WORLD ANTIVIRAL CONGRESS

SAN DIEGO | 28 NOVEMBER - 1 DECEMBER 2022

Broad-Spectrum Antivirals against Respiratory Viruses

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Crestone Inc.

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Crestone Overview

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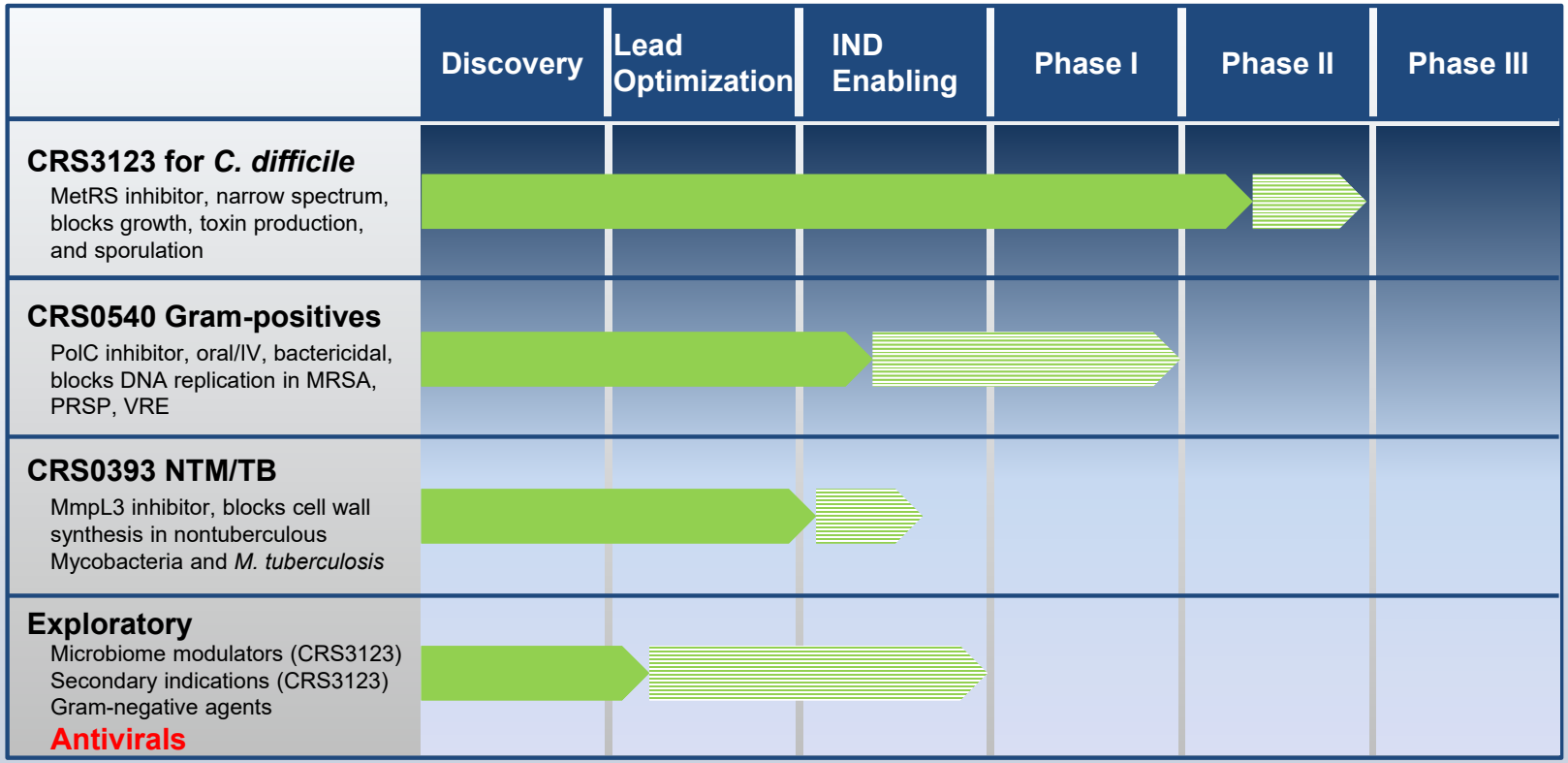
- Located in Boulder, Colorado
- Founded in 2009
- Focus on novel mechanism-of-action anti-bacterial agents, recently antiviral
- Overall mission is to address antibiotic resistance and infection control
- Pipeline of four programs
- Programs advanced to date with non-dilutive support (mostly NIH)
- Owned 100% by founders, employees, and advisors
- Experienced founding and management team

