Drug Development Pathway

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The traditional development pathway for small-molecule biologics includes a linear series of events: basic research and discovery, preclinical testing, human clinical trials, and regulatory and market approvals. Each step in this process is dictated by comprehensive guidelines to ensure proper quality, safety, and product utility standards. In the United States, drug development guidelines are governed by the Food and Drug administration (FDA) and enforced through a rigorous regulatory approval process.[1] The development journey from discovery to consumer use requires significant time and investment, with potential returns met by public offerings, industry partnerships, or various commercialization strategies.

- *Discovery*
    - Research discovery occurs through a variety of experimental models that aim to identify novel insights in therapeutic development.
    - Primarily, these mechanisms include insights toward new molecular profiles, toxicity standards, and disease processes.
- *Preclinical Research*
    - Preclinical laboratory testing in animal models is regulated by the FDA and requires researchers to follow Good Laboratory Practice (GLP) guidelines to identify toxicity profiles and recommended dosing guidelines.
    - Preclinical datasets inform clinical trial design, which are packaged and submitted for FDA review through an Investigational New Drug (IND) application. FDA approval is required to initiate clinical trials.
- *Clinical Research*
    - Human trial testing is conducted in phases to assess safety, tolerability, and therapeutic utility compared to other standard of care treatment options.
    - Clinical trial design is based on prior data outcomes and scaled to meet the objectives and endpoints of a given trial phase.
- *Regulatory Approval*
    - Upon successful completion and review of clinical trial data, the culmination of therapeutic information is submitted to the FDA as a New Drug Application (NDA).
    - NDA review determines therapeutic safety and efficacy for the intended population.
- *Market Approval*
    - Post approval, prescribing information, often referred to as labelling, will be determined to accurately describe intended use.

[1] https://www.fda.gov/patients/learn-about-drug-and-device-approvals/drug-development-process

OxaliTEX Development Strategy

Orphan Drug Designation

Additional market and regulatory approvals may be sought to expedite or de-risk clinical use for an intended population. Under the Orphan Drug Act, the FDA may grant orphan designation (ODD) to a drug or biologic intended to treat a rare disease or condition, defined in the United States as a patient population of fewer than 200,000 individuals, or a patient population greater than 200,000 individuals when there is no reasonable expectation that the cost of developing and making available the drug or biologic will be recovered from sales for that drug or biologic.[2] After the FDA grants ODD, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. ODD does not convey an advantage in or shorten the duration of the regulatory review and approval process.

In the United States, ODD entitles a Sponsor to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, the product is entitled to orphan product exclusivity, restricting FDA approval on other applications to market the same drug for the same indication for seven years, except in limited circumstances of clinical superiority or sufficient available quantities to meet the needs of patients under ODD.

InnovoTEX intends to seek an ODD for its lead candidate, OxaliTEX, as treatment for platinum resistant ovarian cancer. ODD approval will optimize and de-risk regulatory approval timelines towards clinical use.

Additional Indications

OxaliTEX will be further evaluated preclinically for its potential use in additional indications. This strategy is expected to allow the identification of subpopulations that will benefit from the treatment of OxaliTEX and is expected to facilitate further expansion of the OxaliTEX market and support future clinical trial designs. Other tumor types expected to be evaluated include but are not limited to colorectal, lung, and glioblastoma multiforme.

Clinical Design

The Phase I clinical trial will provide information related to regimen, safety, tolerability, and pharmacokinetics (PK). Phase I dose escalation cohorts will establish the maximum tolerated dose and cohort indication for dose expansion.

Post pandemic, innovative clinical trial strategies, such as adaptive or modified trial designs,

[2] https://www.fda.gov/industry/medical-products-rare-diseases-and-conditions/designating-orphan-product-drugs-and-biological-products

have been implemented to ease the burden of data collection and monitoring on patients and administrative staff. The adaptive model is often more efficient and informative as it provides opportunities to streamline and optimize interim data outcomes, and the flexibility to modify the trial course in accordance with the pre-specified methodology.

InnovoTEX will plan to use an innovative, adaptive trial design with a modified treatment regimen for dose escalation in Phase I. Pre-clinical data has shown that OxaliTEX is well-tolerated, tumor localizing, and overcomes platinum resistance in multiple solid tumor indications including ovarian cancer. Therefore, solid tumor indications, primarily platinum resistant ovarian cancer will be evaluated.