



# CHIMERIX

COWEN  
HEALTHCARE CONFERENCE

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CHIEF FINANCIAL OFFICER  
MARCH 11, 2019

# Forward-Looking Statements

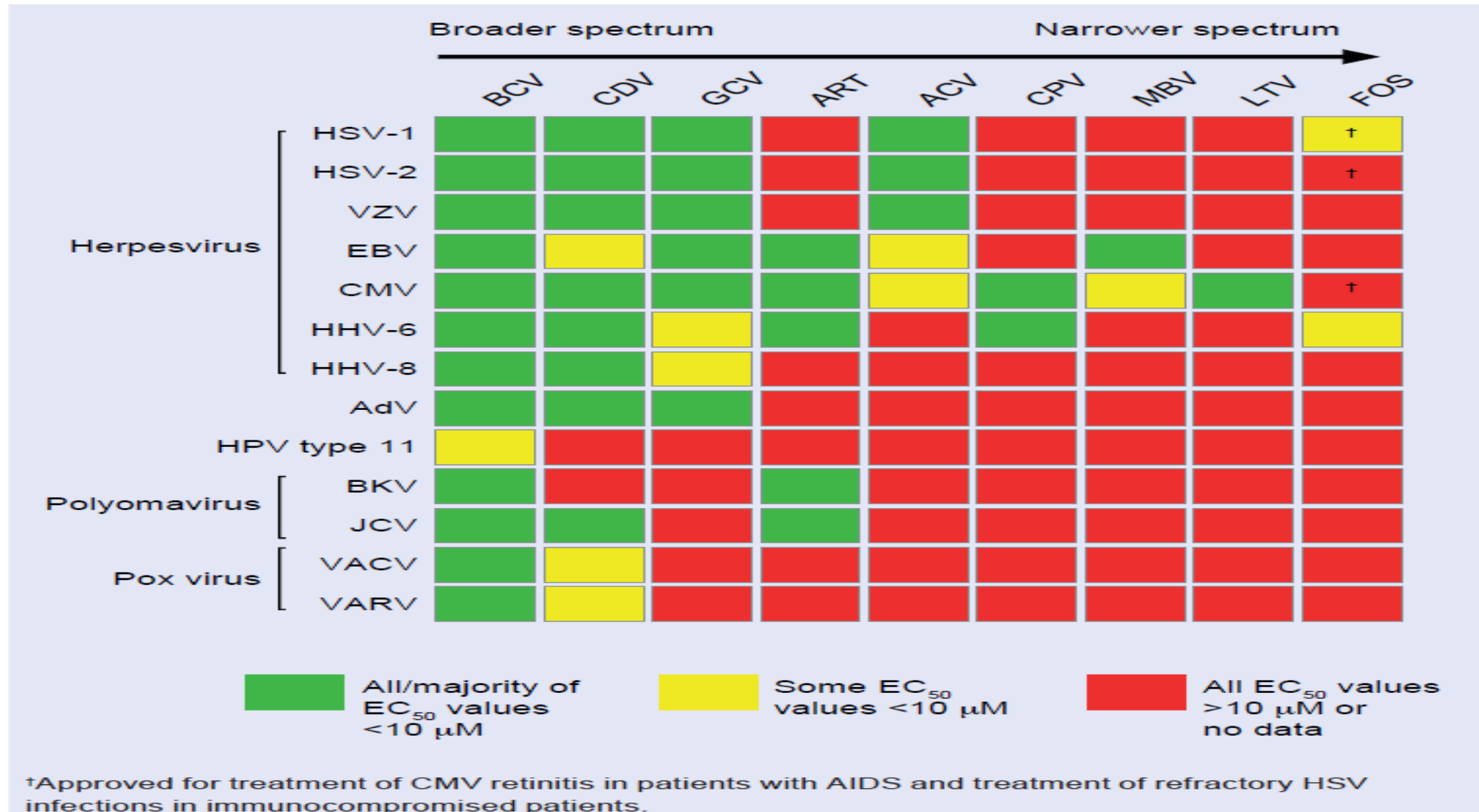
*These slides and the accompanying oral presentation contain forward-looking statements and information within the meaning of the Private Securities Litigation Reform Act of 1995 that are subject to risks, uncertainties and other factors, including the possibility that there may not be a viable continued development path for brincidofovir, that any clinical trials we may conduct will not demonstrate adequate efficacy and safety of brincidofovir, that the FDA and other regulatory authorities may not approve brincidofovir or brincidofovir-based regimens, and that marketing approvals, if granted, may have significant limitations on their use. As a result, brincidofovir may never be successfully commercialized. In addition, Chimerix may be unable to file for regulatory approval for brincidofovir with other regulatory authorities. Similar risks and uncertainties apply to our development of CMX521. These risks, uncertainties and other factors could cause actual results to differ materially from those referred to in the forward-looking statements. The reader is cautioned not to rely on these forward-looking statements. These and other risks are described in detail in Chimerix's Annual Report on Form 10-K for the quarter ended December 31, 2018 and other documents subsequently filed with or furnished to the U.S. Securities and Exchange Commission. All forward-looking statements are based on information currently available to Chimerix, and Chimerix assumes no obligation to update any such forward-looking statements.*



