



May 20, 2020

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**Systems-Based Approaches for Immunological Disease**  
COVID-19 Development Update

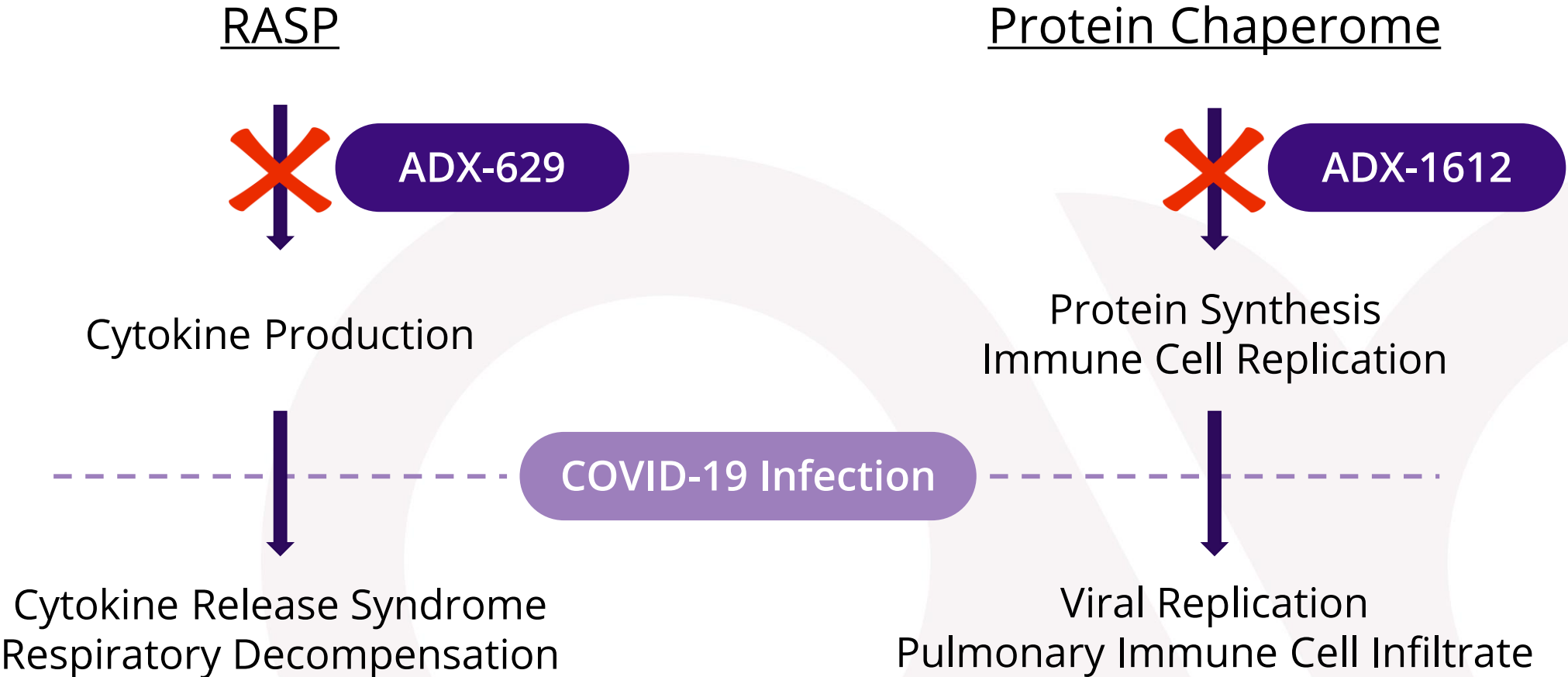
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# For the Treatment of COVID-19, Aldeyra Is Developing Two Systems-Based Approaches That Potentially Modulate Numerous Targets



Aldeyra Therapeutics is developing ADX-629 and ADX-1612 as investigational new drugs for the treatment of immune mediated diseases, including cancer. Aldeyra has initiated communication with the Food and Drug Administration (FDA) about the potential use of ADX-629 for the treatment of COVID-19 related cytokine release syndrome. Aldeyra has not yet communicated with the FDA about the potential use of ADX-1612 to treat COVID-19 related conditions.

