

New HIV Drug Development a Problem
From Jules Levin, NATAP, December 4, 2008
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In the past few years we have seen development of a number of very effective new HIV drugs: raltegravir, darunavir, etravirine, Fuzeon, tipranavir, and CCR5 inhibitor maraviroc, with TMC278 on the way. Tibotec has been very busy developing 3 of these drugs along with a commitment to HCV drug development. Merck displayed quite a high level of commitment to developing raltegravir and also to developing new HCV drugs. All these companies spent money and effort developing these very important HIV therapies. Pfizer developed maraviroc as is Schering Plough developing their CCR5 antagonist vicriviroc, but to a market that has been lukewarm so far to using CCR5 inhibitors. Boehringer Ingelheim developed and launched tipranavir when Fuzeon was the only new drug, and they too have an active HCV drug development program. At the time patients were very anxious for both Fuzeon and tipranavir. Of course Roche's development program of Fuzeon was a trailblazer in new drugs for patients with extensive drug resistance and saved quite a lot of lives.

I sat on the company community advisory boards for all these drugs and witnessed the process companies and patients experienced in development for each of these drugs. At ICAAC Nov 2008 there was an oral presentation by the FDA in essence laying out study requirements for new HIV drugs. It appears as though the FDA and the EMEA have created high barriers for new HIV drug approvals. It also appears as though many HIV researchers/'thought leaders' think we have enough HIV drugs and agree with these high barriers for new HIV drug development.

I emphatically disagree. We need safer, more convenient, drugs with less side effects. We need new classes of drugs that have these characteristics and for patients with drug resistance. In the past I recall there was a movement to fast track new drugs for patients with resistance and I think this helped in the movement to delay studies in naives. This I think helped put naive drug development in a context that it was less important.

More recently a number of well known HIV researchers have made their opinions clear that they think we have enough new HIV drugs and this has played an important role in creating high barriers for new drug development. This development certainly adds to an environment where additional factors discourage new HIV drug development. Developing a new HIV drug is costly, and there are already about 20 HIV drugs so these facts make it potentially much more difficult to justify investing the high cost for developing a new HIV which has been estimated at \$500-750 million to develop a new HIV drug. Of course in addition due to economic reasons all companies are in a situation of having to tighten their financial belts and make decisions about where to invest their research dollars and decide I think where will they make a better profit -- cancer, HIV, cardiovascular disease.

The industry has been under increasing scrutiny by regulators, the public, and politicians, and some of this added scrutiny is at least in part due to bad behavior by certain companies but also due to heightened public and patient undue anger. Drug companies have become the boogie man, the bad guy. Apparently forgotten or pushed to the side is that these companies provide the lifblood for patients. Some companies have had significant trouble. Roche announced leaving HIV but they are still supporting saquinavir use in the field and Fuzeon is still being used but less. They turned to devoting their assets to developing HCV drug development. GSK has had difficulties with AZT and abacavir but are developing a new integrase inhibitor. Abbott had much success with Kaletra but have also turned to HCV drug development. Many drug companies are thankfully devoting much effort to developing HCV drugs.

So, where will our new HIV drugs come from? Will we see new HIV drugs? Will biotech companies devote their efforts to identifying and developing new classes of HIV drugs, will academic and government researchers do this? There are lot of people in this field who share my concerns that new HIV drug development is a problem.