



# **CHIMERIX**

**JP MORGAN  
HEALTHCARE CONFERENCE**

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JANUARY 10, 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 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.*

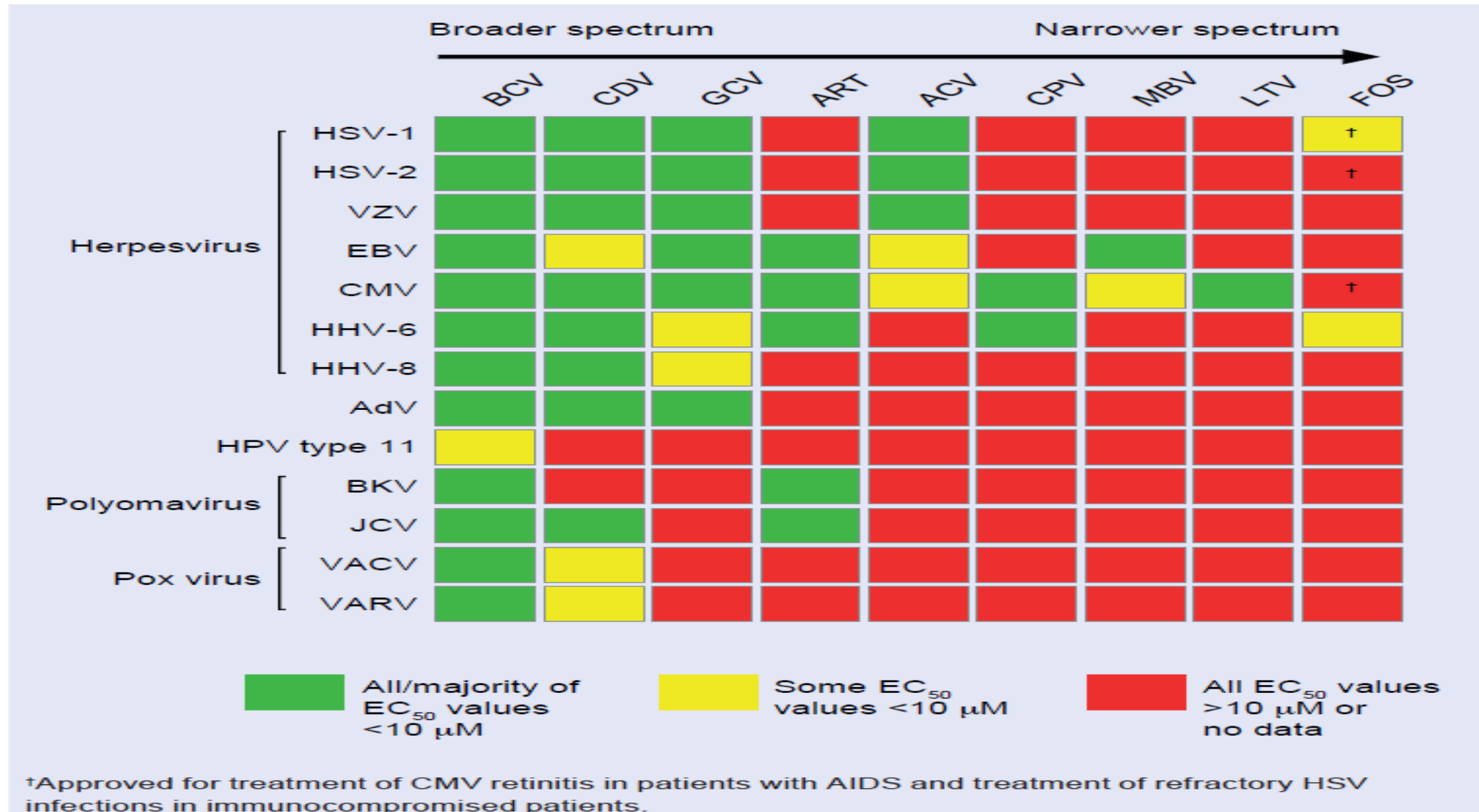


# CMRX: Developing Solutions for Immunocompromised Patients

- **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
  - Data anticipated from oral programs in smallpox, IV programs in adenovirus and BKV
  - Capital to achieve planned milestones, with \$194M at the end of 3Q 2018



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



# BCV Has Been Used to Treat Multiple dsDNA Viral Infections

Viral Family	Virus	BCV	Clinical Efficacy Demonstrated in
Adenovirus	Adenovirus (AdV)	0.02	1500+ patients w AdV have received BCV
Polyoma	BK Virus (BKV)	0.13	New data in animal model confirms BCV activity <sup>1</sup> , Ph 2 study in kidney transplant recipients planned for 2019
	JC Virus (JCV)	0.045	Oral BCV has been used in ~36 pts with PML or JC viremia IV BCV achieves higher CNS penetration
Papilloma	Human Papillomavirus (HPV)	17	BCV used in patients in expanded access trials
Herpes Viruses	Herpes Simplex Virus 1	0.01	BCV cleared acyclovir-resistant HSV-1 after HCT <sup>2</sup>
	Herpes Simplex Virus 2	0.02	BCV cleared acyclovir-resistant HSV-2 after HCT <sup>3</sup>
	Varicella Zoster Virus (VZV, HHV3)	0.0004	BCV demonstrated to prevent shingles post HCT <sup>4</sup>
	Epstein-Barr Virus (EBV, HHV4)	0.03	Anecdotal use in post-HCT viremia and disease
	Cytomegalovirus (CMV, HHV5)	0.001	Antiviral activity demonstrated in Ph 2 <sup>5</sup> and Ph 3 <sup>6</sup> trials
	Human Herpesvirus 6	0.003	Prevention of viremia and disease in subset analysis of Ph 3 HCT
Pox	Human Herpesvirus 8	0.02	
	Variola	0.1	Ongoing pivotal animal studies in collaboration with BARDA
	Vaccinia	0.8	Disseminated vaccinia cleared with BCV treatment <sup>7</sup>

