Progress Report Year 1
Oct, 2003

Results in Year 1

1. Determine the safety and efficacy of pharmacologic inhibiton of the microsomal transfer protein (MTP) in patients with homozygous FH, including the effects on in vivo lipoprotein metabolism and on atherosclerosis.

We have initiated a phase I/II clinical trial of an MTP inhibitor in patients with homozygous FH. Six patients have been enrolled and two have completed the dose escalation treatment phase of the protocol. Tolerability has been surprisingly good, and there have been no major safety issues; a few patients have had increased liver function tests that were dealt with by reduction in dose as per protocol. Excitingly, we have seen major reductions in plasma cholesterol levels, though we await more data before reporting on the efficacy results. In any case, we have already answered our major question with this phase I/II trial—whether we can identify a dose of the MTP inhibitor in these patients that will be acceptably tolerated and result in substantial reduction in cholesterol levels. As a result, we have already begun planning for a larger and longer phase III trial. The current study could not have occurred without the support of the DDCF. I co-authored a review in the Journal of Clinical Investigation about genetic hypercholesterolemia that mentioned the use of MTP inhibition as a potential therapeutic strategy for homozygous FH.

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