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March 13, 2007

Mr. Andrew C. von Eschenbach
Commissioner
US Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20857

Re: Comments on Docket No. 2006N--0062, RIN 0910-AF14

Dear Commissioner von Eschenbach:

We appreciate the opportunity to submit comments in regard to the Proposed Regulation on Expanded Access to Investigational Drugs for treatment Use. Our comments are based upon our experience with medical product development, clinical trial strategy and execution, and interaction with patient groups in the course of building over twenty biotech companies. All of these biotech companies were or are developing products for serious or life-threatening diseases and conditions, including a wide range of cancers, ALS, MS and other neuro-degenerative diseases, end-stage liver disease, and other serious diseases for which there are no genuinely effective treatments available today. Our fund is one of the very, very few nationwide that is willing to invest at an early (i.e., pre-clinical) stage, and invest in fundamentally novel technologies. We take the lead role in working with the founding scientists and building the companies from the pre-clinical stage through to mid-stage and late stage clinical trials and beyond. Consequently, we are involved at a detailed and operational level in clinical trial strategy and execution, on a daily basis, with our companies. We also have considerable interaction with the applicable patient groups.

We have a number of comments in regard to the proposed regs – some general, and some detailed – as follows:

- Our most important overall comment is that expanded access arrangements are urgently needed, and we strongly applaud the FDA's proposal of regs to clarify and increase expanded access.
- In that regard, we also applaud the agency's decision to include an intermediate-size patient population.
- However, the agency is substantially under-estimating the extent of unmet need and demand for expanded access, and the agency's category of intermediate-size patient

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population does not go nearly far enough, and leaves much too big a gap between it and the treatment IND/large population category.

The agency's decision not to adopt more than three categories of expanded access, coupled with the agency's limitation on the size of the intermediate population (only 10 to 100 patients), further coupled with the very high bar that the agency has maintained for treatment INDs/large populations (thousands of patients) leaves a very big gap between the 100-patient level and the thousands-of-patients level. This gap will seriously interfere with the utility of the overall expanded access program.

The way the proposed regs structure the requirements, the category of expanded access most likely to be used will be the intermediate population. Sponsors with multiple individual cases will be requested to consolidate into an intermediate program, and it will be difficult for sponsors to meet the requirements for large population programs.

The key point is that intermediate population programs, as limited in the proposed regs (allowing access for just tens or hundreds of patients), are not going to be anywhere near enough to make a dent in the unmet need and demand.

- **The agency is keeping the bar considerably too high for large populations** by continuing to require that Phase III data or completed Phase II data be provided to support the submission. This limits the use of these programs to very, very late in the drug development process. If Phase III data are required, the large population program will only be providing access months, not years, earlier than simply waiting for marketing approval. That is not much of an acceleration, and will certainly not be enough of an acceleration to fulfill the unmet needs and demands of patients, nor to provide substantial help to small biotech companies. Even if "only" completed Phase II data will be required, that will still limit treatment INDs/large populations to quite late in the development process, and will not provide enough acceleration to fulfill patient and biotech company needs. The balancing approach that is described throughout the proposed regs (under which the severity of the disease and the degree of safety, etc. guide the decision-making) should be sufficient to protect patients and serve social needs.
- **In order to be truly useful, either the large population programs need to be available based upon Phase I data (at least in cases where appropriate under the balancing approach), or the intermediate population program needs to be able to go well above 100 patients (i.e., up to 500 or 1,000 patients), or there needs to a fourth category between the intermediate and the large populations programs.**
- The agency seems to be overlooking the extensive role of small biotech companies in the developing the more novel kinds of investigational drugs, and the potentially large

significance of expanded access programs for such small biotechs. In the proposed reg, the agency states that it “does not believe that the proposed rule will have a significant economic impact on a substantial number of small entities,” and the agency specifically requests comments about the “number of affected small entities” and the likely impact. We respectfully disagree, and think that the agency should expect to see a large number of small biotech companies at least considering, and potentially proceeding with, expanded access programs.

As numerous studies have shown, in recent years it has increasingly been the small biotech companies (rather than big pharma or even big biotech) that have been developing the more novel and innovative therapies. These more innovative therapies are often the ones that offer heightened potential for medical breakthroughs, and that patients most seek access to.

These innovative therapies, and their small biotech company sponsors, also tend to be the ones that have the most difficulty making progress through the development pathway and could be substantially helped (positively impacted) by expanded access programs. Small biotech companies face an extremely severe funding gap – especially at the pre-clinical and early clinical stages. Small biotech companies also face special difficulties in getting their novel therapies through early and mid-stage clinical trials, up to the development stage at which they are able to obtain significant partnering arrangements.

Expanded access programs can play a crucial supporting role in helping small biotech companies to reach larger numbers of patients sooner, to generate larger amounts of supporting data sooner, and to move their novel treatments forward sooner. This would benefit the patients, the small biotech companies and society.

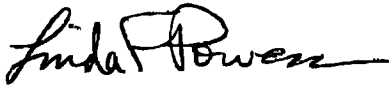
The most powerful boost for small biotech companies and the patients seeking their new therapies would come from the combining expanded access programs with policies allowing cost recovery and reimbursement (the subject of a separate agency proposal).

- The proposed regs seem to place too much emphasis on the efficacy that must be shown before expanded access programs may proceed. It is certainly appropriate and necessary to be very rigorous about safety requirements and to require demonstration of safety before expanded access programs proceed. In contrast, only minimal showing of efficacy (or reason to expect efficacy) should be required before expanded access programs may proceed. From a sponsor’s perspective, a primary reason to conduct expanded access programs would be to flesh out the picture on efficacy much sooner and faster. If the sponsor must show efficacy beforehand, that will significantly limit the utility of the expanded access programs. In addition, taking the approach of minimal efficacy requirements beforehand will not impose substantial costs on society

or the healthcare system because the sponsor will be paying for the costs of producing and supplying the therapy in most of the expanded access programs. And, if such programs enable a product to reach marketing approval sooner than otherwise, this will greatly reduce the costs that the sponsor must recoup in the pricing of the product on the commercial market.

Again, thank you for this opportunity to submit comments. We strongly applaud the agency's effort to increase expanded access programs. Such programs are sorely needed.

Sincerely,



Linda F. Powers
Managing Director