1. Naderer et al; Poster # SA-PO641 Kidney Week October 23-October 28, 2018, San Diego CA
2. Voight S et al. Transpl Infect Dis 2016;18:791–794
3. El-Haddad D et al. Antiviral Res. 2016;134:58-62.
4. Lee YJ et al. Transpl Infect Dis. 2018 Dec;20(6):e12977

5. Marty FM et al, NEJM 2013; doi: 10.1056/NEJMoa1303688
6. Marty FM et al. Biol Blood Marrow Transplant 2018; doi: 10.1016/j.bbmt.2018.09.038
7. Lederman E et al. J Infect Dis. 2012;206:1372-85.



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

## ■ Oral BCV for Adenovirus:

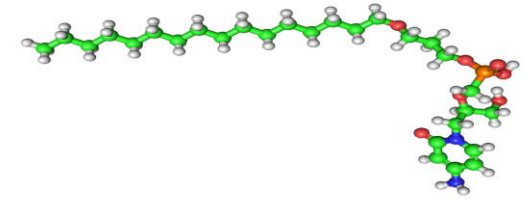
- ❖ potent antiviral activity retained across all AdV types
- ❖ rapid reduction in AdV viral load
- ❖ first prospectively randomized trial expected to complete enrollment in 2019

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

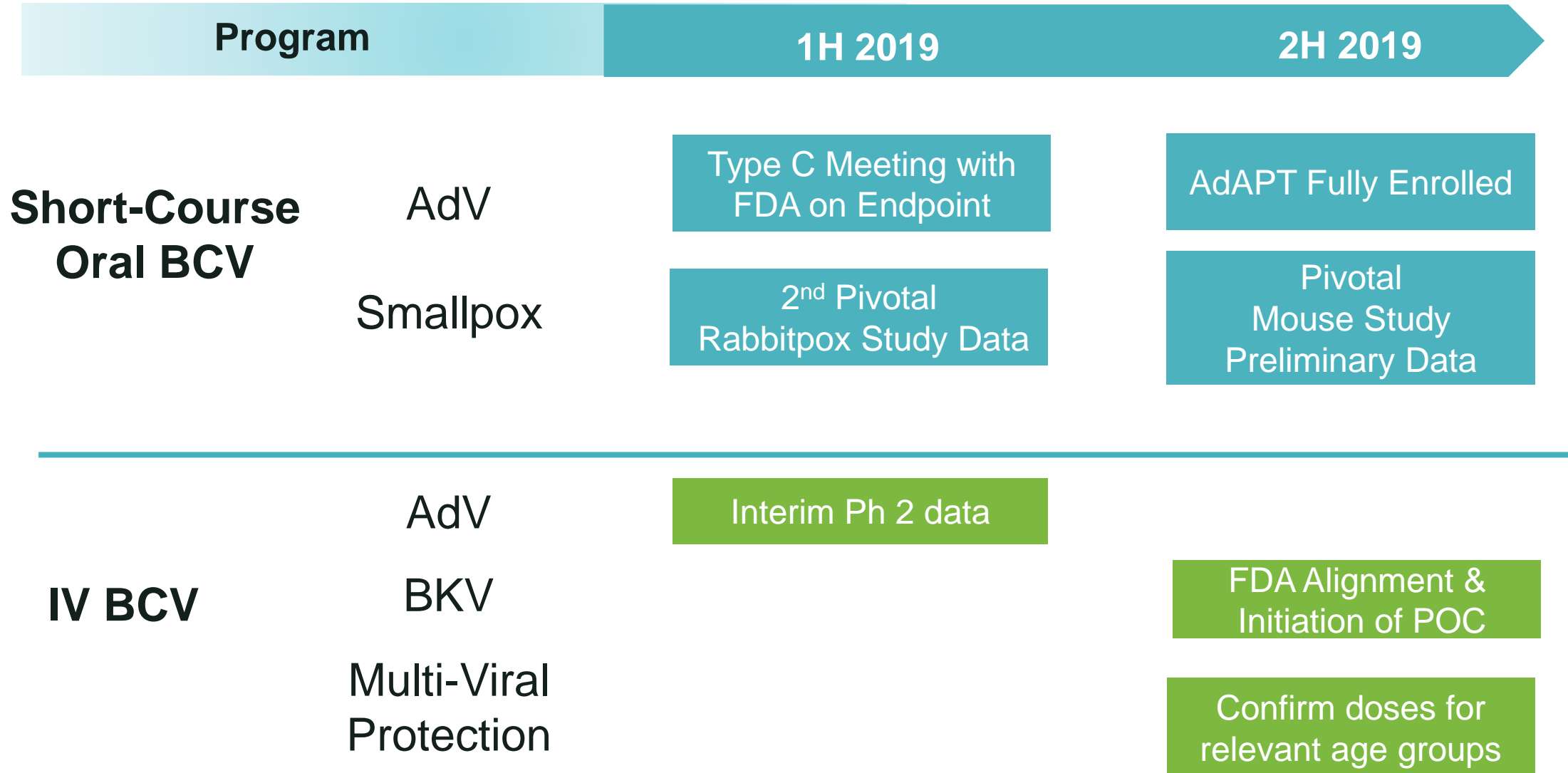
- ❖ high barrier to resistance
- ❖ convenient once-weekly oral dosing
- ❖ demonstrated activity in multiple animal models and isolated orthopoxvirus cases (progressive vaccinia, monkeypox, cowpox infections)

