Heteroarylphenylamine inhibitors of HIV reverse transcriptase

**OCR Number:** OCR 4081

**Description:**
Yale inventors have designed, synthesized, and tested a novel series of non-nucleoside reverse transcriptase inhibitors (NNRTIs) for treatment of wildtype and, more importantly, drug resistant mutant HIV-1 strains. The AIDS crisis continues with over 40 million people infected with HIV-1, and 3 million deaths in 2004, alone. 1.4 Million patients are in the US and Western Europe and account for $5.6 Billion in drug sales, annually. Of these sales, current NNRTI therapies account for almost $850 Million (2002), but are increasingly ineffective. The need for new drugs and points of attack to combat HIV is profound. The compounds available for license have excellent pharmaceutical and economic properties, and have been demonstrated to be effective inhibitors of HIV-1 mutant replication in industry standard cell-based models.

**Value Proposition:** HIV-1 is continually renewing itself as an unmet medical need as new drug-resistant mutants evolve. Reverse transcriptase, a well-established target for treatment of HIV, requires new inhibitors as old ones become obsolete. Current therapies are impotent against many mutant strains and have poor pharmaceutical characteristics. Potent small molecule inhibitors with favorable pharmaceutical properties and low cost of goods are not currently available. The compounds available for license could capture a significant portion of a $1Billion dollar market.

**Field of Application:** Antiviral therapy targeting reverse transcriptase (HIV, HBV, HCV, etc.).

**Advantages:**
- High potency (low nM, high pM)
- Superior solubility compared to marketed NNRTIs
- Excellent efficacy against mutant strains
- Low predicted cost of goods
- Low molecular weight
- Low predicted toxicity

**Stage of Development:** Numerous class representatives have been tested against wildtype and mutant strains. Many show equal or superior potency and solubility characteristics.

**Publications:**

HIV Background: http://hivmedicine.com/
Journal Articles:

1. Jorgensen, et al., 2005, Computer-aided design of NNRTIs
2. Ruiz-Caro, et al., 2005, Optimization of diarylamines as NNRTIs
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