Crestone Pipeline



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What COVID-19 Can Do to You

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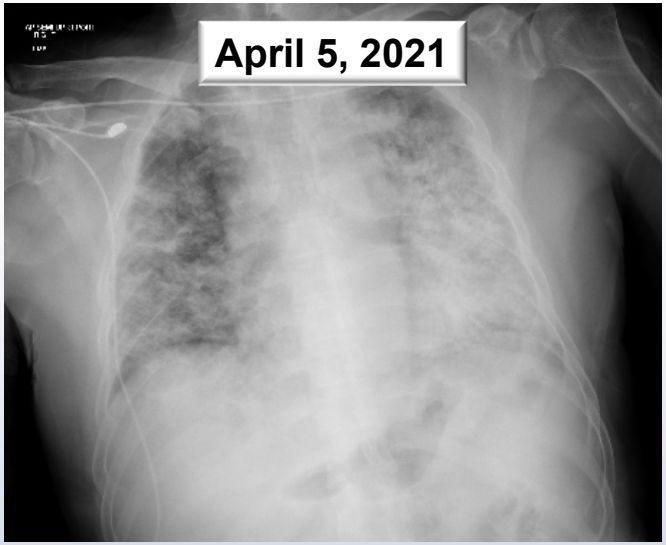

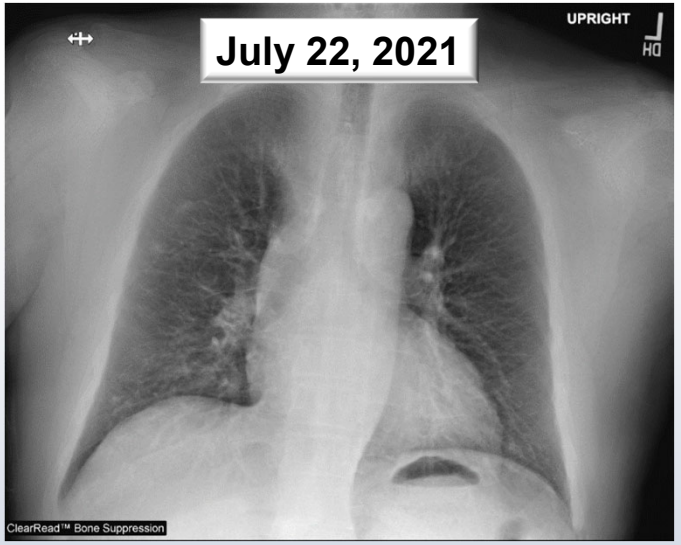

- Infected with SARS-COV-2 on 3/16/2021, hospitalized on 3/23/2021
- Hospitalized for 30-days including 8 days of ICU
- Rehabilitation two weeks, home recovery one month

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The Good News is YOU are Fighting For Better Tools!