## ■ 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

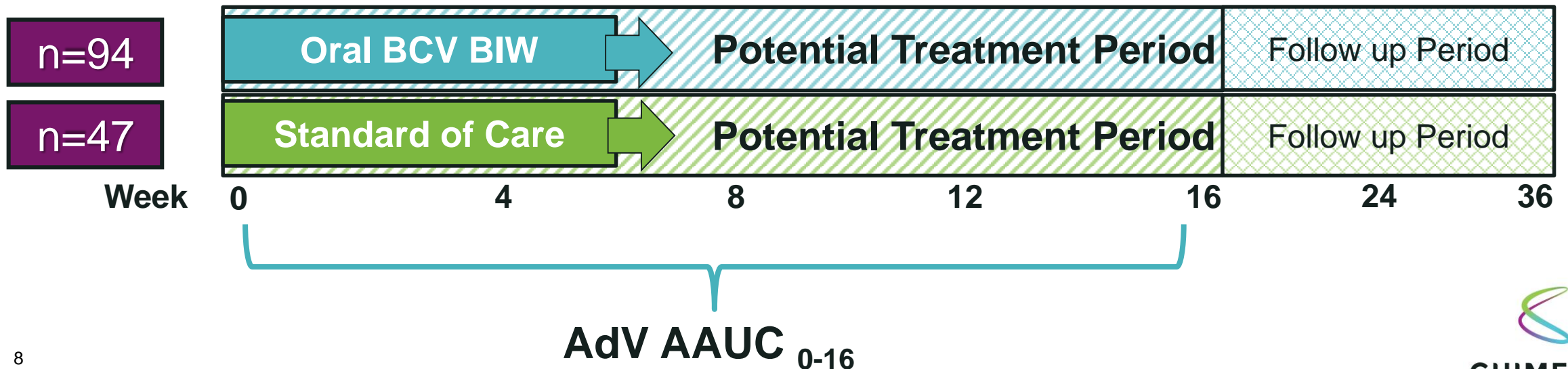


# Multiple Milestones Anticipated in 2019



# AdAPT: Adenovirus after Allogeneic Pediatric Transplantation

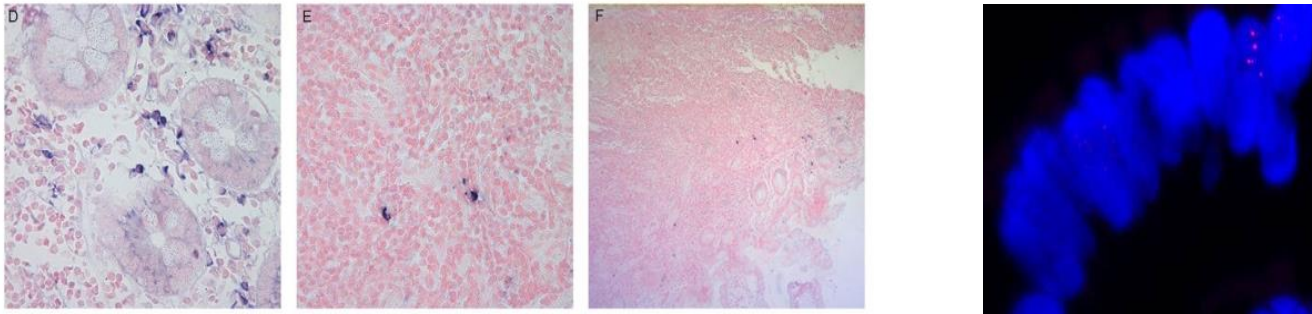
- **Open label, comparative study of oral BCV vs. standard of care (SoC) in AdV viremia**
  - Pediatric T-cell depleted allo-HCT recipients in 1<sup>st</sup> 100 days of HCT with AdV  $\geq 1000$  copies/mL
- **Short course therapy: “Treat-to-clear” paradigm**
  - BCV (or SoC) administered until AdV 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)**





# AdV Persists in the Gut of Children..... and Reactivates from the Gut after Transplant

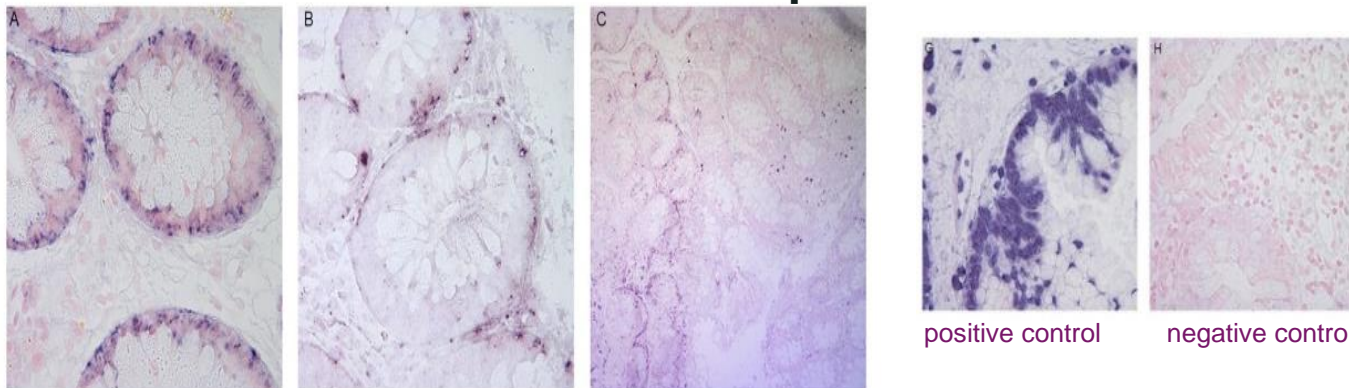
## Persistent AdV in gut of immunocompetent children