# CMRX: Developing Solutions for Immunocompromised Patients

- **The Team:** Experienced and committed management team with proven track records developing first-in-class antivirals and first-in-indication commercial launches
- **The Molecule:** Brincidofovir (BCV, CMX001) remains the only broad-spectrum antiviral in advanced development
  - Demonstrated antiviral potency in 2000+ patients
  - Multiple formulations to prevent and treat acute and chronic viral infections
- **The Year:** Regulatory, Clinical and Financial Alignment
  - Emerging programs at FDA focusing on Expanded Access and Rare Diseases
  - Well capitalized, with \$186M at the end of 4Q 2018

# BCV Has Broad Spectrum Activity and High Potency: Results from a Systematic Literature Review



# Brincidofovir's Broad Spectrum of Activity Provides a Potential “Pipeline in a Product” with Patent Protection Through 2034

## ■ Oral BCV for Adenovirus:

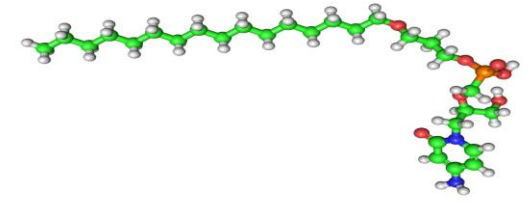
- ❖ potent antiviral activity retained across all AdV types
- ❖ rapid reduction in AdV viral load
- ❖ first prospectively randomized trial

## ■ Oral BCV for Smallpox: medical countermeasure for smallpox

- ❖ high barrier to resistance
- ❖ convenient once-weekly oral dosing
- ❖ demonstrated activity in multiple animal models and isolated orthopoxvirus cases (progressive vaccinia, monkeypox, cowpox infections)

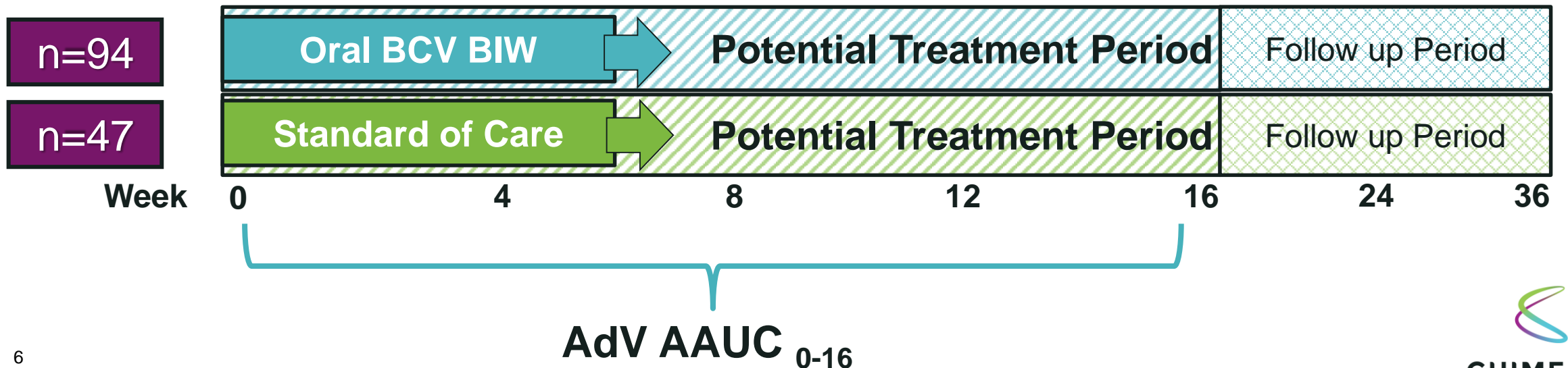
## ■ IV BCV for BK, JCV, HHV6 and other CNS viral infections:

- ❖ improved safety and tolerability after four doses
- ❖ improves delivery to the CNS in animal studies
- ❖ allows for dose-ranging to determine activity for additional pathogenic viruses

