OTHER ANTIRETROVIRAL DRUGS IN DEVELOPMENT

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.

GENE THERAPIES

Several products are being developed to interfere with genes used by HIV.

- **HGTV43** by Enzo Biochem is an "antisense" therapy designed to produce CD4 cells (T-cells) that resist infection by HIV. It is in Phase I trials.
- **M87o** by EUFETS AG is a gene therapy that makes T-cells resist infection by HIV. It is being studied in a Phase I trial.
- M**ifepristone (VGX410, also known as RU486)** by Viral Genomix, interferes with the viral protein vpr. It is in a Phase I/II trial.
- **Modified CD4 and CD8 cells** by Cell Genesys are genetically modified to block attachment by HIV.
- **RRz2** by Johnson & Johnson is a ribozyme that attacks HIV's tat gene. It is in Phase II trials.
- **VRX496 by VIRxSYS** is in Phase II trials. It appears to bind to the RNA (genetic code) of HIV and disrupt it.

INTEGRASE INHIBITORS

After HIV's genetic code is changed from a single strand to a double strand by the reverse transcriptase enzyme, it gets inserted (integrated) into the genetic code of the infected cell. Then the HIV genetic code gets "read", producing new viruses. Scientists hope that integration will be another point in the HIV life cycle that can be targeted by drugs.

Elvitegravir (also known as Gilead 9137 and JTK-303) is now in a phase III study. The drug is used boosted with ritonavir. It is eliminated almost entirely via the feces so no dose adjustments are needed for patients with kidney problems.

GSK364735 by GlaxoSmithKline and Shionogi is in Phase I trials.

Raltegravir (Isentress, MK-0518) by Merck was approved in 2007. See fact sheet 471 for more information.

MATURATION INHIBITORS

A new type of drug inhibits the development of HIV's internal structures in a new virus. The first "maturation inhibitor" being tested is **bevirimat (PA457)** by Panacos Pharmaceuticals. It is moving into Phase III trials. Early results show strong antiretroviral activity. Side effects are mild. PA457 will probably be a once-a-day drug.

ZINC FINGER INHIBITORS

The inner core of HIV is called the nucleocapsid. It is held together by structures called "zinc fingers". Zinc finger inhibitors (or zinc ejectors) are drugs that can break apart these structures and prevent the virus from functioning.

Scientists believe that the nucleocapsid core cannot mutate very easily, so a drug that works against zinc fingers might be effective for a long time. Unfortunately, zinc fingers are not only used by the HIV virus. Drugs that attack them could have serious side effects.

One zinc finger inhibitor - azodicarbonamide (ADA) - has been tested in a Phase I/II trial, but there are no recent reports on its development.

VIRAL DECAY ACCELERATOR

A new type of drug under development is KP-1461. It encourages mutations in HIV to the point that the virus is no longer functional. Results from a Phase II study are expected by the middle of 2008.

DRUGS NO LONGER IN DEVELOPMENT

BI201 by BioInvent
L870810 integrase inhibitor by Merck
S-1360, GW810781 (integrase inhibitor) by Shionogi and GlaxoSmithKline