RASP = Reactive Aldehyde Species



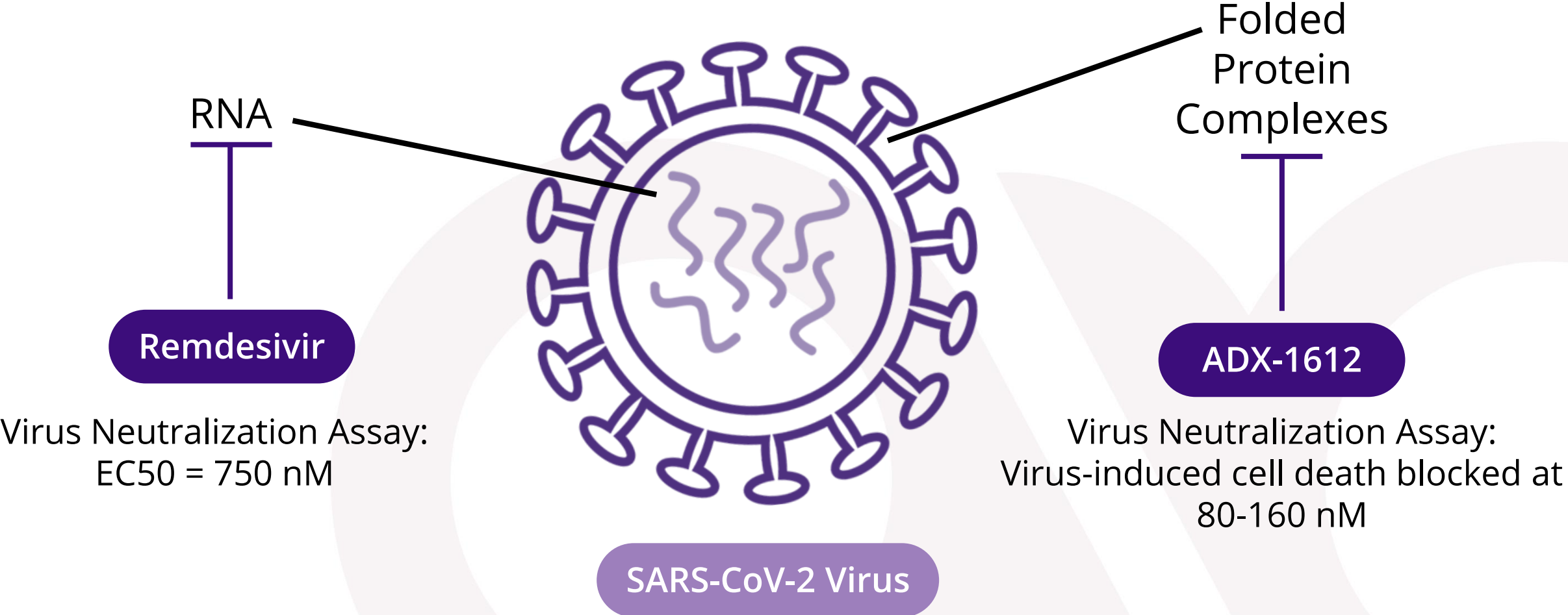
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**COVID-19 DEVELOPMENT UPDATE**