Ideal Antiviral Drug

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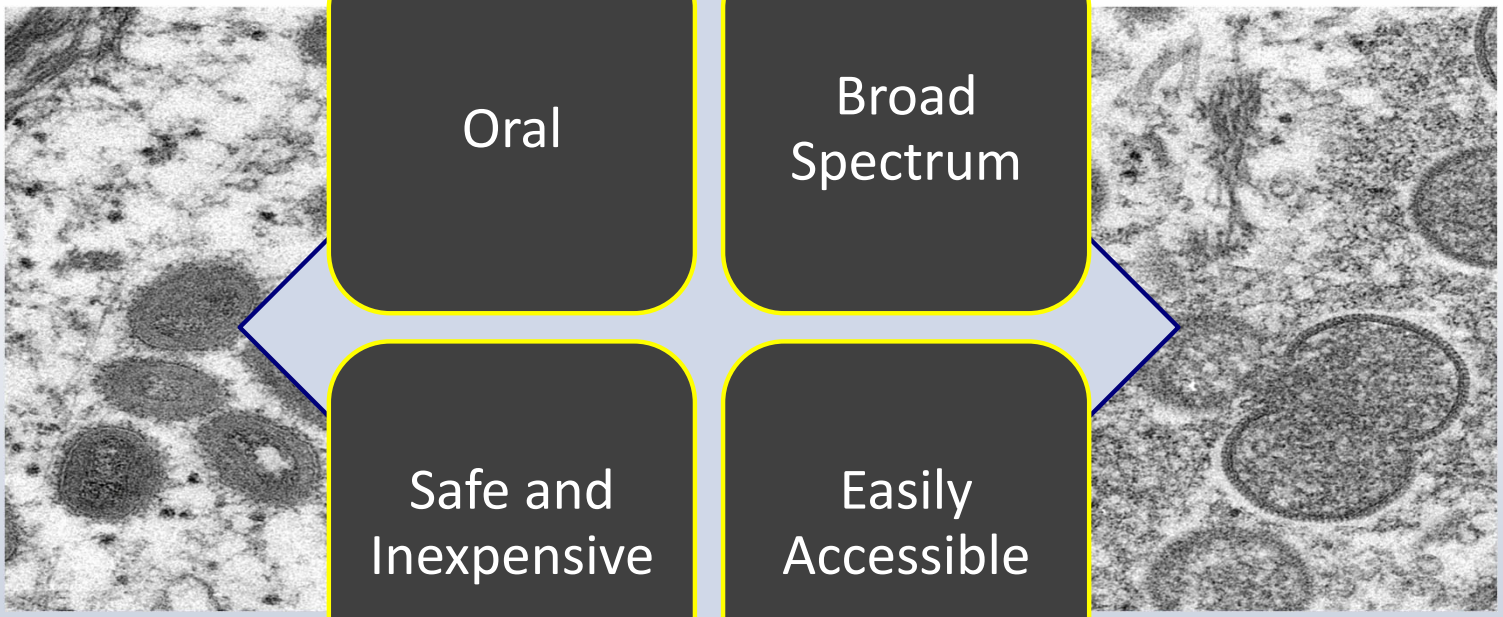