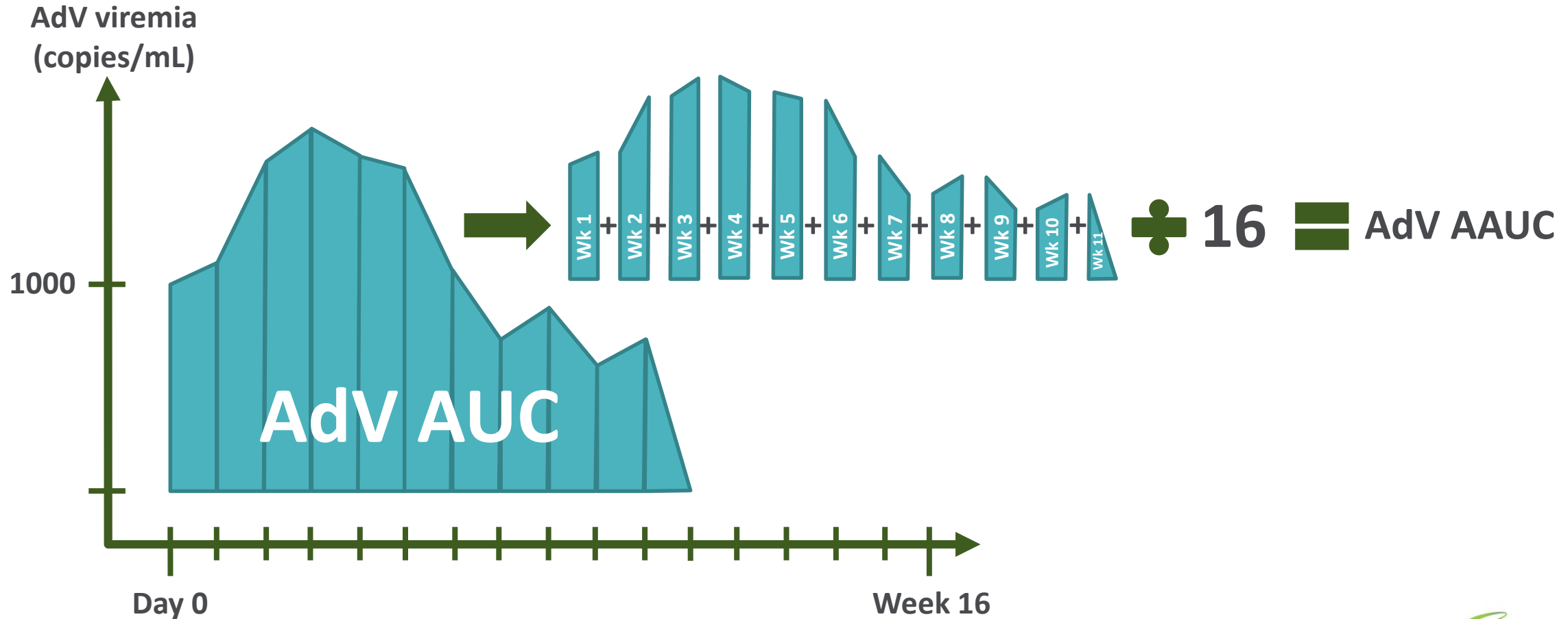
***Oral BCV provides targeted therapy for AdV after pediatric HCT:***

- Delivers drug to gut (source of viral replication in pediatric HCT patients)
- 100-fold greater potency vs. IV CDV