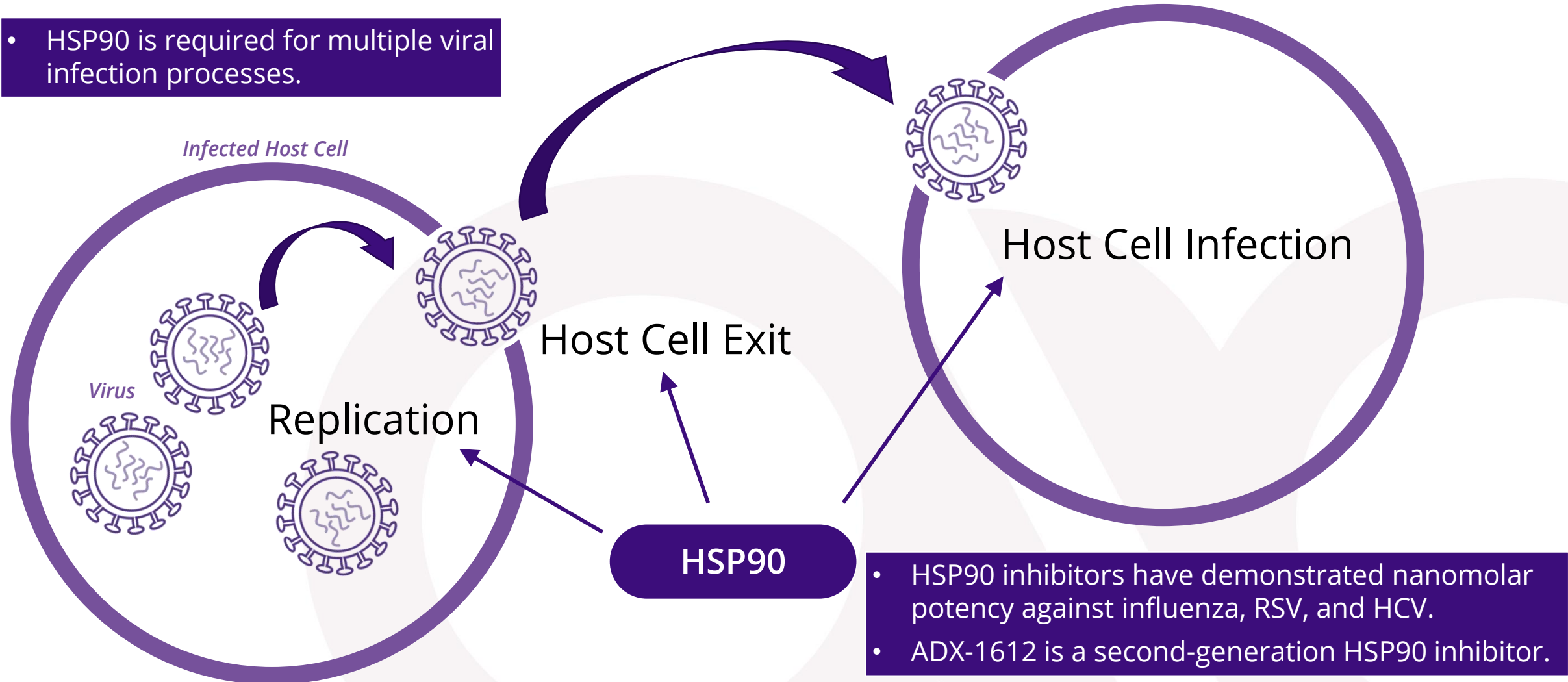
# ADX-1612: A Potential COVID-19 Antiviral with Nanomolar Potency