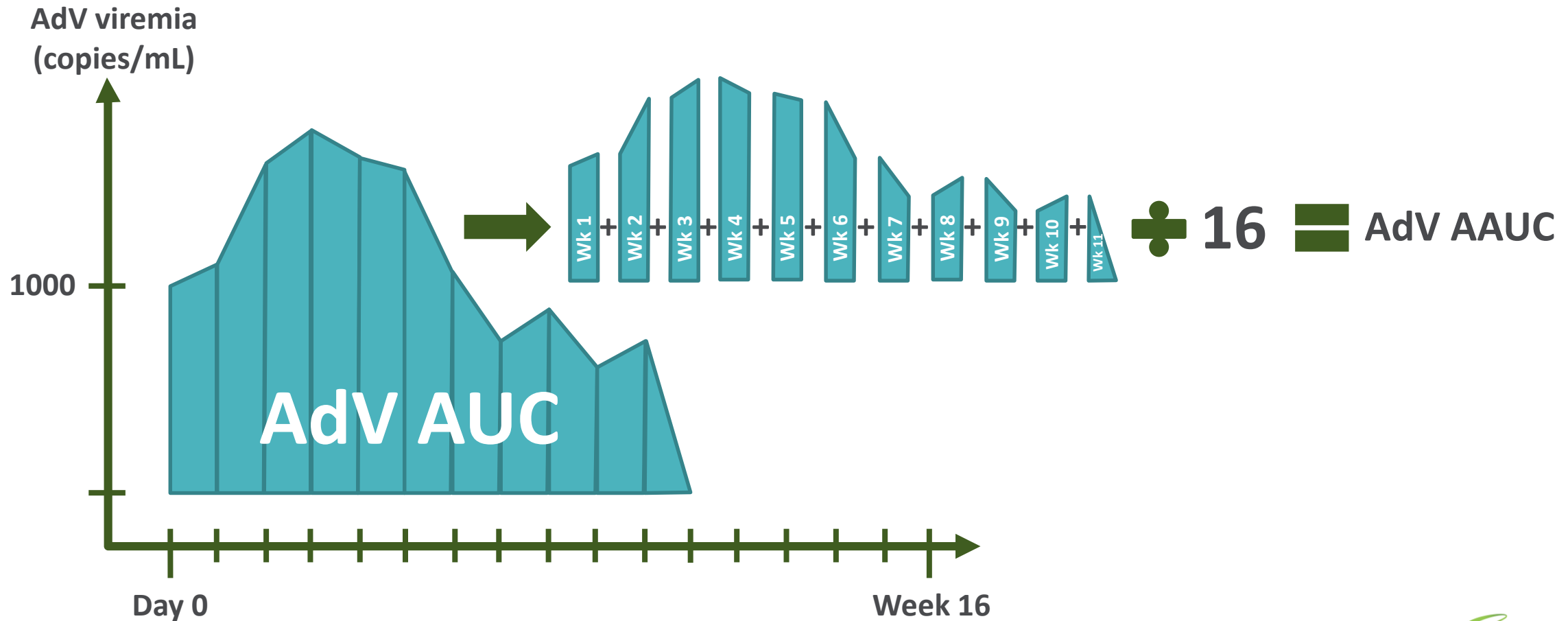


# AdAPT: Adenovirus after Allogeneic Pediatric Transplantation

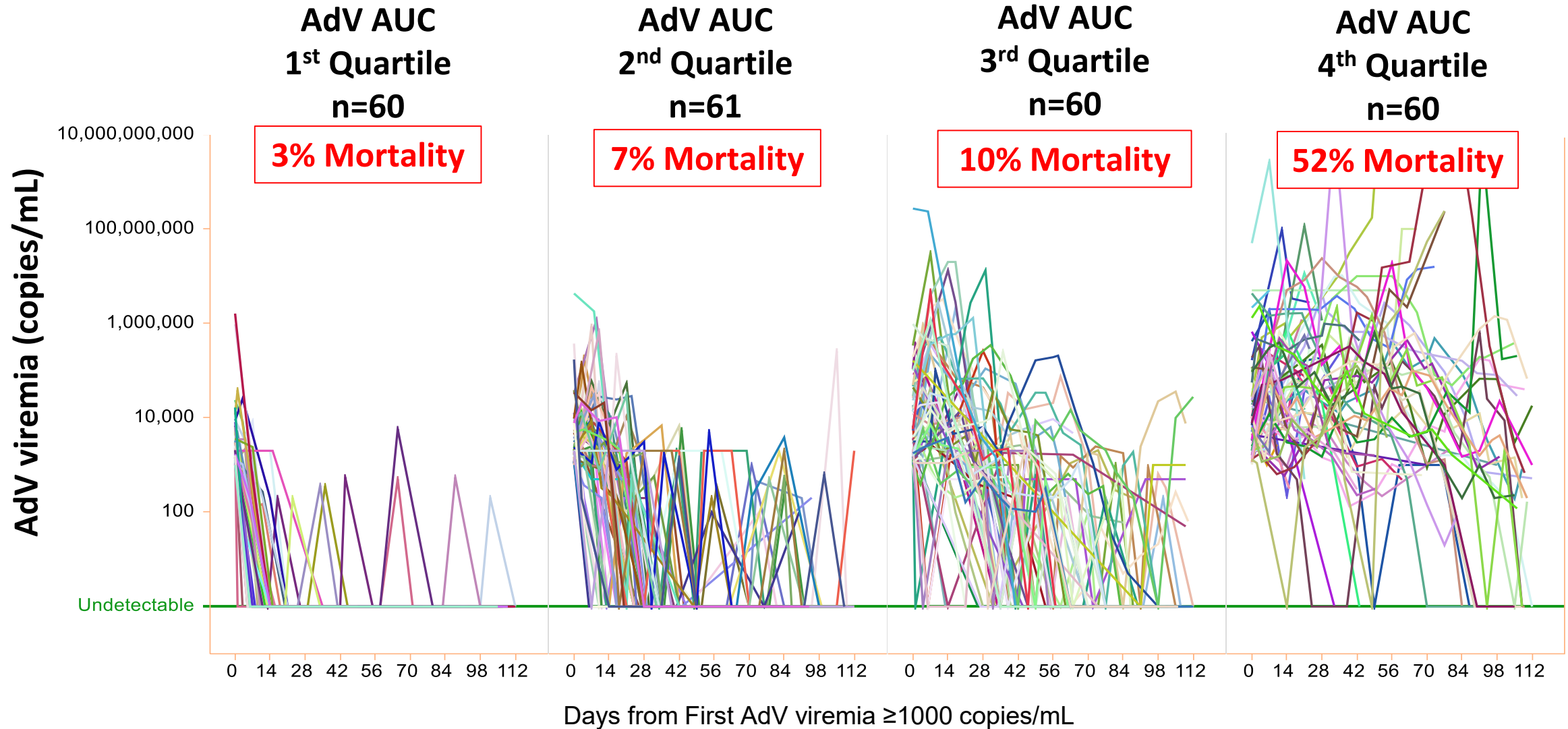
- **Open label, comparative study of oral BCV vs. standard of care (SoC) in AdV viremia**
  - Pediatric T-cell depleted allo-HCT recipients in 1<sup>st</sup> 100 days of HCT with AdV  $\geq 1000$  copies/mL
- **Short course therapy: “Treat-to-clear” paradigm**
  - BCV (or SoC) administered until AdV is cleared from plasma
- **Primary endpoint: AdV Average Area Under the Curve over 16 weeks (AdV AAUC<sub>0-16</sub>)**
  - Powered to detect 0.6 log<sub>10</sub> difference in AdV AAUC<sub>0-16</sub>
- **Small study: N=141 (2:1 randomization)**