- Oral
- Broad Spectrum
- Safe and Inexpensive
- Easily Accessible

https://phil.cdc.gov

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Reality

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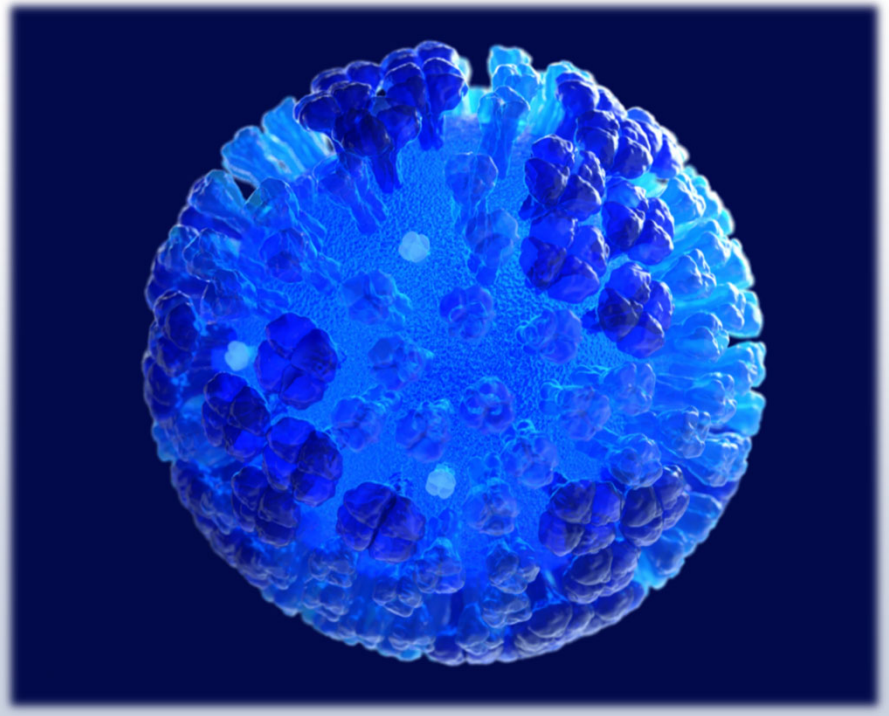
- No such antiviral drug today
- Viruses are very diverse
- Viruses emerge and re-emerge presenting challenges for clinical trials
- Development of therapeutics for some viral infections is not economically attractive



https://phil.cdc.gov

Antiviral Spectrum of Activities

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- Vaccine/monoclonal antibody
  - Very specific for one virus
- Viral targeted antiviral
  - Specific virus or its viral family
- Host viral life cycle targeted
  - Spectrum can be broader
- Immune-modulators
  - Broadest spectrum

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Where to Start?

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Identify target(s) most essential for as many viruses as possible, if not all virus replication

Research the current broad-spectrum antivirals

Start with existing leads

-Identify partners for testing

NIAID PCS Support

Under Antiviral Program for Pandemic (APP)

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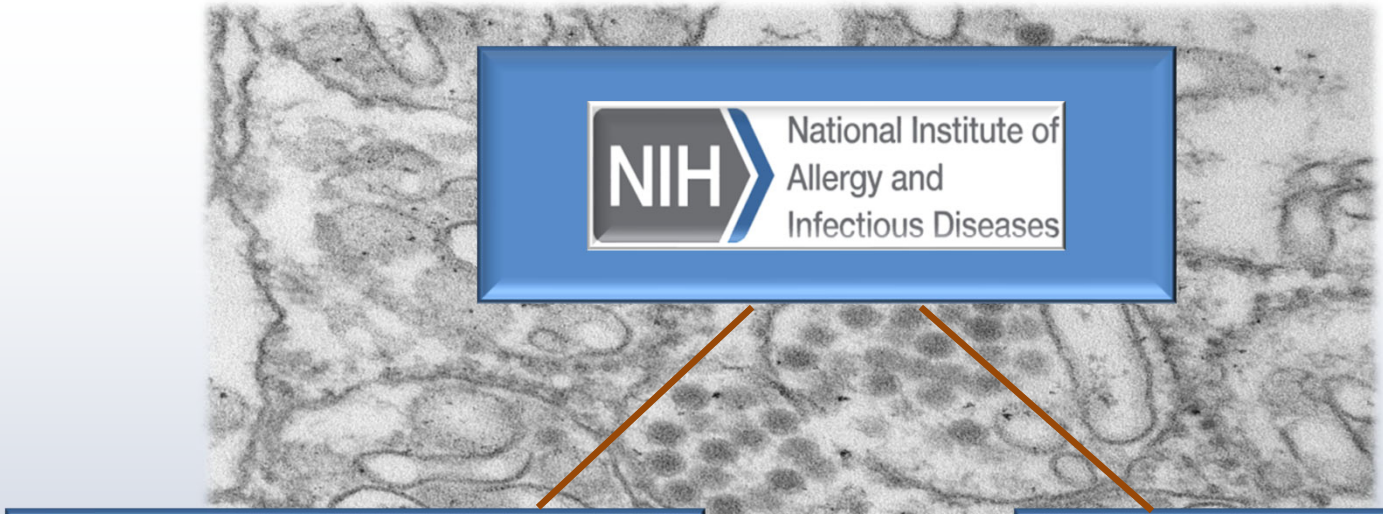