## Reactivated AdV post HCT



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



# AdV AUC: Most Predictive Viral Measure for All-Cause Mortality

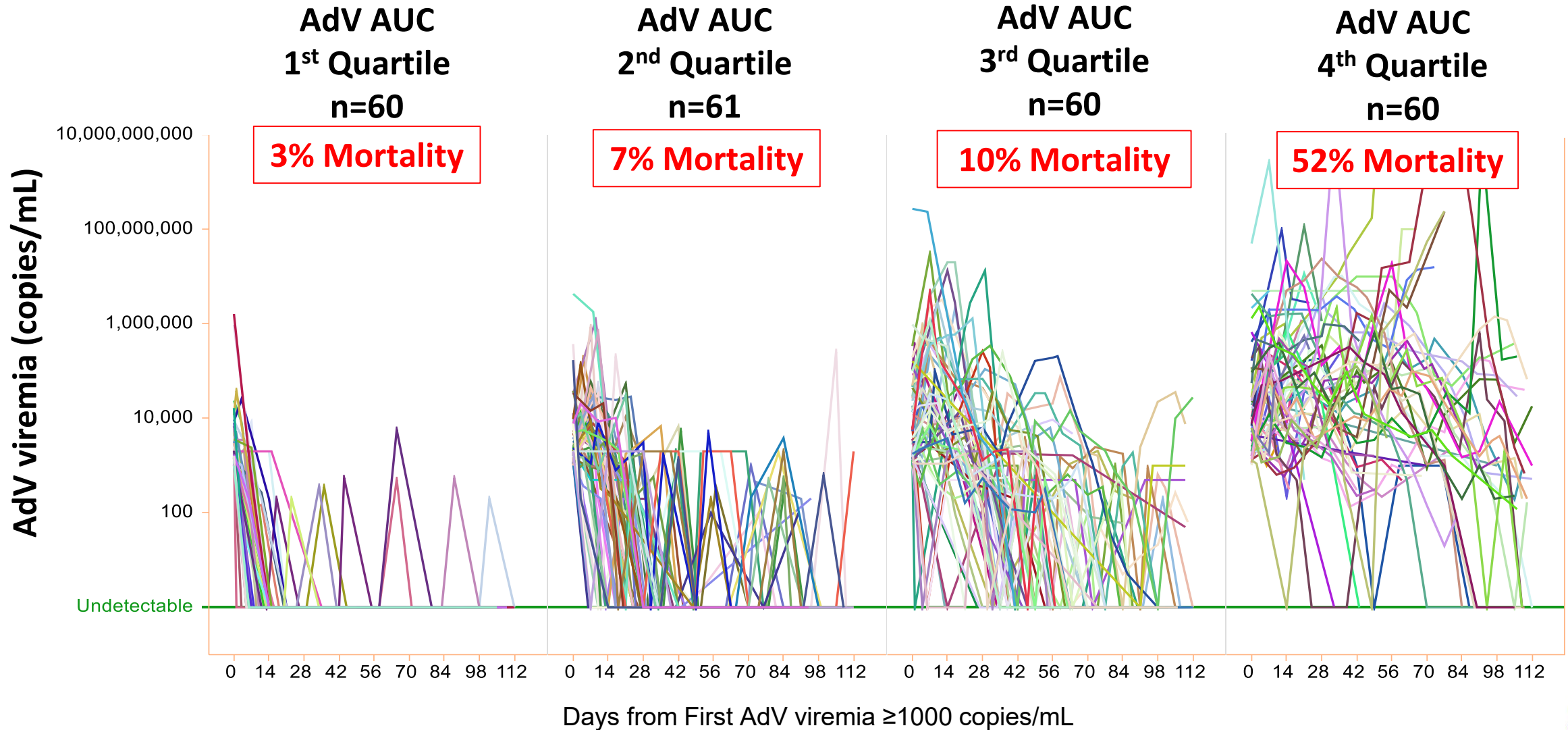
## *Each 1 log<sub>10</sub> Increase in AdV AUC Doubles Hazard for Mortality*

Viral Measurement (95% CI)		Peak AdV viremia	Days AdV viremia <1000 c/mL	Days with undetectable AdV viremia	2-week change in AdV viremia	AdV viremia over time	AdV AAUC
<b>Hazard for all-cause mortality</b>		<b>1.31</b> (1.13 - 1.53)	<b>0.96</b> (0.95 - 0.97)	<b>0.96</b> (0.95 - 0.97)	<b>1.24</b> (1.04 - 1.47)	<b>1.37</b> (1.22 - 1.55)	<b>1.91</b> (1.57 - 2.32)
Lymphocyte count	≥ 900	1.00	1.00	1.00	1.00	1.00	1.00
	300-899	1.88 (0.47 - 7.53)	1.82 (0.45 - 7.35)	1.71 (0.43 - 6.89)	1.80 (0.45 - 7.18)	1.64 (0.41 - 6.50)	2.19 (0.54 - 8.86)
	<300	7.81 (2.22 - 27.46)	5.20 (1.48 - 18.32)	5.09 (1.44 - 17.96)	7.97 (2.27 - 27.95)	4.87 (1.35 - 17.52)	6.82 (1.92 - 24.22)
Renal replacement therapy	No	1.00	1.00	1.00	1.00	1.00	1.00
	Yes	13.10 (5.54 - 30.97)	5.09 (1.85 - 14.02)	6.12 (2.21 - 16.98)	14.56 (6.30 - 33.67)	6.90 (2.74 - 17.39)	5.91 (2.38 - 14.72)
AdV disease	No	1.00			1.00		
	Yes	1.79 (0.92 - 3.48)			1.90 (1.00 - 3.63)		
Maximum GvHD stage	0					1.00	
	1,2					0.89 (0.34 - 2.33)	
	3,4					2.31 (1.08 - 4.92)	

- Associations were independent of lymphocyte immune reconstitution in all models