# Calculating AdV Average Viral Burden = AdV AAUC<sub>0-16</sub>



# Higher AdV AUC<sub>0-16</sub> Correlates with Higher Mortality

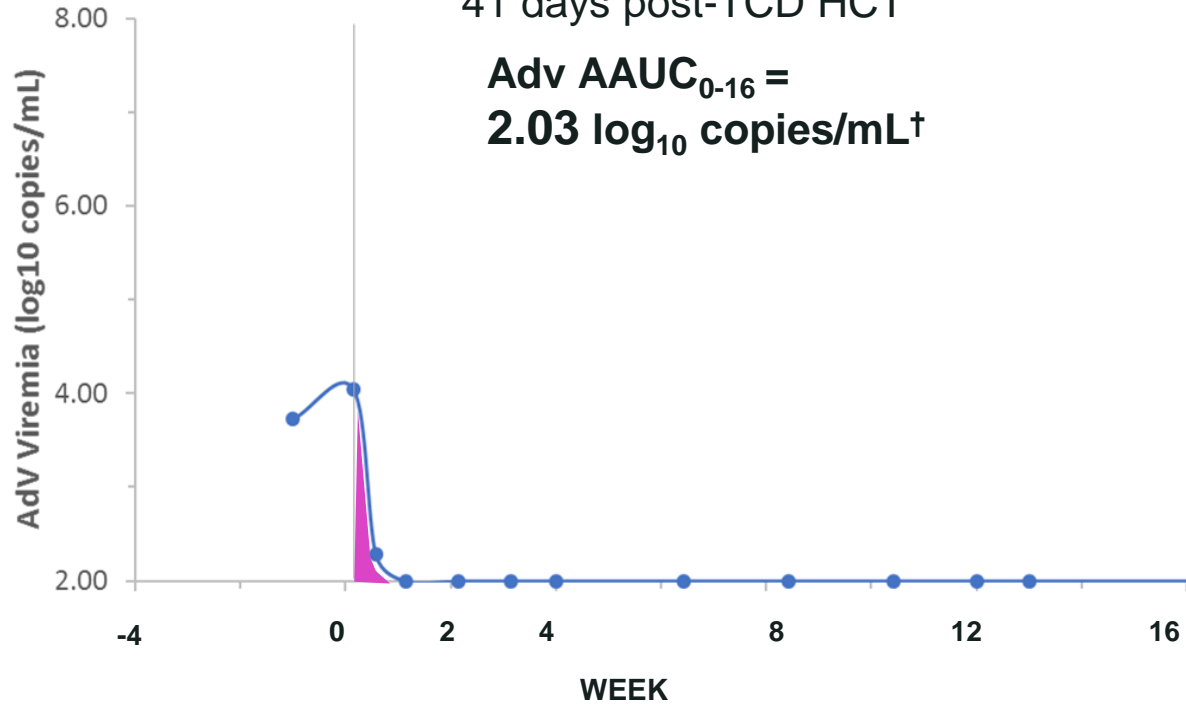




# AdAPT Is Designed for Success

**Oral BCV from Advise**  
 3 yr old pt  
 41 days post-TCD HCT

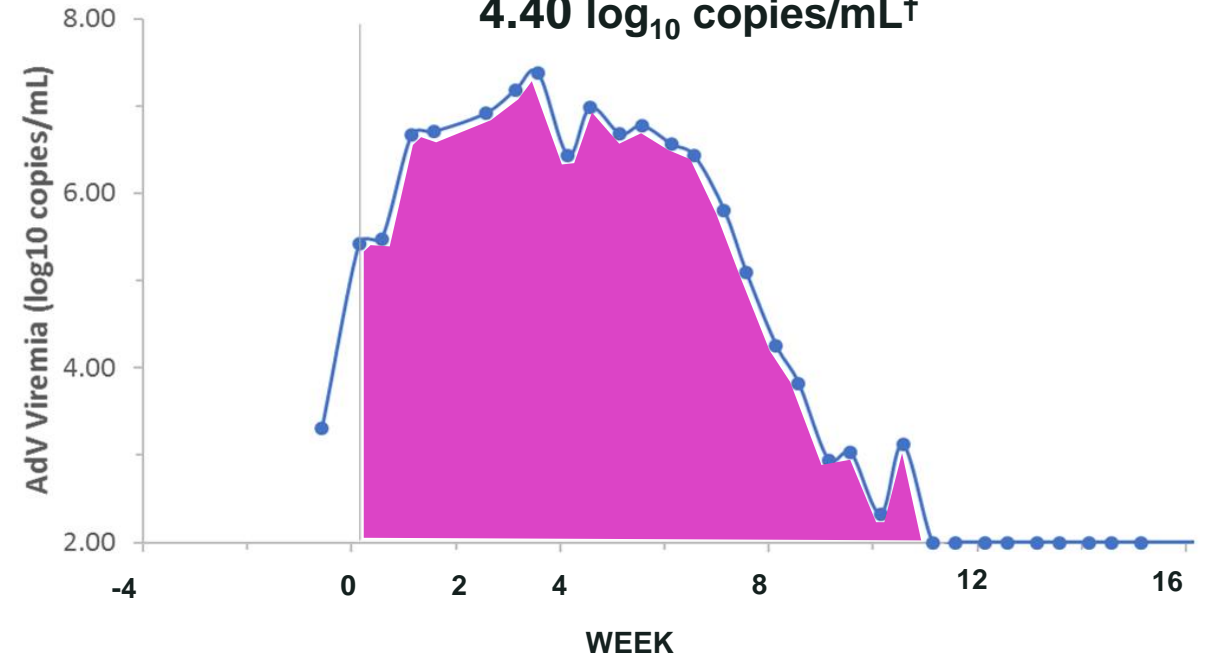
**Adv AAUC<sub>0-16</sub> =**  
**2.03 log<sub>10</sub> copies/mL†**



**Local Standard of Care (SoC)**  
**from Advance\***

2 yr old pt  
 19 days post-HCT

**Adv AAUC<sub>0-16</sub> =**  
**4.40 log<sub>10</sub> copies/mL†**



**[AdV AAUC for local SOC] – [AdV AAUC with BCV] = potential difference in AdAPT**  
**[4.40] – [2.03] = 2.37 log<sub>10</sub>**

\*Local standard-of-care may include reduction of immunosuppressants or off-label IV cidofovir

† Lower limit of detection: 2 log<sub>10</sub> copies/mL



# Maximizing the Probability of Success for AdAPT

- Study design incorporates key learnings for oral brincidofovir:
  - Includes highest risk patients: pediatric recipients of T-cell depleted HCT prior to immune reconstitution
  - Short-course oral BCV therapy begun as soon as feasible following first reading  $>1000$  copies/mL
    - Rapidly clears virus
    - Minimizes side effects
  - Primary endpoint is AdV burden over time, the most sensitive measure to differentiate the antiviral effect of oral BCV from SoC
  - $>90\%$  power to show superiority of brincidofovir over available SoC
  - Open-label study – randomized but not blinded
- Study sites are experienced with BCV, prospectively monitor for AdV and have expertise in treating AdV infections in high-risk patient populations

# Status of FDA Discussions on AdAPT

- Type C Meeting Requested to review data supporting use of AdV AAUC as a surrogate marker
  - AdVance data and other independent studies demonstrate AdV AAUC correlation with mortality
  - Briefing Package submitted to FDA in late February
  - FDA response received on March 7 indicating plans to invite CMRX to participate in public workshop on the development of antivirals for the treatment of AdV infection in immunocompromised patients
  - Proposed meeting is targeted for late summer and would provide an opportunity to discuss virologic endpoints with the FDA and scientific community; FDA indicated that specific discussion of AdAPT would be more appropriate when results of AdAPT are available
- Leveraging Real-World Treatment Experience from Expanded Access Protocols
  - At the Nov 2018 Workshop on Expanded Access by Reagan-Udall Foundation, FDA expressed willingness to review expanded access data with hard endpoints such as survival and hospitalizations; cited need to obtain and evaluate all data in rare diseases
  - Currently Expanded Access protocol (Study 351) in US and NPP program in Europe provide oral brincidofovir for adenovirus infection

