

## CLINICAL TESTING & GOVERNMENT REGULATION PROFILE

### CLINICAL TESTING

Clinical trials involve the administration of the pharmaceutical product to healthy volunteers or to patients identified as having the condition for which the product is being tested. The pharmaceutical product is administered under the supervision of a qualified principal investigator. Clinical trials are conducted in accordance with protocols previously submitted to the FDA as part of the IND application that detail the objectives of the trial, the parameters used to monitor safety and the efficacy criteria that are being evaluated. Each clinical trial is conducted under the auspices of an institutional review board ("IRB") at the institution at which the trial is conducted. Clinical trials are typically conducted in three sequential phases that may overlap.

**Phase I Clinical Studies** - emphasis on testing for safety (adverse effects), dosage tolerance, metabolism, distribution, excretion and clinical pharmacology in healthy human volunteers. Phase I trials may be divided between Phase Ia - single doses of the drug, or, Phase Ib - multiple doses of the drug.

**Phase II Clinical Studies** – designed to determine the effectiveness of the pharmaceutical for specific targeted indications, to determine dosage tolerance and optimal dosage and to identify possible adverse side effects and safety risks in a limited patient population. The "Simon" trial design used by ADVENTRX, is a common experimental format for conducting a Phase II trial. It features two stages, whereby certain parameters must be reached in the first stage in order to continue on to the second stage.

**Phase III Clinical Studies** - provide expanded evaluation of clinical effectiveness as well as extended testing for safety within an expanded patient population at multiple clinical study sites.

The FDA reviews both the clinical trial plans and the results of the trials at each phase, and may discontinue the trials at any time if there are significant safety issues.

The results of the preclinical tests and clinical trials are submitted to the FDA in the form of an NDA for marketing approval. The testing and approval process requires substantial time and effort, and FDA approval may not be granted on a timely basis or at all. The approval process is affected by a number of factors, including the severity of the disease, the availability of alternative treatments and the risks and benefits demonstrated in clinical trials. Additional animal studies or clinical trials may be requested during the FDA review process and may delay marketing approval.

Upon approval, a drug may be marketed only for the FDA approved indications in the approved dosage forms. Further clinical trials are necessary to gain approval for the use of the product for any additional indications or dosage forms. The FDA may also require post-market reporting and may require surveillance programs to monitor the side effects of the drug, which may result in withdrawal of approval after marketing begins.

### ORPHAN DRUG DESIGNATION

CoFactor™ was granted Orphan Drug designation in the United States and European Union for the treatment of pancreatic cancer in 2004.

#### United States

Orphan drug designation provides ADVENTRX with tax incentives for clinical development of CoFactor for trials conducted in the U.S., and seven years of marketing exclusivity following drug approval. Orphan drug status is granted by the FDA's Office of Orphan Products Development and is eligible for products to treat diseases that affect fewer than 200,000 people in the U.S.

#### European Union

Orphan medicines are drugs for treating life threatening medical conditions that affect fewer than 5 out of every 10,000 people in the European Union (EU). EU orphan status provides incentives, such as reduced fees for protocol assistance and scientific advice, and increased time for market exclusivity following drug approval.

## FDA FAST TRACK PROGRAM

ADVENTRX believes that CoFactor™ may qualify for the FDA fast track program toward rapid approvals of new drugs for cancer therapy.

The Food and Drug Administration Modernization Act of 1997 (FDAMA) included a Section 112, which mandated the Agency to facilitate the development and expedite review of drugs and biologics intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs through the implementation of a *fast track program*. *Fast track* adds to existing programs, such as accelerated approval, the possibility of a “rolling submission” for a marketing application. To be eligible for the *fast track* program, an applicant must submit a request with supporting documentation for fast track designation for a product and its proposed use. The FDA is required by the statute to decide within 60 days of receipt of the request whether the conditions for fast track designation have been met.

## GOVERNMENT REGULATION

The manufacture, distribution, marketing and sale of therapeutic drugs are subject to government regulation in the U.S. and in various foreign countries including Japan and the member countries of the European Union. In the U.S., rules and regulations established by the Food and Drug Administration (“FDA”) requiring the presentation of data indicating that products are safe and efficacious and are manufactured in accordance with current Good Manufacturing Practice (“cGMP”) regulations must be followed. Japan, the member countries of the European Union and various other countries have similar rules and regulations.

The steps required before a new prescription drug may be marketed in the U.S. include (i) preclinical laboratory and animal tests, (ii) the submission to the FDA of an Investigational New Drug (“IND”) application, which must be evaluated and found acceptable by the FDA before human clinical trials may commence, (iii) adequate and well-controlled human clinical trials to establish the safety and effectiveness of the drug, (iv) the submission of a New Drug Application (“NDA”) to the FDA and (v) FDA approval of the NDA. Prior to obtaining FDA approval of an NDA, the facilities that will be used to manufacture the drug must undergo a pre-approval inspection to ensure compliance with the FDA’s cGMP regulations.

Preclinical tests include laboratory evaluation of product chemistry or biology and animal studies to assess the safety and effectiveness of the product and its formulation. The results of the preclinical tests are submitted to the FDA as part of an IND application, and unless the FDA objects, the IND application will become effective 30 days following its receipt by the FDA, after which clinical trials can begin. If the FDA has concerns about the proposed clinical trial, it may delay the trial and require modifications to the trial protocol prior to permitting the trial to begin.

## About ADVENTRX

ADVENTRX Pharmaceuticals, Inc. is a biopharmaceutical research and development company committed to the commercialization of new therapies to treat cancer and viral disease. The company seeks to improve upon existing therapies or to develop novel treatments to address significant medical problems such as drug metabolism, bioavailability and resistance. Common stock for ADVENTRX is traded on the American Stock Exchange under the trading symbol ANX. More information on ADVENTRX can be found by visiting our website at [www.adventrx.com](http://www.adventrx.com).



*This Clinical Testing and Government Regulation Profile contains forward-looking statements about ADVENTRX Pharmaceuticals, Inc. (the “Company”) including, without limitation, the benefits and performance expected from the use of our potential products, the timing and success of clinical trials and the receipt of required approvals from the United States Food and Drug Administration and other regulatory agencies. Forward-looking statements are based on certain assumptions and expectations of future events that are subject to risks and uncertainties. Actual results and trends may differ materially from historical results or those expressed or implied in any such forward-looking statements depending on a variety of factors. For a discussion of such risks and uncertainties, which could cause actual results to differ from those contained in any forward-looking statement in this Corporate Profile, see the section titled “Risk Factors” in the Company’s Annual Report on Form 10-KSB filed with the Securities and Exchange Commission, as well as other reports that the Company files from time to time with the Securities and Exchange Commission. The Company undertakes no obligation to update publicly any forward-looking statement for any reason, except as required by law, even as new information becomes available or other events occur in the future. This material is intended for informational purposes only and is not intended to solicit the purchase or sale of the Company’s securities.*