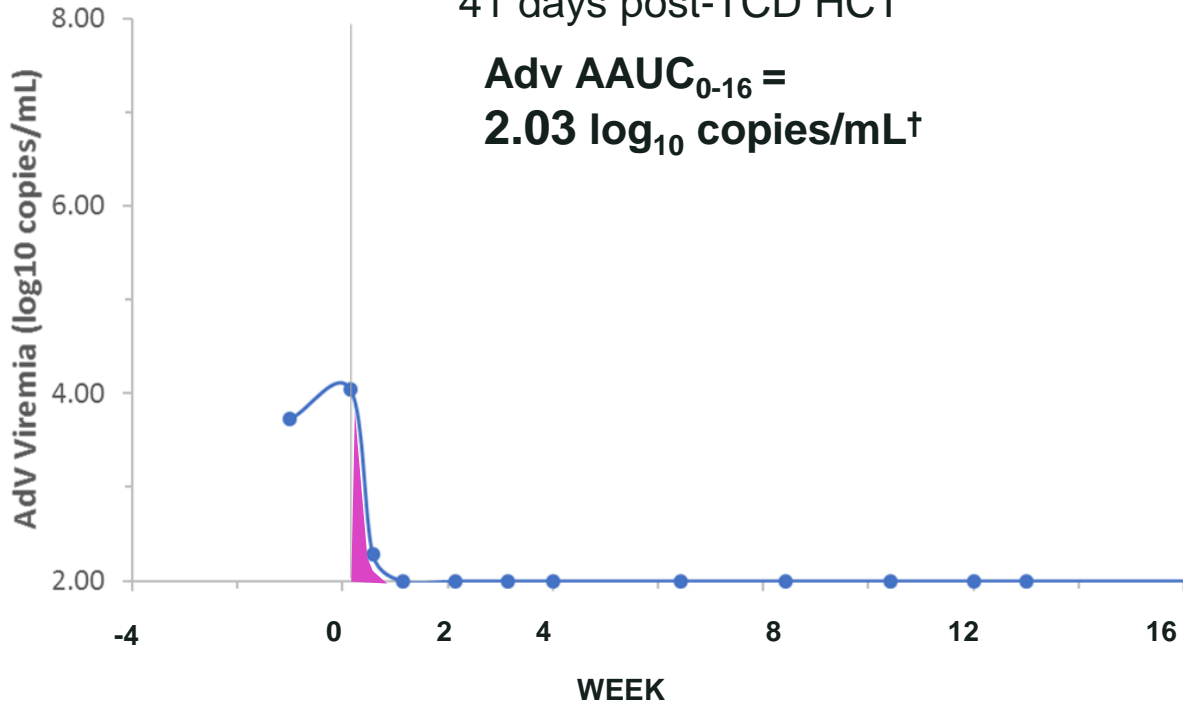


# Higher AdV AUC<sub>0-16</sub> Correlates with Higher Mortality

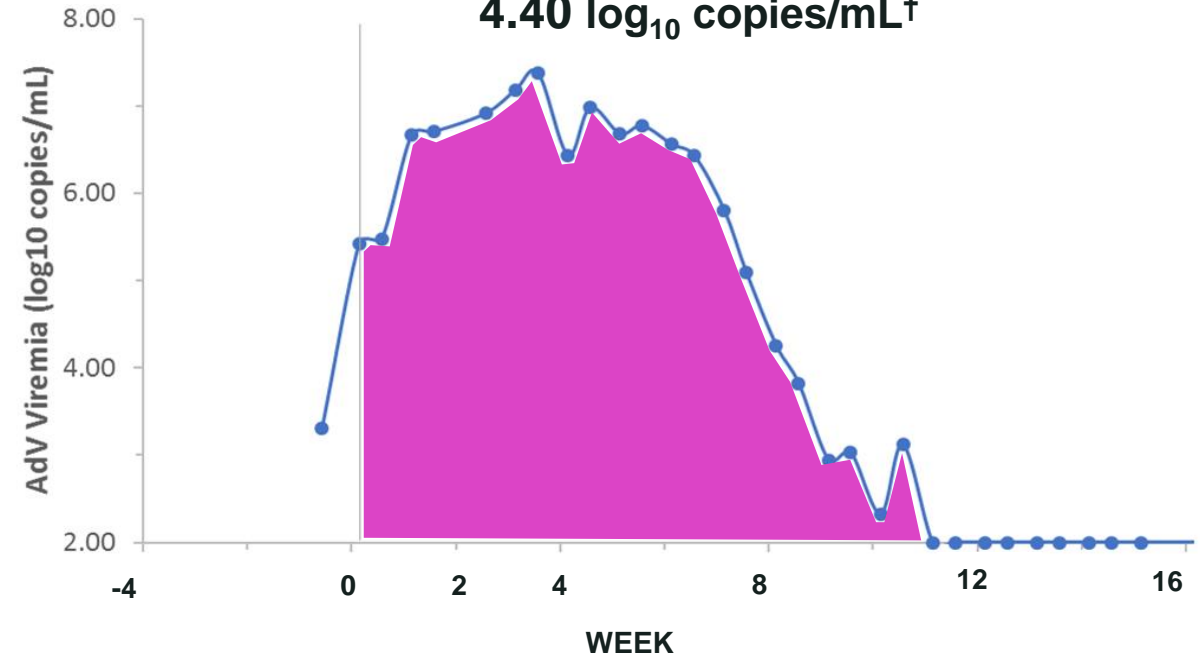


# AdAPT Is Designed for Success

**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>**



# 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 within the first three weeks of adenoviremia
    - 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

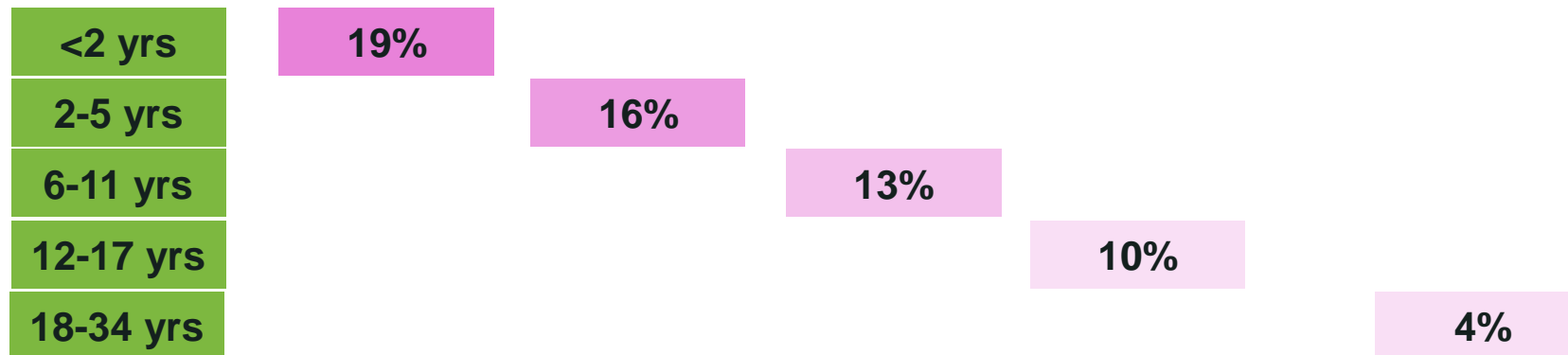
# Multiple Options for Discussing Surrogate Endpoint with FDA