# ADX-1612 Represents a Potentially Synergistic Treatment with Antivirals that Target Viral Nucleic Acids



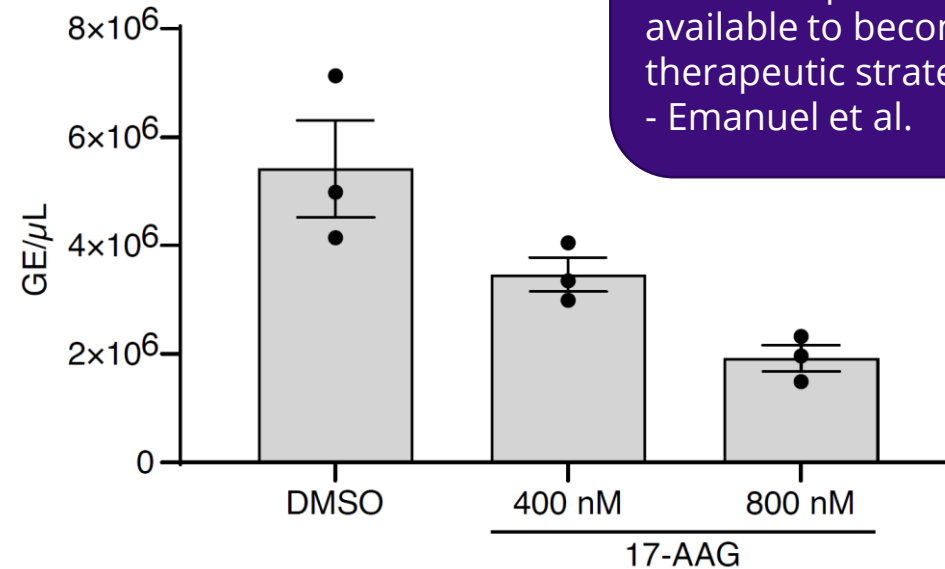
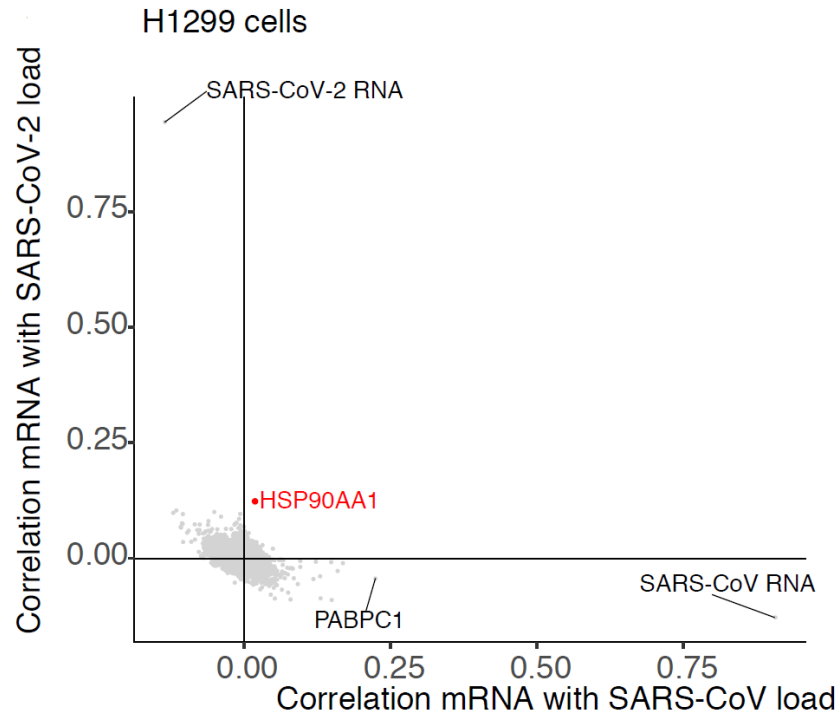
# ADX-1612 Inhibits HSP90, Which is Required for Multiple Processes Associated with Viral Infection

- HSP90 is required for multiple viral infection processes.





