

## ANTI-VIRAL COMPOUNDS THAT INHIBIT HIV ACTIVITY

### SUMMARY

The National Cancer Institute (NCI) Molecular Targets Laboratory is seeking parties interested in collaborative research to co-develop antiviral tropolone derivatives developed by systematic medicinal chemistry on the lead series.

### REFERENCE NUMBER

E-081-2011

### PRODUCT TYPE

- Therapeutics

### KEYWORDS

- HIV
- AIDS, RNase H
- tropolone derivative
- ribonuclease H
- viral replication

### COLLABORATION OPPORTUNITY

This invention is available for licensing and co-development.

### CONTACT

John D. Hewes  
NCI - National Cancer Institute  
240-276-5515

[John.Hewes@nih.gov](mailto:John.Hewes@nih.gov)

### DESCRIPTION OF TECHNOLOGY

Several novel tropolone derivatives have been identified that inhibit HIV-1 RNase H function and have potential for anti-viral activity due to reduced cellular toxicity. Inhibiting RNase H function is a potential treatment for many viral infections, since RNase H function is essential for viral replication for many pathogenic retroviruses such as HIV-1 and HIV-2. Although many hydroxytropolone compounds are potent RNase H inhibitors binding at the enzymatic active site, they are limited as therapeutic candidates by their toxicity in mammalian cells. The toxicity thought to be a result of inhibition of multiple essential mammalian metalloenzymes. We reasoned that the potential beneficial application of tropolone RNase H inhibition might be of therapeutic use if the toxic effects in mammalian cell were eliminated. By selectively adding steric bulk to add new drug-enzyme contacts for the RNase H active site, a number of

novel compounds, that have initially demonstrated reduced cytotoxicity, have been produced. Importantly, these novel compounds appear to retain antiviral activity essential for use as therapeutics.

## POTENTIAL COMMERCIAL APPLICATIONS

As an HIV-1 therapeutic

## COMPETITIVE ADVANTAGES

- Potentially reduced toxicity
- Availability of x-ray crystallographic information to guide analog design

## INVENTOR(S)

[John Beutler](#) (NCI), [Stuart LeGrice](#) (NCI), [Craig Thomas](#) (NHGRI)

## DEVELOPMENT STAGE

- Discovery (Lead Identification)

## PUBLICATIONS

[Chung S, et al. Synthesis, activity and structural analysis of novel alpha-hydroxytropolone inhibitors of human immunodeficiency virus reverse transcriptase-associated ribonuclease H. J Med Chem 2011 Jul 14;54\(13\):4462-4473.](#)

## PATENT STATUS

- U.S. Issued: US 8,993,768
- Foreign Issued: WO2012154904

## RELATED TECHNOLOGIES

- [E-183-2009 - Novel Analogues of the Natural Product Schweinfurthin with Specificity for Tumors and Other Disease Manifestations Associated with Neurofibromatosis Type 1](#)

## THERAPEUTIC AREA

- Infectious Diseases