FDA has publicly proposed new options for development:

- **Type C Meeting** to review data supporting use of AdV AAUC as a surrogate marker
  - Briefing Package will be submitted at the time of the meeting request
  - Following submission of the request, a meeting should be scheduled within 75 days
  - Data from AdVance and other independent studies confirm relevance of AUC over other virologic endpoints
- **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
  - Expanded access protocols can be considered for outbreak situations

# High Mortality in All Age Groups with Adenovirus After HCT

- AdVance collected data from 4000+ HCTs in Europe during 2013-2015
- Risk factors, timing, and outcomes from adenovirus infections in adult and pediatric transplant recipients were collected from de-identified chart reviews
  - Incidence of AdV post-HCT highest in children <2 yrs, and declined into early adulthood



- Measures of AdV viral load in blood were found to be highly predictive of survival: peak viral load, rate of increase in viral load, and persistence over time
  - Viral measure most correlated with mortality was AdV Area Under the Curve (AdV AAUC<sub>0-16</sub>)



# 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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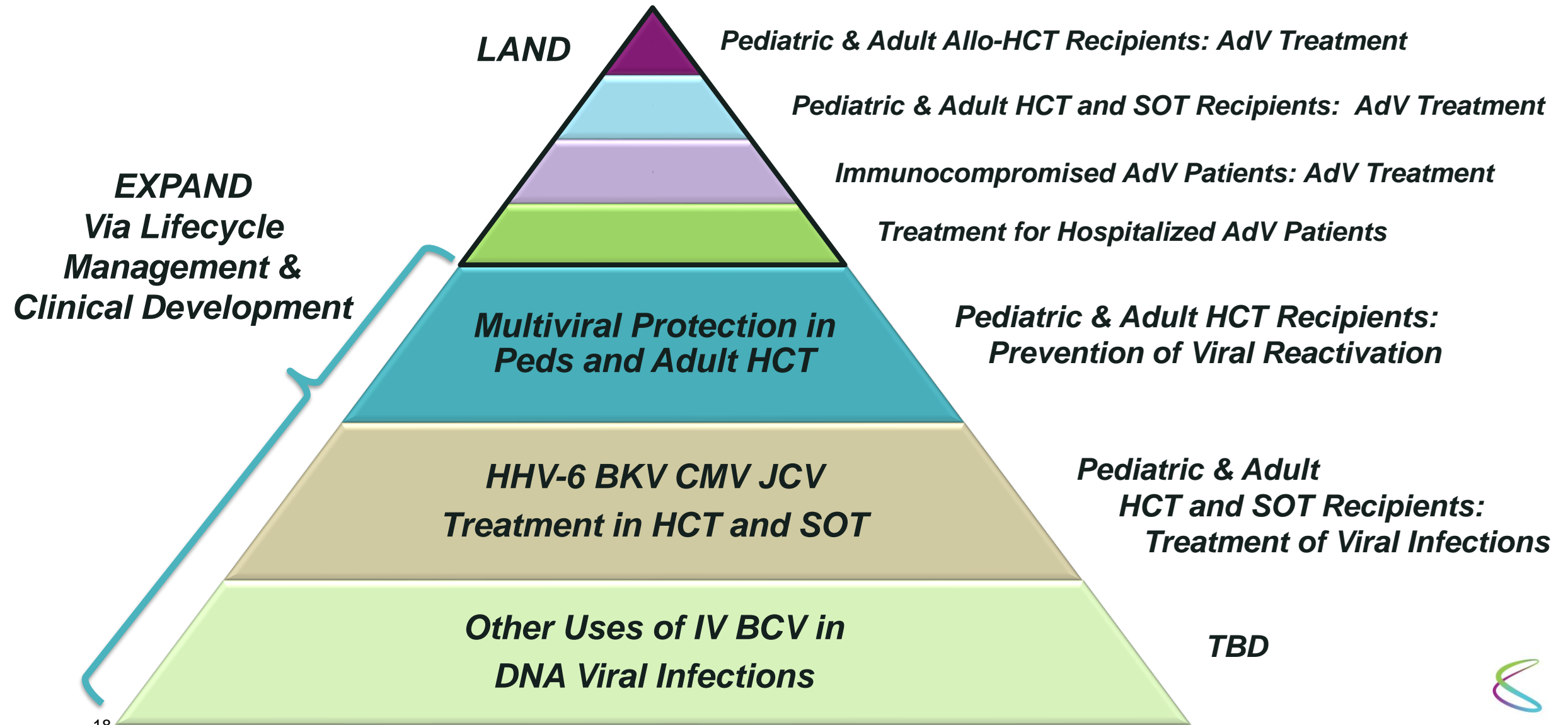


30 sickened in adenovirus outbreak in New Jersey, including 10 children who have died

