical trials both at home and abroad. The ultimate success relies on comprehensive reports that required "proof of data integrity, proof of relevance, documentation of informed consent, and oversight of a local institutional review board."[22]

Once a product has successfully passed phase III, The Center of Biologics Evaluation and Research is responsible for evaluating an NDA. The review will have 12 months to reach a conclusion and it will determine if the "drug was either approved, approved under certain

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[21] Spar, Debora, and Adam Day. "Drug Testing in Nigeria (A)." *Drug Testing in Nigeria (A) - Case - Faculty & Research - Harvard Business School*, 11 July 2006, https://www.hbs.edu/faculty/Pages/item.aspx?num=32953.

[22] Spar, Debora, and Adam Day. "Drug Testing in Nigeria (A)." *Drug Testing in Nigeria (A) - Case - Faculty & Research - Harvard Business School*, 11 July 2006, https://www.hbs.edu/faculty/Pages/item.aspx?num=32953.

conditions, or not approved because of major problems with the committee's findings."[23] After FDA approval, the manufacturer is free to distribute the product immediately. Lastly, phase IV will commence post-launch and will monitor the safety and efficacy of the drug. Phase IV is primarily testing for new or expanded indications for a drug or changes in dosing.[24]

Contrary to the standard FDA new drug approval process is the accelerated approval and priority review process from the FDA. Novazyme underwent this procedure and created a timeline to launch their innovative Pompe disease treatment in 10 quarters.

1. Preclinical stage: 3-6 months
2. Investigational New Drug: 3 months
3. Phase I/II Clinical Trials: 6 months
4. Phase III: 6 months
5. Preparing Biologic License Agreement: 3 months
6. BLA: 6 months
7. Launch[25]

The accelerated approval and priority review process is intended to deliver superior treatments to seriously endangered populations. Overall it will rely on a fast track, breakthrough therapy, accelerated approval, and priority review. The fast track and breakthrough therapy is unconventional because it requires the company to designate clinically significant endpoints that strongly suggest the potential of the new drug for a meaningful effect on the underlying illness.[26] It will have to offer evidence of similar efficacy as the unaccelerated track, but not to great

[23]Bohmer, Richard, and Bradley Campbell. "A Father's Love: Novazyme Pharmaceuticals, Inc." *Harvard Business Publishing Education*, 22 Oct. 2022, https://hbsp.harvard.edu/product/603048-HCB-ENG.
[24]Bohmer, Richard, and Bradley Campbell. "A Father's Love: Novazyme Pharmaceuticals, Inc." *Harvard Business Publishing Education*, 22 Oct. 2022, https://hbsp.harvard.edu/product/603048-HCB-ENG.
[25]Bohmer, Richard, and Bradley Campbell. "A Father's Love: Novazyme Pharmaceuticals, Inc." *Harvard Business Publishing Education*, 22 Oct. 2022, https://hbsp.harvard.edu/product/603048-HCB-ENG.
[26]FDA. "Fast Track, Breakthrough Therapy, Accelerated Approval, Priority Revie." *U.S. Food and Drug Administration*, FDA, https://www.fda.gov/patients/learn-about-drug-and-device-approvals/fast-track-breakthrough-therapy-accelerated-approval-priority-review.

extents. Therefore, it saves valuable time as it does not alter scientific standard approval or the quality of evidence. The accelerated approval will come if the FDA approves the clinically significant endpoints and the data to demonstrate increased effectiveness in treatment, prevention, or diagnosis of the condition.[27] Therefore, Novazyme underwent this process to get their Pompe disease treatment approved as fast as possible.

Novazyme's first CEO, Crowley, ensured to create a profitable business model surrounding a cure for Pompe disease. Crowley attracted funds and felt the pressure of time because his two children suffered from Pompe disease while there was no effective treatment. Therefore, one can argue Novazyme was different from a typical pharmaceutical company because they were not in pursuit of profit, but used millions in funds to support a moralistic cause. This is apparent with their approach to using enzyme therapies, for a small population, because it was uncommon and expensive to manufacture. However, it seemed to be the best method of treating Pompe disease. Crowley's internal debate regarding the future of his company also accentuates Novazyme's values.

