



# 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. One of them, **mifepristone (VGX410, also known as RU486)** by Viral Genomix, interferes with the viral protein vpr. It is in a Phase I/II trial. **BI-201** by BioInvent is an antibody designed to block HIV's tat gene. It is in Phase I/II trials.

## 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.

**Gilead 9137 (also known as JTK-303)** is in Phase I/II studies. The drug was discovered by Japan Tobacco and is licensed to Gilead Sciences.

**GSK364735 by GlaxoSmithKline** and Shionogi is in Phase I trials.

**MK-0518 by Merck** is being studied in Phase III trials. It is available through an expanded access program.

## 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 **bevrimat (PA457)** by Panacos Pharmaceuticals. It is currently in Phase II 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.

## ANTISENSE DRUGS

These are a "mirror image" of part of the HIV genetic code. The drug locks onto the virus to prevent it from functioning. One antisense drug, **HGTV43** by Enzo Therapeutics, is starting Phase II trials. VIRxSYS has completed a Phase I trial of its product, VRX496.

## DRUGS NO LONGER IN DEVELOPMENT

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

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