# Adenovirus Increasingly Recognized in Community Outbreaks

- Highly pathogenic strains of AdV have been reported in otherwise healthy adults and children
- Relatively immunocompromised patients may be at increased risk of fatal outcomes
- Extrapolation from viral panels and known community pneumonia epidemiology indicates ~12,000 cases of adenovirus annually in the US

THE BALTIMORE SUN

MONDAY DEC. 17, 2018

## Five more adenovirus cases confirmed at University of Maryland, bringing total to 35



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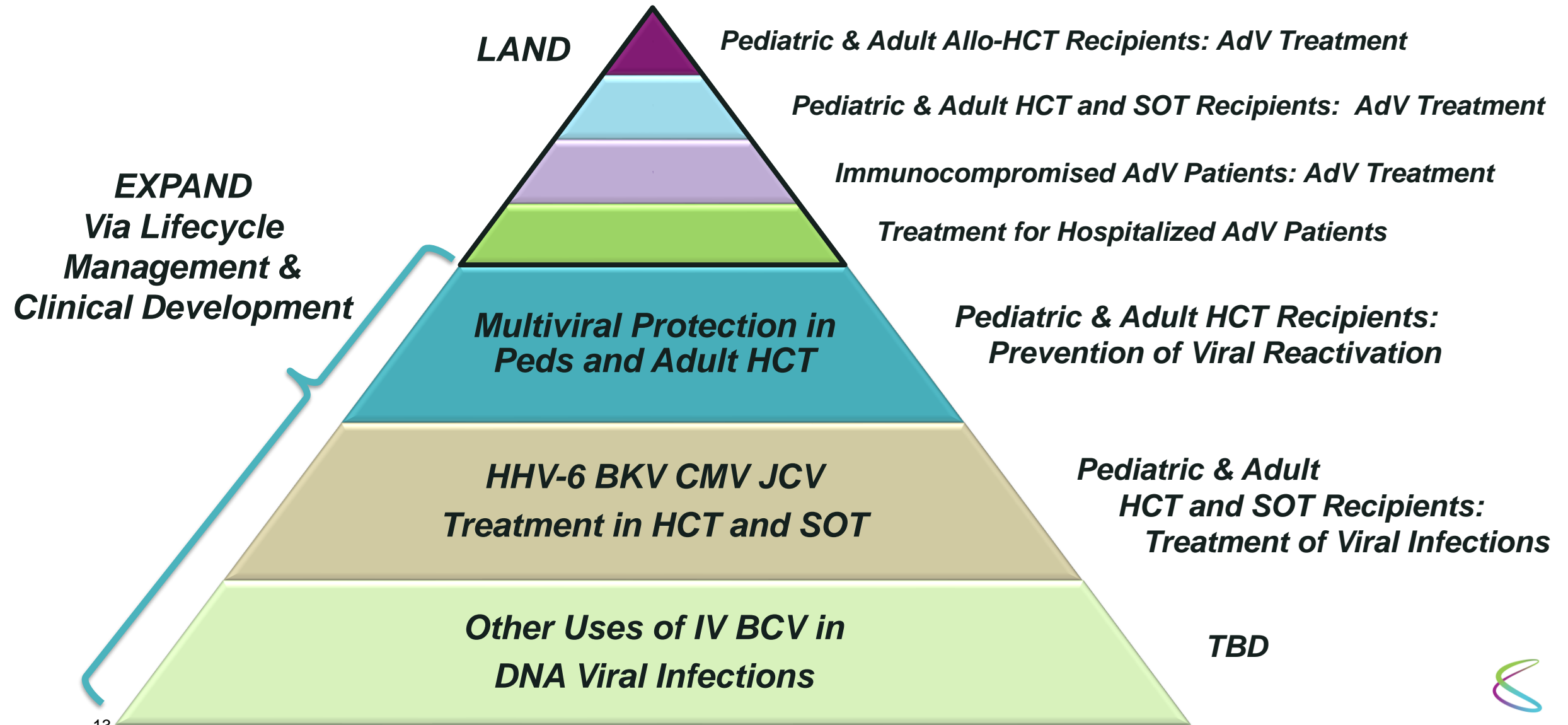


30 sickened in adenovirus outbreak in New Jersey, including 10 children who have died