Crowley accepted Genzyme's offer to buy Novazyme for $137.5 million upfront because he believed it would be the best way to allow his Pompe treatment to reach the market. Genzyme had expertise in manufacturing, clinical development, and commercialization, which would all help reduce the risk in bringing HP-GAA to market.[28] Genzyme also had strong experience with LSDs and developed a Pompe program with early successes. Therefore, instead of competing against a big pharmaceutical company, Crowley decided to give up his investor's potential

[27]FDA. "Fast Track, Breakthrough Therapy, Accelerated Approval, Priority Revie." *U.S. Food and Drug Administration*, FDA, https://www.fda.gov/patients/learn-about-drug-and-device-approvals/fast-track-breakthrough-therapy-accelerated-approval-priority-review.

[28]Bohmer, Richard, and Bradley Campbell. "A Father's Love: Novazyme Pharmaceuticals, Inc." *Harvard Business Publishing Education*, 22 Oct. 2022, https://hbsp.harvard.edu/product/603048-HCB-ENG.

upside. Crowley entrusted Genzyme to combine both their expertise and continue producing successful treatments for LSDs and eventually a treatment for Pompe.

Crowley's decision was not run by profit and his investment bankers laid out pros and cons in regards to which company will increase the probability of HP-GAA reaching the market. It is evident that not all pharmaceutical companies are in this market for profit. However, the Orphan Drug Act is still necessary to support the development of unprofitable drugs. This is understandable because of the high costs associated with drug development. Therefore, there will still be diseases that might never experience treatment. I wonder how unfair it will feel for those that understand the pharmaceutical industry has the resources to find cures for them, but refuse to do so due to expected profits being low. Awareness must continue to spread, pass the Orphan Drug Act, so society can force change in the system or raise independent funds for people that suffer from rare diseases.

Bibliography

Berry, Marissa. “FDA Designations for Rare Disease Products, Part 2: Orphan Drug Designation.” *Premier Consulting*, 1 Apr. 2022, https://premierconsulting.com/resources/blog/fda-designations-for-rare-disease-products-part-2-orphan-drug-designation/.

Bohmer, Richard, and Bradley Campbell. “A Father's Love: Novazyme Pharmaceuticals, Inc.” *Harvard Business Publishing Education*, 22 Oct. 2022, https://hbsp.harvard.edu/product/603048-HCB-ENG.

FDA. “Fast Track, Breakthrough Therapy, Accelerated Approval, Priority Revie.” *U.S. Food and Drug Administration*, FDA, https://www.fda.gov/patients/learn-about-drug-and-device-approvals/fast-track-breakthrough-therapy-accelerated-approval-priority-review.

Gormley, Brian. “Biotech Ipos Slow after Record-Breaking 2021.” *The Wall Street Journal*, Dow Jones & Company, 24 Feb. 2022, https://www.wsj.com/articles/biotech-ipos-slow-after-record-breaking-2021-11645700402#:~:text=U.S.%20biotech%20startups%20raised%20%2429.66,year%20before%2C%20according%20to%20SVB.

Kreutzer, Laura. “OrbiMed Seeks $4.75 Billion for Fresh Slate of Healthcare-Focused Funds.” *The Wall Street Journal*, Dow Jones & Company, 29 Apr. 2022, https://www.wsj.com/articles/orbimed-seeks-4-75-billion-for-fresh-slate-of-healthcare-focused-funds- 11651248801?mod=business_minor_pos1.

Mikulic, Matej. “Global Pharmaceutical Market Size 2001-2019.” *Statista*, 4 May 2021, https://www.statista.com/statistics/263102/pharmaceutical-market-worldwide-revenue-since-2001/#:~:text=The%20global%20pharmaceutical%20market%20has,about%201.27%20trillion%20U.S.%20dollars.

Publishing, BCC. “Global Markets for Orphan Drugs.” *Orphan Drugs Market Size, Share & Growth Analysis Report*, https://www.bccresearch.com/market-research/pharmaceuticals/orphan-drugs-market-report.html#:~:text=The%20global%20orphan%20drugs%20market,,period%20of%202021%20to%202026.

Silverman, Ed. “Developing a Drug Costs $2.6 Billion, but Not Everyone Believes This.” *The Wall Street Journal*, Dow Jones & Company, 18 Nov. 2014, https://www.wsj.com/articles/BL-270B-1036.

Spar, Debora, and Adam Day. “Drug Testing in Nigeria (A).” *Drug Testing in Nigeria (A) - Case - Faculty & Research - Harvard Business School*, 11 July 2006, https://www.hbs.edu/faculty/Pages/item.aspx?num=32953.

“U.S. Pharmacy Market Size.” *Business Fortune Insights*, https://www.fortunebusinessinsights.com/u-s-pharmacy-market-106306.