# HSP90 Recently Identified as a Potential Therapeutic Target of SARS-CoV-2

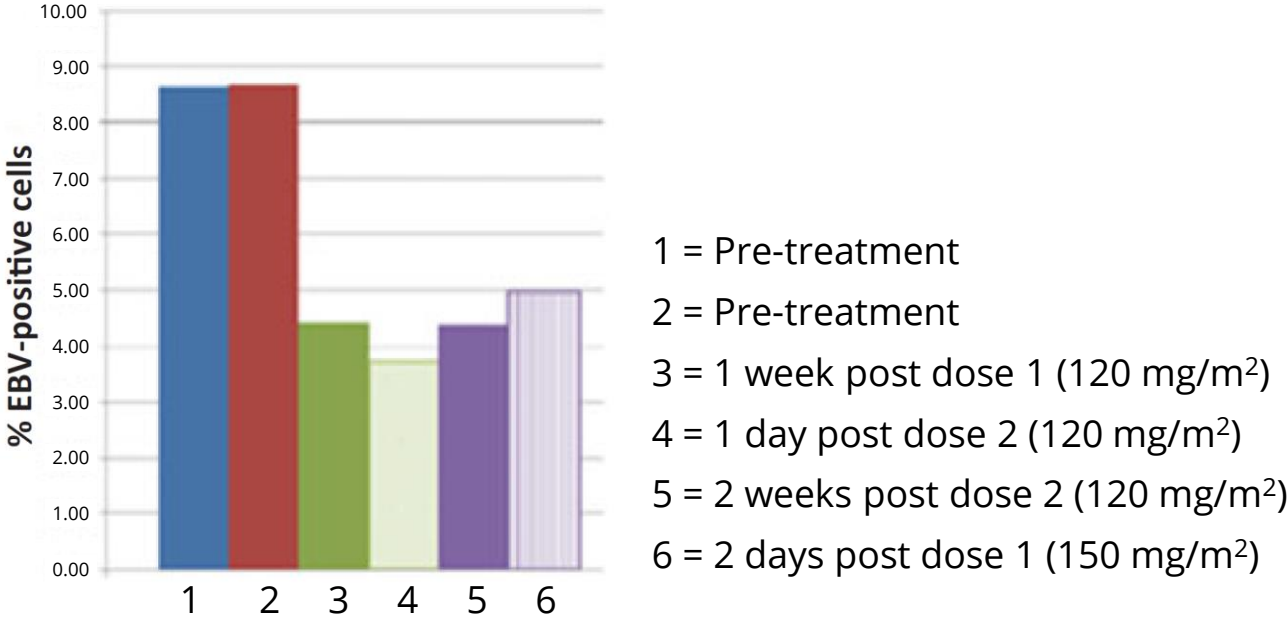


“Since several inhibitors of HSP90 with higher affinities have been in clinical development ... some of these compounds could be readily available to become part of a therapeutic strategy for COVID-19.”  
- Emanuel et al.

**Elevated HSP90 RNA found in SARS-CoV-2, and a low-potency HSP90 inhibitor reduced viral load in cell culture**

Emanuel et al. *Bulk and single-cell gene expression profiling of SARS-CoV-2 infected human cell lines identifies molecular targets for therapeutic intervention*, bioRxiv preprint, May 5, 2020. DOI:10.1101/2020.05.05.079194. Not certified by peer review.

# ADX-1612 Has Been Tested in Over 1600 Cancer Patients to Date, and Has Clinically Demonstrated Antiviral Activity in a Viral-Induced Cancer

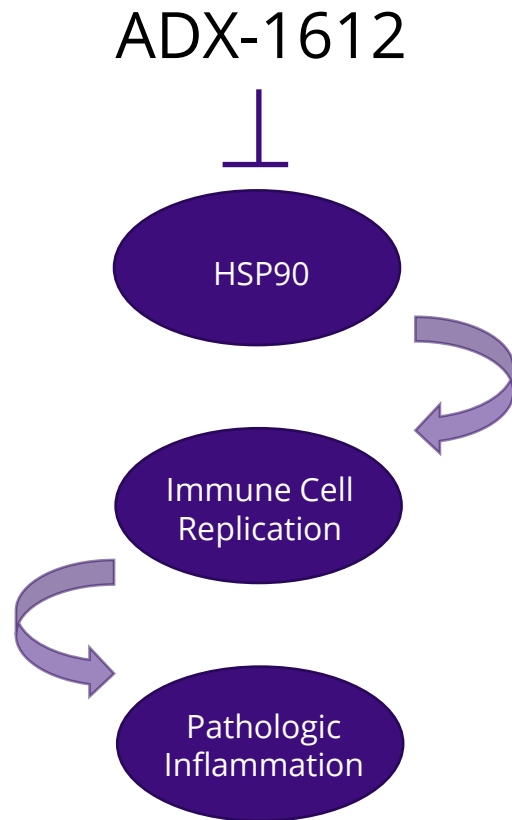


**In an EBV-infected patient, ADX-1612 reduced the percentage of circulating EBV-positive cells.**

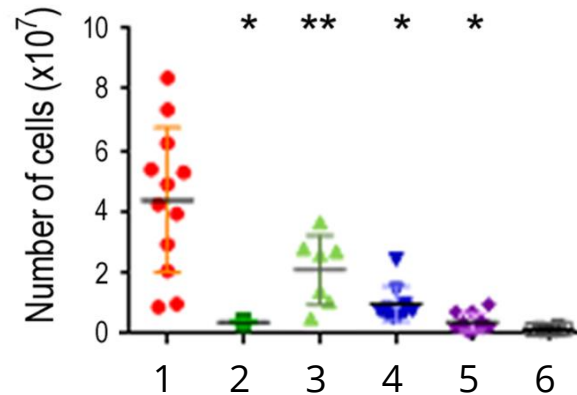
Shatzer et al. *Ganetespib, an HSP90 inhibitor, kills Epstein-Barr virus (EBV)-infected B and T cells and reduces the percentage of EBV-infected cells in the blood*, *Leukemia & Lymphoma*, 2016, DOI: 10.1080/10428194.2016.1213823