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Crestone's Antiviral Approach

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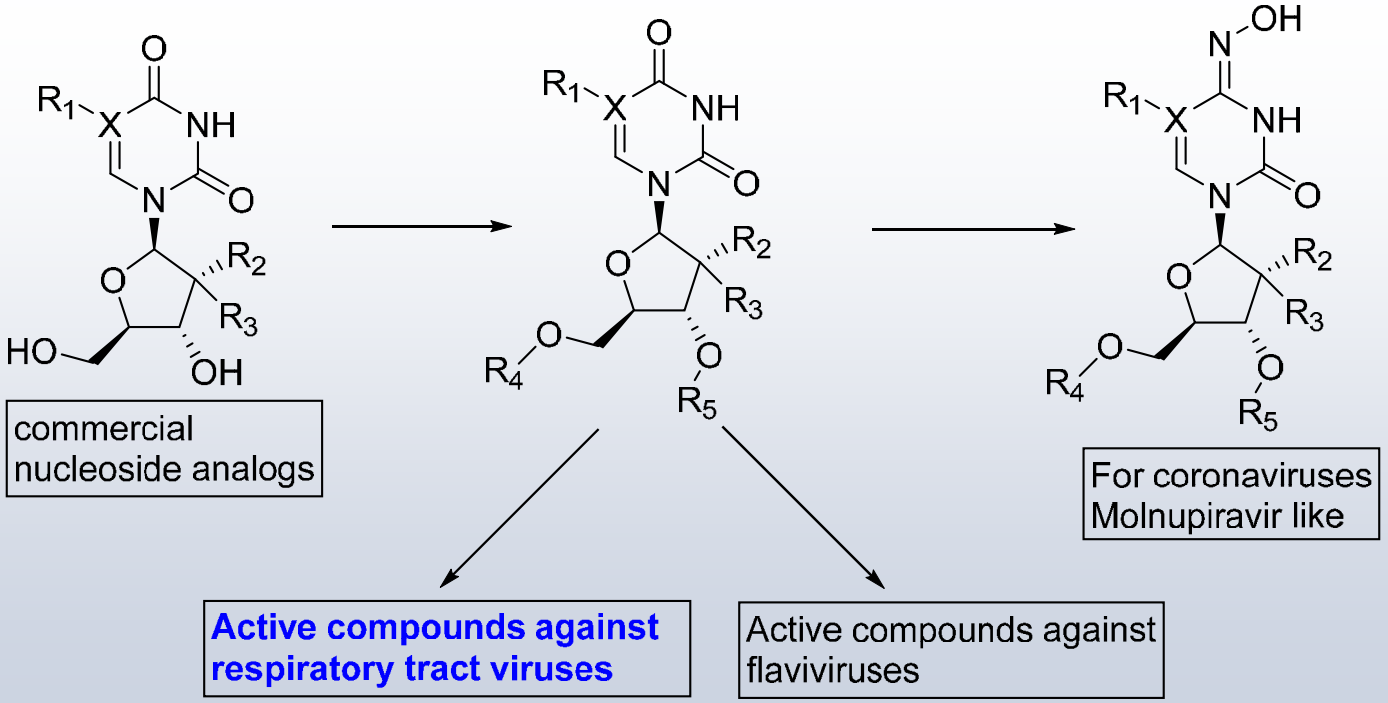

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Broad Spectrum Antivirals for Respiratory Viruses

