

# Potential Treatment for the Respiratory Syncytial Virus Infections (HRSV)

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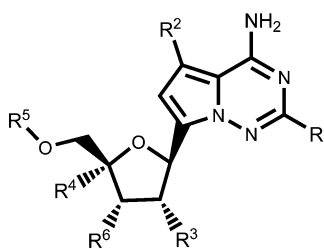
<b>Title:</b>	Pyrrolo[1,2- <i>f</i> ][1,2,4]Triazines Useful for Treating Respiratory Syncytial Virus Infections		
<b>Patent Application Number:</b>	WO 2015/069939 A1	<b>Publication date:</b>	14 May 2015
<b>Priority Application:</b>	US 61/902,544	<b>Priority date:</b>	11 November 2013
<b>Inventors:</b>	Clarke, M. O. H.; Doerffler, E.; Mackman, R. L.; Siegel, D.		
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<b>Disease Area:</b>	Pneumovirinae virus infections	<b>Biological Target:</b>	Human Respiratory Syncytial Virus (HRSV)
<b>Summary:</b>	The invention in this patent application relates to tetrahydrofuranpyrrolo[1,2- <i>f</i> ][1,2,4]-triazine-4-amine derivatives represented generally by formula (I). These compounds possess antiviral activities and may potentially be useful for the treatment of pneumovirinae virus infections, including respiratory syncytial virus infections.		

Pneumovirinae viruses, which include the human respiratory syncytial virus (HRSV), are a subfamily of the Paramyxoviridae viruses' family. They are negative-sense, single-stranded, RNA viruses that are responsible for many prevalent human and animal diseases. HRSV infects almost all children by their second birthday causing lower respiratory tract infections in infancy and childhood resulting in mild respiratory illness in most cases, but in some cases the infection can become serious. Statistically, nearly 5–20 infections in every thousand cases require hospitalization. HRSV also infects the elderly and adults and may cause severe infections in patients with high risk factors such as chronic heart and lung disease or immunosuppressed patients.

Ribavirin is the only approved antiviral agent to treat HRSV infections, but it has limited efficacy. Currently, there is no available vaccine to prevent HRSV infections; however, monoclonal antibody palivizumab is available for limited use for immunoprophylaxis. Its use is restricted to cases involving infants at high risk, such as premature infants or those with either congenital heart or lung disease. It also comes at a high cost that often makes it prohibitive for general use.

There are several reported examples of the structurally related pyrrolo[2,3-*d*]pyrimidine derivatives at variable stages of development that show antiviral activities and may be useful in treating viral infections. However, there remains a need for the discovery of new effective antiviral compounds that display acceptable toxicity profiles for treating viral infections by the Paramyxoviridae viruses' family, including Pneumovirinae viruses such as HRSV.

## Important Compound Classes:



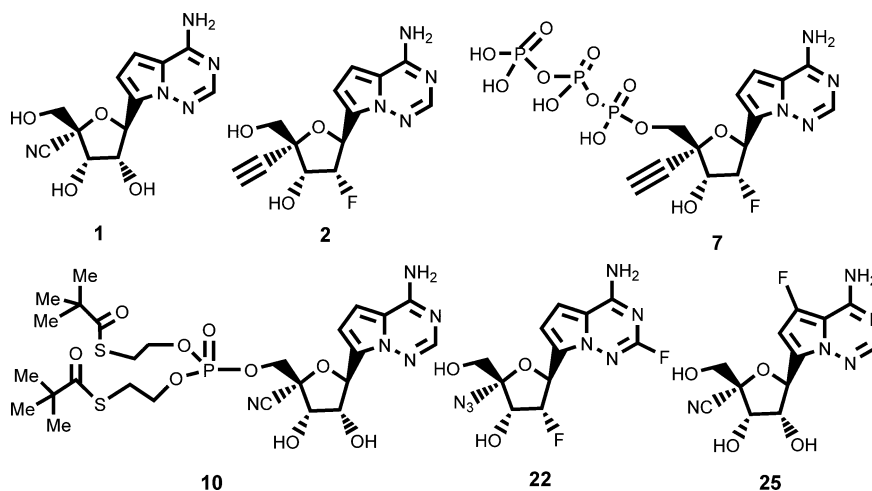
Formula (I)

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## Key Structures:

The inventors listed the structures of 35 examples of formula (I) including the following compounds:



## Biological Assay:

Respiratory syncytial virus (RSV) antiviral activity and cytotoxicity assays:

- Anti-RSV Activity
- Cytotoxicity Assay in HEp-2 Cells
- Cytotoxicity Assay in MT-4 Cells
- RSV RNP Assay

## Biological Data:

The following table contains assay data obtained from the above representative examples:

Compound	Anti-RSV EC <sub>50</sub> (μM)	HEp-2 CC <sub>50</sub> (μM)	MT-4 CC <sub>50</sub> (μM)	RSV RNP IC <sub>50</sub> (μM)
<b>1</b>	7.3	>50	>53	--
<b>2</b>	9.6	>100	>106	--
<b>7</b>	--	--	--	1
<b>10</b>	1.0	39	7.3	--
<b>22</b>	0.57	>100	32	--
<b>25</b>	9.2	>100	>93	--

## Recent Review Articles:

1. Gomez, R. S.; Guisle-Marsollier, I.; Bohmwald, K.; Bueno, S. M.; Kalergis, A. M. *Immunol. Lett.* **2014**, *162* (1-Part A), 237–247.
2. Najarro, P.; Angell, R.; Powell, K. *Antiviral Chem. Chemother.* **2012**, *22* (4), 139–150.
3. Olszewska, W.; Openshaw, P. *Expert. Opin. Emerg. Drugs* **2009**, *14* (2), 207–217.

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### Notes

The authors declare no competing financial interest.