# In Addition to Antiviral Activity, ADX-1612 Has Demonstrated Potential Suppression of Pathologic Inflammation



Immune cell count reduction in animal model of lupus<sup>1</sup>



- 1 = Vehicle
- 2 = Cyclophosphamide
- 3 = Cyclophosphamide/2
- 4 = ADX-1612
- 5 = ADX-1612 + cyclophosphamide
- 6 = Normal animal

Clinical response in patient with chronic vasculitis after a single dose



<sup>1</sup>Liu et al. *The HSP90 Inhibitor Ganetespib Alleviates Disease Progression and Augments Intermittent Cyclophosphamide Therapy in the MRL/lpr Mouse Model of Systemic Lupus Erythematosus*, PLoS One, May 14, 2015.

DOI:10.1371/journal.pone.0127361

# ADX-1612 Planned Phase 2 COVID-19 Clinical Trial Synopsis\*

- **Patient Population:**

Adults and children hospitalized for COVID-19 with an oxygen saturation (SpO<sub>2</sub>) ≤ 94% on room air, or requiring supplemental oxygen, mechanical ventilation, or extracorporeal membrane oxygenation

- **Size:**

Up to 30 subjects, randomized 2:1 drug:placebo

- **Treatment Period:**

Two doses 72 hours apart

- **Endpoints:**

Time to discharge, days in intensive care unit, days in hospital, global clinical score

# Expected ADX-1612 Development Milestones and Clinical Plans\*

- Coronavirus Treatment Acceleration Program application **May 2020**
- COVID-19 IND submission **Q3 2020**
- Initiation of clinical testing for COVID-19 **Q3 2020**
- Completion of enrollment for ovarian cancer (the Phase 2 EUDARIO Trial) **June 2020**



