

New Inhibitors of Cytomegalovirus DNA Polymerase

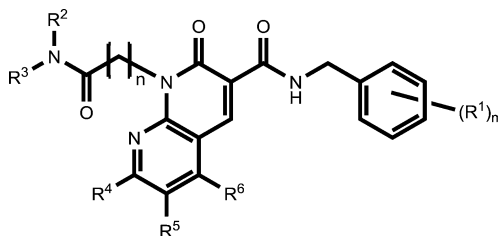
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Title:	Cytomegalovirus Inhibitor Compounds		
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Priority Application:	US 61/620,752	Priority date:	5 April 2012
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Disease Area:	Treatment and prevention of Human cytomegalovirus (HCMV) disease and/or infection	Biological Target:	HCMV DNA polymerase

Summary: The invention in this patent application relates to 1,8-naphthyridin-2(1H)-one analogs represented generally by formula (I). These compounds are inhibitors of human cytomegalovirus (HCMV) DNA polymerase and may potentially be used for the treatment and prevention of CMV disease and/or infection.

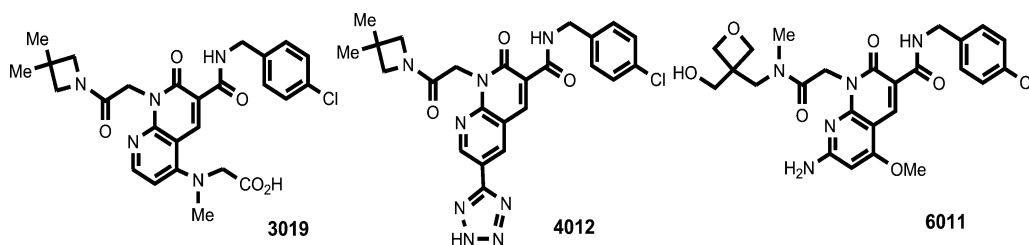
Human cytomegalovirus (HCMV), also known as CMV or human herpes virus 5 (HHV-5), is a β -herpes virus. CMV is widespread virus that infects people of either sex and any age group with all ethnic backgrounds worldwide. HCMV infection is typically unnoticed in healthy people, but can be life threatening for those with immunocompromised systems whether adults or children. The currently approved drugs for the treatment of HCMV include Valganciclovir, Ganciclovir, Cidofovir, and Foscarnet. Each of these therapies inhibits CMV DNA polymerase (pUL54), an enzyme essential for viral replication. However, emergence of drug-resistant HCMV has been reported for all of them. The compounds of this application have similar activities and may provide additional treatment against HCMV infections.

Important Compound Classes:

Formula (I)

Key Structures:

The inventor reported the structures and synthesis procedures for 231 analogues of formula (I); the following three are represented examples:

**Biological Assay:**

HCMV Polymerase Scintillation Proximity Assay
HCMV Polymerase LANCE TR-FRET Assay

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Biological Data:

IC₅₀ values in the range of 40 μM were reported for about 40 compounds; examples **3019**, **4012**, and **6011** have some of the lower IC₅₀ values.

Data from HCMV Polymerase LANCE TR-FRET Assay	
Compound	IC ₅₀ (nM)
3019	50
4012	30
6011	22

Claims:

Claims 1–13: composition of matter; variations of formula (I)

Claims 14–15: use as medicament

Claims 16–19: pharmaceutical composition

Claims 20–25: method of treating or preventing CMV disease

Recent Review Articles:

1. James, S. H.; Prichard, M. N. *Infect. Disord.: Drug Targets* **2011**, *11* (5), 504–513.

2. Schreiber, A.; Haerter, G.; Schubert, A.; Bunjes, D.; Mertens, T.; Michel, D. *Expert Opin. Pharmacother.* **2009**, *10* (2), 191–209.

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Notes

The authors declare no competing financial interest.