



FUSION AND ATTACHMENT INHIBITORS

NOTE: several fact sheets describe drugs that are being tested against HIV:

- Fact sheet 410: nucleoside analog reverse transcriptase inhibitors (nukes)
 - Fact sheet 430: non-nucleoside analog reverse transcriptase inhibitors (NNRTIs or non-nukes)
 - Fact sheet 440: protease inhibitors
 - Fact sheet 460: attachment and fusion inhibitors
 - Fact sheet 480: immune therapies
- These drugs have not been approved by the Food and Drug Administration (FDA) for use against HIV.**

ATTACHMENT AND FUSION INHIBITORS

This is a new class of anti-HIV drugs. They are intended to protect cells from infection by HIV by preventing the virus from attaching to a new cell and breaking through the cell membrane. Researchers hope that these drugs can prevent infection of a cell by either free virus (in the blood) or by contact with an infected cell.

Because digestive acids break them down, most of these drugs are given by injections or intravenous infusion. Fusion and attachment inhibitors in human trials include AK602, AMD070, BMS-378806, HGS004, INCB9471, Maraviroc, PRO 140, SCH532706, SP01A, TAK-652, TNX-355 and Vicriviroc (SCH 417690),

AK602 is a CCR5 blocker being developed by Kumamoto University in Japan. It is in early human trials.

AMD070 by AnorMed blocks the CXCR4 receptor on CD4 T-cells to inhibit HIV fusion. It is in Phase II trials.

BMS-378806 is an attachment inhibitor that attaches to gp120, a part of the virus, not the target cell. It is in Phase I trials.

HGS004 by Human Genome Sciences, a monoclonal antibody CCR5 blocker, successfully completed a Phase II trial.

INCB9471 by Incyte Corporation has successfully completed Phase II trials in healthy volunteers. It is being tested as a 200 mg dose once a day. It has shown very good tolerability.

Maraviroc (Celsentri, MVC, UK-427,857) was approved by the FDA in July 2007. See fact sheet 462.

PRO 140 by Progenics is now in Phase II trials. It blocks fusion by binding to a receptor protein on the surface of CD4 cells. PRO 140 has been granted fast-track status by the FDA. It is being studied as an intravenous infusion and by subcutaneous injections.

SCH532706 by Schering is in Phase I studies. It is best used as part of a regimen that includes ritonavir where it can be administered once daily.

SP01A by Samaritan Pharmaceuticals is an HIV entry inhibitor in a Phase III trial.

TAK-652 by Takeda blocks binding to the CCR5 receptor. A Phase I study has been completed.

TNX-355 by Tanox blocks the CD4 receptor. It is a genetically engineered drug, a "monoclonal antibody." It may be administered by intravenous infusion or as a twice-monthly injection. No significant side effects have shown up yet. It is in Phase II trials.

Vicriviroc (SCH 417690, formerly called Schering D) by Schering Plough blocks the CCR5 receptor on CD4 cells. No serious toxicities have been seen. Phase III trials are starting.

DRUGS NO LONGER IN DEVELOPMENT

The following drugs are no longer being developed for use against HIV:

AMD3100 (fusion inhibitor) by AnorMed

Aplaviroc (GW873140) by GlaxoSmithKline. Development was suspended due to liver toxicity.

BMS488043 and BMS806 (attachment inhibitors by Bristol-Myers Squibb, replaced by BMS378806

FP21399 (CCR5 blockers) by Fujii Pharmaceuticals

PRO542 by Progenics is no longer being developed. Instead, Progenics is focusing on PRO140.

T-1249 (fusion inhibitor) by Roche and Trimeris – development was halted in early 2004.

Revised May 4, 2008