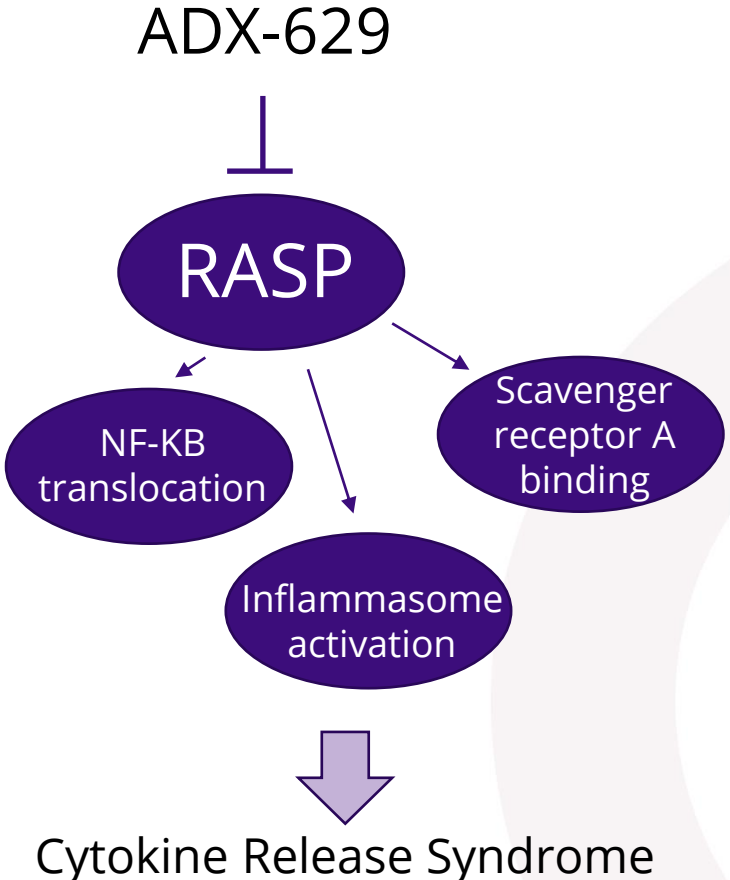
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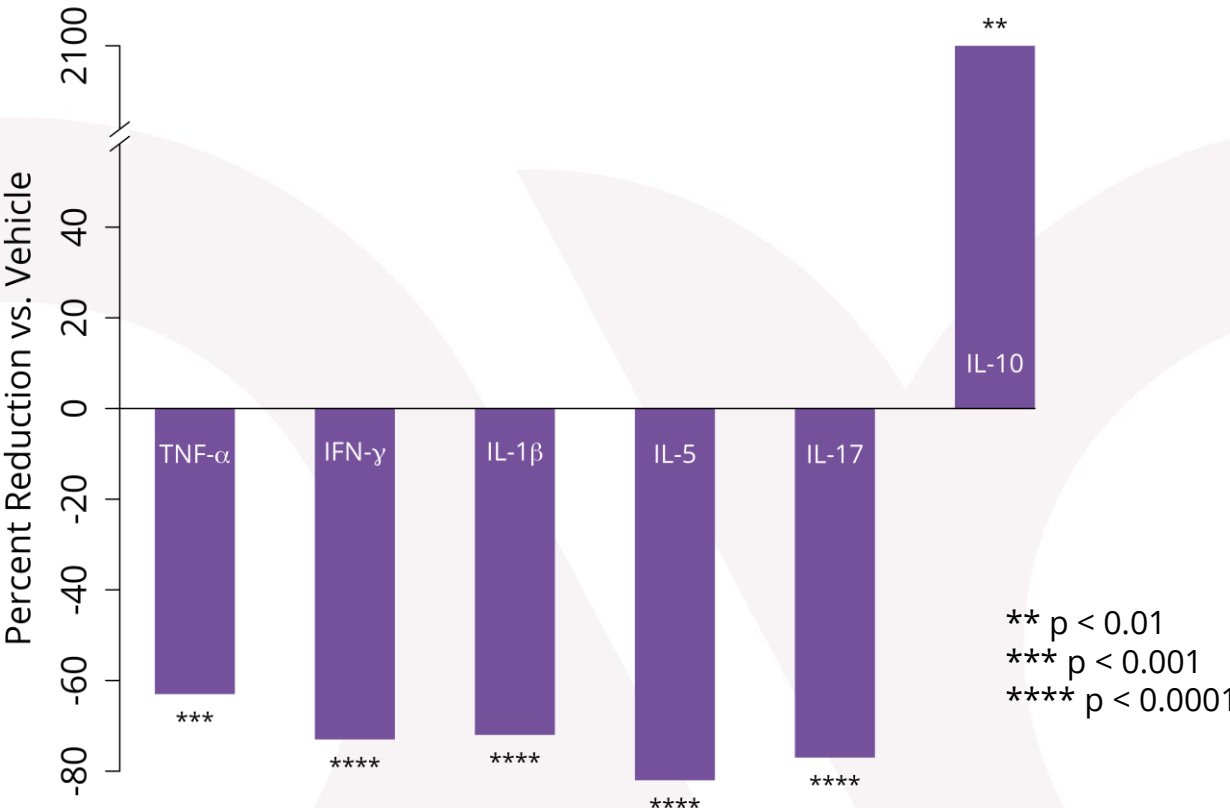
**COVID-19 DEVELOPMENT UPDATE**

# ADX-629 For The Potential Treatment of Cytokine Release Syndrome

# ADX-629 is a Pre-Cytokine, Systems-Based Approach with the Potential to Mitigate Cytokine Responses in COVID-19



LPS Animal Model of Cytokine Storm



# ADX-629 Planned Phase 2 COVID-19 Clinical Trial Synopsis\*

- **Patient Population:**  
COVID-19 patients recently admitted to hospital for respiratory compromise
- **Dosing:**  
600mg oral twice daily
- **Size:**  
Up to 30 subjects, randomized 2:1 drug:placebo
- **Treatment Period:**  
Up to 28 days
- **Endpoints:**  
Proportion on mechanical ventilation, time to discharge, cytokine profile



# Expected ADX-629 Development Milestones and Clinical Plans\*

- ✓ Coronavirus Treatment Acceleration Program (CTAP) application **March 2020**
- ✓ BARDA CoronaWatch application **May 2020**
- ✓ BARDA CoronaWatch meeting accepted (to be scheduled)
- ✓ Pre-IND FDA discussion (Pulmonary Division)
- COVID-19 IND submission **June 2020**
- COVID-19 clinical trial initiation **Q3 2020**
- Psoriasis and atopic asthma clinical trial initiations **H2 2020**



# Systems-Based Approaches for Immunological Disease

