



# NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS 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 440: protease inhibitors
- Fact sheet 460: attachment and fusion inhibitors
- Fact sheet 470: new classes of antiretroviral drugs
- Fact sheet 480: immune therapies

***These drugs have not been approved by the Food and Drug Administration (FDA) for use against HIV.***

## **NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS**

These drugs stop HIV from multiplying by blocking the reverse transcriptase enzyme. This enzyme changes HIV's genetic material (RNA) into the form of DNA. This step has to occur before HIV's genetic code gets combined with an infected cell's own genetic codes. Non-nucleoside reverse transcriptase inhibitors, called NNRTIs or non-nukes, physically prevent the reverse transcriptase enzyme from working.

### **NNRTIs IN DEVELOPMENT**

NNRTIs (also called non-nukes) in development include BILR 355 BS, Calanolide A, IDX899, MIV-150, RDEA806, Rilpivirine (TMC278) and UK 453,061.

**BILR 355 BS** by Boehringer Ingelheim is being developed against wild type virus and virus already resistant to

NNRTIs. A Phase II study is in progress.

**(+)-Calanolide A** by Sarawak MediChem Pharmaceuticals was derived from a rain forest plant. It can easily cross the blood-brain barrier, and seems to stay in the bloodstream for a long time. It is in Phase II human trials.

**Etravirine (TMC125)** by Tibotec is active against some strains of HIV that are resistant to other NNRTIs. It was approved in 2008. For more information, see fact sheet 434.

**IDX899** by Idenix Pharma successfully completed a Phase I/II study in treatment-naïve patients. All rights to IDX899 have been sold to GlaxoSmithKline.

**MIV-150** by Medivir and Chiron shows good results in the laboratory against HIV that is resistant to other NNRTIs. It takes a long time for HIV to develop resistance to MIV-150. Phase II trials are in progress.

**RDEA806** by Ardea has completed a Phase II trial. The drug is active against HIV that is resistant to efavirenz. Viral resistance does not develop easily.

**Rilpivirine (TMC278)** by Tibotec is active against some strains of HIV that are resistant to other NNRTIs. It is being developed as a once-daily medication. Good results from a Phase IIb dose finding study in treatment-naïve patients were reported in August. A slow-release formulation is being studied.

**UK 453,061** by Pfizer has been studied in Phase I trials. It appears to be active against resistant strains of HIV. This includes virus resistant to efavirenz.

### **NNRTIs NO LONGER IN DEVELOPMENT**

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

**Ateviridine** by Upjohn

**Capravirine** by Pfizer / Agouron Pharmaceuticals

**Dapivirine (TMC120)** by Tibotec was abandoned due to low blood levels. However, it may still be useful as a microbicide.

**DPC083** by Bristol-Myers Squibb

**Emivirine (Coactinon)** by Triangle Pharmaceuticals

**GW5634, GW678248** by GlaxoSmithKline

**Loviride** by Janssen Pharmaceuticals

**HBV-097** by Hoechst-Bayer

**PNU142721** by Pharmacia & Upjohn

**TMC120** by Tibotec

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