By Michael Nedelman, CNN

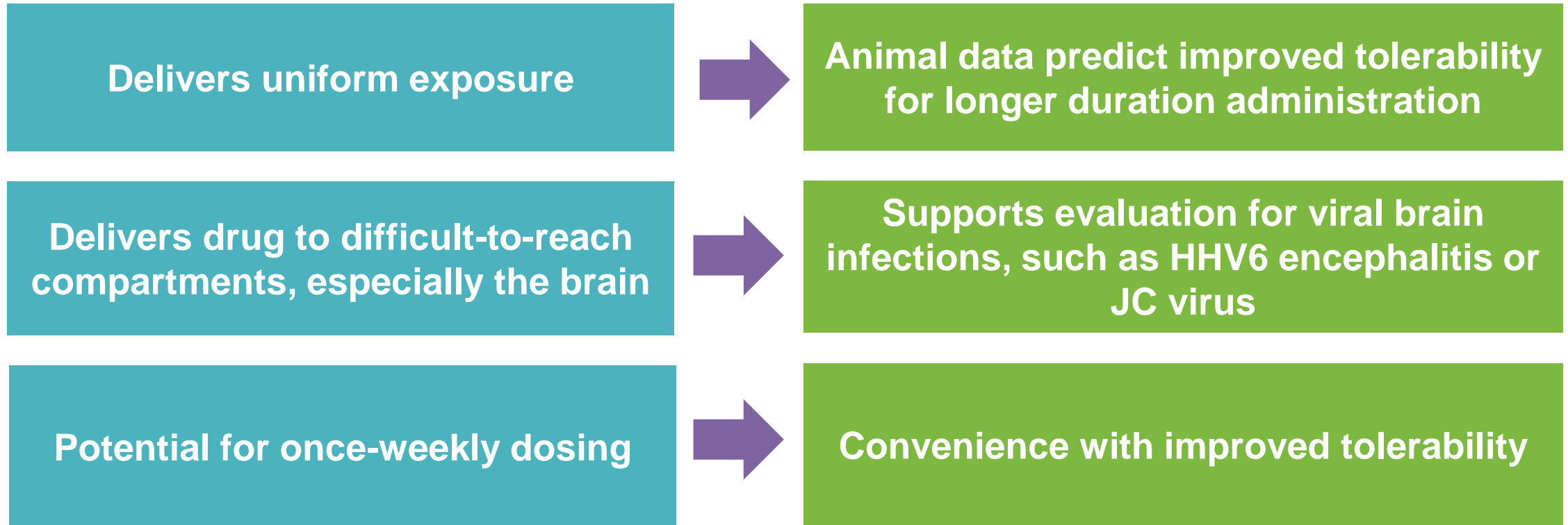


# Building Value for Oral and IV Brincidofovir: “Land and Expand”



# IV BCV: Fulfilling the Potential for Prevention and Treatment

Early development work shows great promise for IV BCV

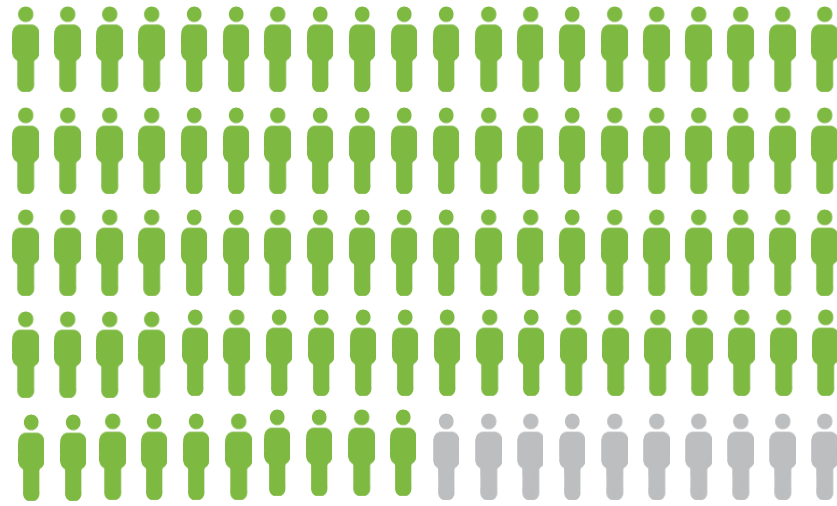


# IV BCV: Multiple Dose Study Demonstrates Improved Tolerability

- IV BCV x 4 doses in healthy adult subjects (Multiple Ascending Dose study)
  - Confirmed IV BCV 10 mg achieves exposure of oral BCV 100 mg
  - No diarrhea at 10 mg twice weekly
  - No dose-limiting clinical adverse events
- Phase 2 patient studies initiating in the US, UK and Europe
  - Studies 210/211: BCV drug levels and safety/tolerability of multiple doses in adult HCT recipients; assess AdV viral decay curves (secondary endpoint)



# IV BCV for Prevention: High Risk of Disease or Death from New or Reactivated Viruses in Stem Cell Transplant Recipients



