ImClone Oversight Alliance
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November 5, 2001

Dr. Harlan Waksal
Chief Operating Officer
ImClone Systems
180 Varick Street
New York, NY 10014

Dear Dr. Waksal:

Thank you for convening the conference call on Monday, October 29. The signatories of this letter are members of the ImClone Oversight Alliance. The primary focus of this alliance is to provide clear communication to cancer patients and cancer patient advocates about the development and availability of IMC-C225.

The ImClone Oversight Alliance believes that it is time for ImClone to begin planning for an expanded access program for IMC-C225. We fully support your goal to get IMC-C225 approved and available to cancer patients -- clearly approval is everyone's highest priority. At the same time, a well-designed expanded access program would make IMC-C225 available to a pre-defined group of cancer patients between now and the time that IMC-C225 receives FDA approval. Such a program would also provide safety information about IMC-C225 in a 'real world' setting, and increase patient/provider knowledge and 'buzz' about the drug before it hits the market. Thus, both patients and the company would benefit from a properly designed expanded access program.

During the October 29th conference call, you confirmed a statement made by Samuel Waksal during his June 20, 2001 testimony before the House Government Reform Committee hearing chaired by Representative Dan Burton. During his testimony, he stated:

> *"We have completed construction of our own large-scale biologic production facility, which will be dedicated to production of IMC-C225. Once that facility is producing material, we will consider once again instituting a compassionate use IND program or, if we are at the appropriate stage of the approval process, an even larger 'Expanded Access' program."*
> http://www.house.gov/reform/hearings/healthcare/01.06.20/

In addition, since the June Congressional hearing, ImClone officials have publicly stated that they believe IMC-C225 will be approved early in 2002, perhaps after the February 26-27 Oncology Drugs Advisory Committee (ODAC) meeting:

"ImClone/Bristol-Myers Squibb's anti-EGF monoclonal antibody IMC-C225 is expected to be considered for irinotecan-refractory colorectal cancer by FDA's Oncologic Drugs Advisory Committee at its Feb. 27-28 meeting, ImClone said.

"We feel very comfortable...with the data that we have accumulated thus far, that we will be on the February ODAC panel meeting," ImClone CEO Samuel Waksal, PhD, told analysts during a Sept. 19 conference call." – Health News Daily

Because of these facts the ImClone Oversight Alliance believes that now is the time to launch an IMC-C225 expanded access program.

The time available to implement an expanded access program is short. If the drug is approved on or before January 1, 2002 an expanded access program would be moot. On the other hand, since you do not believe that approval will occur that quickly, it may be four or more long months before cancer patients can have access. This is a very long time in the life of a critically ill cancer patient. Therefore, we believe that we must begin planning immediately for the IMC-C225 expanded access program that will commence no later than January 1, 2002 and remain in place until marketing approval has been granted by the FDA.

During the June Congressional hearings, Dr. Samuel Waksal stated that the principal barrier to providing expanded access to IMC-C225 for cancer patients was the limited manufacturing capacity. Since that time, ImClone has stated publicly that manufacturing capacity for IMC-C225 has been increased to meet the expected market demand:

ImClone's partnership with Lonza -- July 7, 2000 "We are confident that Lonza Biologics, an industry leader in antibody manufacturing, will be able to meet our production and quality goals and timetables as a supplemental supplier of IMC-C225," stated Samuel D. Waksal, Ph.D., President and Chief Executive Officer of ImClone Systems. "This agreement is a major step toward helping to ensure that IMC-C225 will be available to oncologists and their patients once FDA approval is obtained. The antibody supply we have contracted for from Lonza will help support our ongoing clinical development program with IMC-C225, as well as our potential commercial needs." Lonza.com press release

Increasing capacity in general -- August 2001 "Because of what Waksal termed the "paucity of biologic manufacturing capacity in the world," ImClone built its own 55,000-ft2 pilot manufacturing facility to provide product for clinical trials. More recently, the company contracedt with Lonza Biologics (www.lonza.com) to produce initial commercial supplies. Asked to produce as much as possible in its New Hampshire contract manufacturing facility, Lonza is making more than 20 runs a year of IMC-C225 in two -5,000-L fermentors. ImClone will use chemistry, manufacturing, and controls (CMC) data from Lonza to support a rolling biologics license application (BLA) that it submitted to CBER a few weeks

ago. The company hopes to gain conditional FDA approval for a limited indication for the therapy next year.

"Meeting future demands. *Meanwhile, ImClone is constructing an 80,000-ft2 commercial manufacturing facility next to its New Jersey pilot plant in anticipation of market approval. The $55 million plant will have three 12,500-L fermentors and will produce twice what Lonza is now making. ImClone has begun production runs and intends to complete validation early next year so that CMC data from the new plant will be available for a subsequent BLA filing. The company has been able to establish a new plant relatively quickly because it is building it from the ground up -- instead of retrofitting an old facility -- and modeling it directly on the nearby pilot plant."*
http://www.pharmaportal.com/articles/bp/bp0801_36-40_wash.pdf

Therefore, it's clearly time for ImClone Systems to step up to the plate and begin implementing an expanded access program.

The ImClone Oversight Alliance proposal calls for using ImClone's existing process and infrastructure so that the program can be initiated quickly. Here are some potential parameters which can be used to begin the discussion:

a. **Patient profile:** Patients with irinotecan-refractory colorectal cancer who are ineligible for ongoing trials -- for example, they could be too young, too ill or could have received prior therapy that's inconsistent with trial protocol.

b. **Timing:** Expanded access to start 4 weeks after the Phase 3 trials open, no later than January 1, 2002 to last until FDA approval is granted and the drug is widely available to practicing oncologists.

c. **Location:** Phase 3 trial sites

d. **Capacity:** Up to 3 patients per site per month, in order to provide benefit to significant number of people compared to the clinical trials without interfering w/ the clinical trials

e. **"Picking" mechanism:** We're prepared to discuss various mechanisms.

f. **Infrastructure:** Use existing infrastructure (call center, packaging, treatment protocols)

Because we only have a short time to execute the expanded access program, the ImClone Oversight Alliance will be scheduling a conference call with you and the members of the ImClone team no later than November 6 to discuss this proposal in detail. At that time, we would also like to schedule the sequence of calls from now until IMC-C225 has received FDA approval. Please call Bob Erwin at (443) 857-7651 to arrange the call.

We look forward to working with you.

Douglas Baxter
In Memory of David Baxter

Frank Burroughs, President
Abigail Alliance for Better Access to Developmental Drugs

Bob Erwin, Director
Marti Nelson Cancer Research Foundation

Jullian Grante, Senior Partner
J. Irving and Draper

Nancy Roach
Colorectal Cancer Patient Advocate

cc: The Honorable Dan Burton
United States House of Representatives

The Honorable Jo Ann Davis
United States House of Representatives

Cancer Leadership Council
Ellen Stovall, Chair

Colon Cancer Alliance
Kevin Lewis, Chair
Amy Kelly, Program Director

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Support for People with Oral and Head and Neck Cancer
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