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Compound ID	Respiratory Syncytial Virus (A2) - CPE (NR) - MA-104			Influenza A (H1N1, California/07/2009) - CPE (NR) - MDCK			Human Rhinovirus-14 (1059) - CPE (NR) - Hela Ohio			Measles (CC) - CPE (NR) - Vero 76			Measles Virus (CC)- VYR - Vero 76		
	EC_{50} (μM)	CC_{50} (μM)	SI_{50} (μM)	EC_{50} (μM)	CC_{50} (μM)	SI_{50} (μM)	EC_{50} (μM)	CC_{50} (μM)	SI_{50} (μM)	EC_{50} (μM)	CC_{50} (μM)	SI_{50} (μM)	EC_{50} (μM)	CC_{50} (μM)	SI_{50} (μM)
CRS700072	0.34	> 32	> 94	2.7	> 32	> 12				0.56	15	27	5.2	> 100	> 19.0
CRS700062	0.39	> 100	> 250	7.3	> 100	> 14				4.3	> 100	> 23	5.6	> 100	> 18.0
CRS700018	0.85	> 100	> 117	12	> 100	> 8.3									
CRS700012	5.1	20	3.9	1.2	> 100	> 83	1.1	> 100	> 91	21	> 100	> 4.8			
CRS700010	1.4	20	14	5	> 100	> 20	1.5	87	58	2.2	> 100	> 45			
Ribavirin	15.02	> 500	> 33	7.32	> 500	> 68									

* $SI_{50} = CC_{50}/EC_{50}$, CPE = cell pathetic effect, NR = neutral red

- CRS700072, CRS700062 and CRS700018 show potent activity against RSV
- CRS700072 and CRS700062 active against Measles in both CPE and VYR assays
- Broad-spectrum against respiratory viruses
- Novel chemical entities
- Much improved potency compared to ribavirin, the ONLY small molecule drug approved for RSV
- Provisional patent filed April 2022
- Continued support from NIAID PS

NIH National Institute of Allergy and Infectious Diseases

Synonyms	MIC: Saur 29213 (ug/mL)	MIC: Calbicans 10231 (ug/mL)
CRS700062	> 64.0	16
CRS700018	> 64.0	16
CRS700012	> 64.0	> 64.0
CRS700010	> 64.0	> 64.0

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Spectrum of Activities against Select Agents

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Compound ID	CellType	PathogenID	Strain	EC_{50} [µM]	EC_{90} [µM]	CC_{50} [µM]	*SI_{50}
CRS700010	HeLa	EBOV	Duncan/Makona	8.79	78	≥30.0	≥3.4
CRS700012	HeLa	EBOV	Duncan/Makona	29.94	51	≥30.0	≥1
CRS700018	HeLa	EBOV	Duncan/Makona	1.47	-	≥30.0	≥20
CRS700062	HeLa	EBOV	Duncan/Makona	1.57	-	≥30.0	≥19
CRS700010	VeroE6	JUNV	Romero	2.96	4	≥30.0	≥10
CRS700012	VeroE6	JUNV	Romero	1.57	3	29.8	19
CRS700018	VeroE6	JUNV	Romero	0.88	1	27.7	31
CRS700062	VeroE6	JUNV	Romero	1.12	2	29.0	26
CRS700010	VeroE6	LASV	Josiah	4.55	-	≥30.0	≥6
CRS700012	VeroE6	LASV	Josiah	1.36	9	≥30.0	22
CRS700018	VeroE6	LASV	Josiah	1.07	4	27.0	25
CRS700062	VeroE6	LASV	Josiah	1.97	9	≥30.0	15
CRS700010	HeLa	RVFV	ZH 501	≥30.0	-	≥30.0	ND
CRS700012	HeLa	RVFV	ZH 501	≥30.0	-	≥30.0	ND
CRS700018	HeLa	RVFV	ZH 501	≥30.0	332	≥30.0	ND
CRS700062	HeLa	RVFV	ZH 501	≥30.0	481	≥30.0	ND