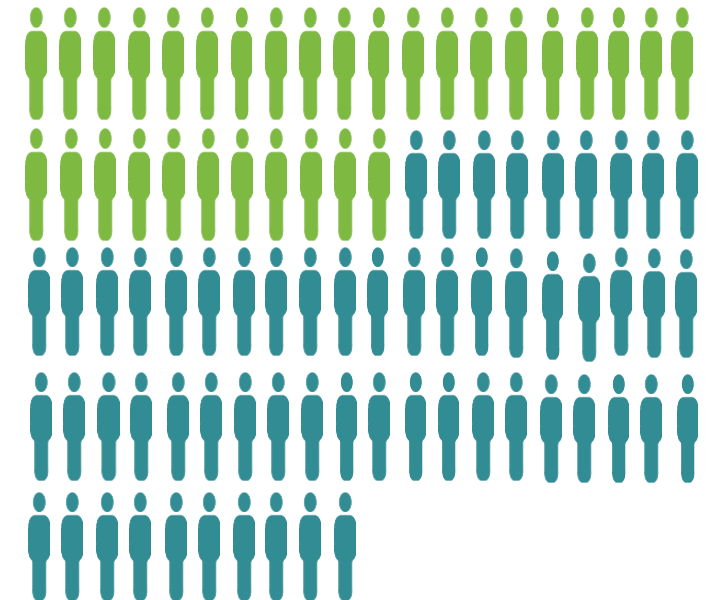
At least one DNA Virus in  
363/404=

**90%**

2/3 have two or  
more DNA viruses

**66%**

1 in 3  
HCT recipients had  $\geq 3$   
DNA viral infections  
detected





# Oral and IV BCV May Address Growing Opportunities to Address Viral Infections in Stem Cell and Solid Organ Transplantation



TRANSPLANTS PER YEAR (population)	US (320M)	EU (550M)	Japan (130M)	ROW	Total
<b>HCT</b>					
Allogeneic	8,700	16,400	3,700	6,454	35,254
Autologous	15,000	21,700	1,800	4,715	43,215
<b>HCT TOTALS</b>	<b>23,700</b>	<b>38,100</b>	<b>5,500</b>	<b>11,169</b>	<b>78,469</b>
<b>SOT</b>					
Kidney	19,860	20,000	1,648	39,052	80,560
Liver	7,800	7,400	438	10,062	25,700
Other SOT	5,940	4,500	124	1,276	11,840
<b>SOT TOTALS</b>	<b>33,600</b>	<b>31,900</b>	<b>2,210</b>	<b>50,390</b>	<b>118,100</b>
<b>TOTAL TRANSPLANT</b>	<b>57,300</b>	<b>70,000</b>	<b>7,710</b>	<b>61,559</b>	<b>196,569</b>

US HCT: 2015 figures from CIBMTR. Auto-HCT are increased by 20% to account for under-reporting to CIBMTR. US SOT: 2016 figures from Organ Procurement and Transplantation Network (OPTN)

EU HCT: JR Passweg, et al., HCT in Europe 2014, nature.com/bmt, 2016. ROW HCT: 2013 figures from EBMT Activity Office (Bone Marrow Transplantation 2015 (50);476-482)

Japan: Clarivate Japan assessment (HCT for 2015; Kidney/Liver for 2016; Other SOT for 2015)



# BCV for Smallpox: Nearing Completion of Animal Studies Under Development with BARDA

- Oral BCV has demonstrated substantial survival benefit in two animal models of fatal orthopoxvirus infections:
  1. **Rabbitpox** virus model: Two studies completed with 100% survival demonstrated in animals that received treatment with brincidofovir immediately after the onset of fever (study 1), or 3 days after infection with the virus (study 2). Results from these studies will be submitted to FDA in support of the efficacy of brincidofovir under the animal efficacy rule.
  2. **Mousepox** / ectromelia replicates respiratory infection route of human smallpox infection. Pivotal mousepox study started in early 2019.
- Regulatory submissions in US and Europe planned for 2020
- Stockpiling opportunities are being pursued in the US via BARDA, and following regulatory approval in Europe/ROW

## Second Rabbitpox Study Shows Significant Survival Advantage in Animals Treated with BCV

	BCV treatment 3 days post-infection	BCV treatment 4 days post-infection	BCV treatment 5 days post-infection	BCV treatment 6 days post-infection	No treatment (placebo)
Overall Survival	29/29 (100%)	26/29 (90%)	20/29 (69%)	20/29 (69%)	8/28 (29%)
P-value vs. Placebo	<0.0001	<0.0001	0.0014	0.0014	-

- The study was designed to determine the effect of administering BCV to animals at certain times (3, 4, 5 or 6 days) after inoculation with the rabbitpox virus

# CMRX: Four Active Clinical Programs in 2019

Program	Indication	Pre-clinical	Phase 1	Phase 2	Phase 3	Status
Short-course Oral BCV	AdV Treatment					AdAPT enrolling
	Smallpox Treatment					Animal Rule Pivotal Studies Progressing
IV BCV	Other Viral Indications					Ph 2 trials initiated

- Brincidofovir represents a high-probability of success small molecule with multiple shots-on-goal for marketing approvals in the US and Europe
- Chimerix remains well-capitalized with \$186M at the end of 4Q2018