* $SI_{50} = CC_{50}/EC_{50}$

USAMRIID United States Army Medical Research Institute of Infectious Diseases
Biodefense solutions to protect our nation

Expanded the viral panel to viruses other than in respiratory tract in preparation for future pandemic

NIH National Institute of Allergy and Infectious Diseases

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Desired Product Profile for Respiratory Tract Viruses

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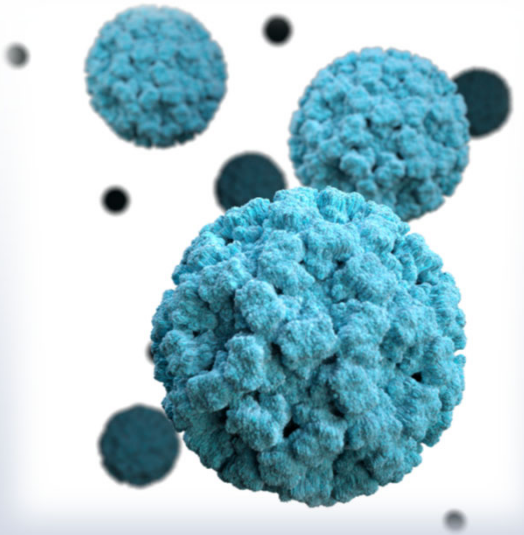
- ✓Oral
- ✓Early intervention
- ✓Broad spectrum: respiratory tract infections
- ✓Safe for acute conditions, less than 10 days
- ✓Dosing regimen: once or twice a day
- ✓Low cost, readily available
- ✓Combination potential for broader coverage of viruses



Current Position: Respiratory Syncytial Virus (RSV)

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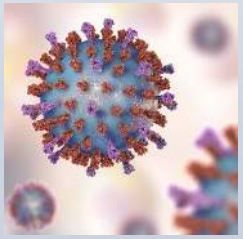
- A common, contagious virus that causes infections of the respiratory tract
  - Negative-sense, single-stranded RNA virus
- Ribavirin is the only small molecule antiviral medication currently approved for the treatment of RSV in children
  - Guanosine analog that acts by inhibiting viral RNA synthesis and capping. It was originally approved in 1986 for treatment of RSV infection
  - The use of ribavirin remains controversial due to unclear evidence regarding efficacy, concerns about toxicity to exposed staff members, as well as cost
- Recognize late-stage vaccine trials, but therapeutics will always be complementary as we learned from COVID-19 pandemic



Near Future Plan

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- PK, tissue distribution of the lead compounds
- Efficacy of lead compounds in cotton rat RSV infection model
- Tolerability in animals
- Viral resistance and mechanism of action
- Collaboration welcome: xsun@crestonepharma.com
  - https://crestonepharma.com

Acknowledgements

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Final Remarks

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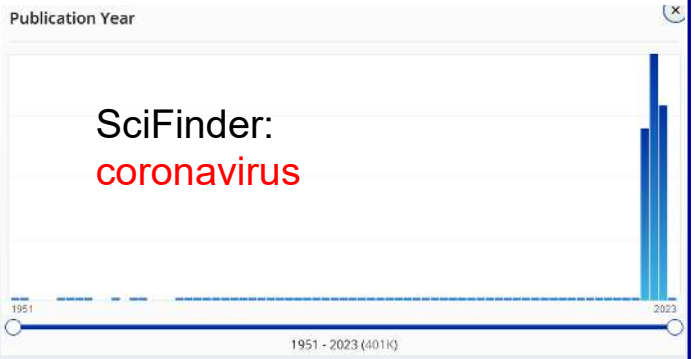
- Be proactive, not reactive to pandemic
- One can not change the world
  - ➢ Together we can make a difference!!!
- Keep up the fight



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Thank You for Your Attention!