By Michael Nedelman, CNN

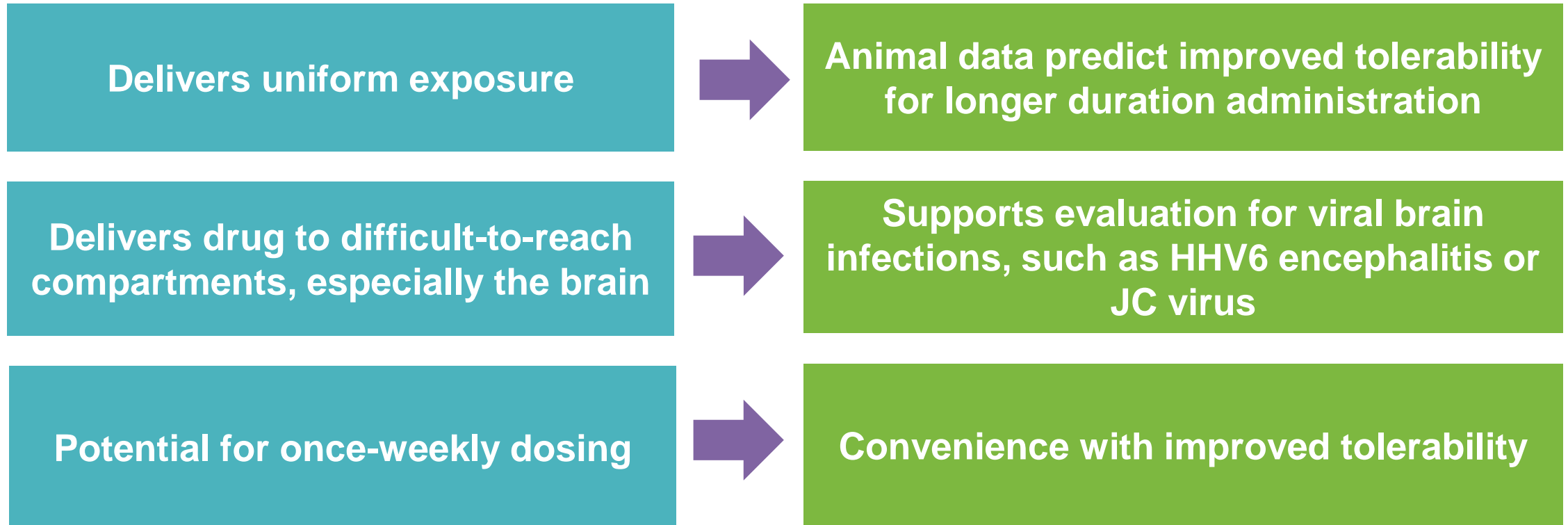


# Building Value for Oral and IV Brincidofovir: “Land and Expand”



# 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: Confirm AdV viral decay curves, BCV drug levels and safety/tolerability of multiple doses in adult HCT recipients; interim data expected in 2019
  - Proof-of-concept in the first study targeting polyomaviruses expected to initiate in 2019



## IV BCV Could Address Loss of Kidney Transplants Due To BKV

- ***In vitro***: BCV has low micromolar potency against BKV in epithelial cells<sup>1</sup>
- **Animal Model**: In a recently-described animal model of polyomaviruses, BCV resulted in a 100-fold reduction in viral load in the kidney<sup>2</sup>
  - Weekly administration showed comparable efficacy to daily administration, confirming efficacy is driven by CDV-PP
- **Clinical Data**:
  - In SUPPRESS, oral BCV reduced the rate of reactivation of BK during the relevant early weeks post-transplant (oral BCV vs placebo)<sup>3</sup>
  - Study 201, the Phase 2 study of oral BCV for CMV prevention, demonstrated improved renal function in patients who were on efficacious doses of oral BCV<sup>4</sup>

1. Tylden GD, et al. Antimicrob. Agents Chemother. doi:10.1128/AAC.00238-15  
2. Naderer et al; Poster # SA-PO641 Kidney Week October 23-October 28, 2018, San Diego CA  
3. Marty FM et al. Biol Blood Marrow Transplant 2018; doi: 10.1016/j.bbmt.2018.09.038  
4. FM Marty et al, NEJM 2013; DOI: 10.1056/NEJMoa1303688



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



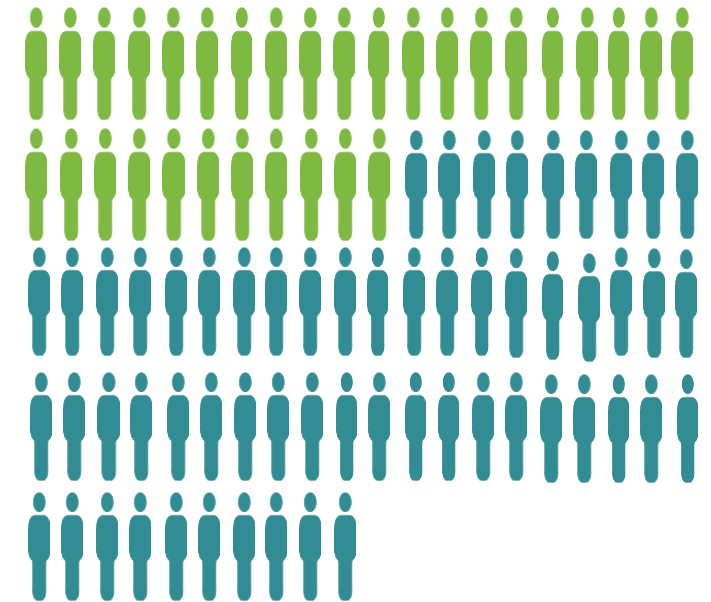
At least one DNA Virus in  
363/404=

**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: 100% survival demonstrated in animals that received immediate treatment with brincidofovir. Results from this study will be submitted to FDA as “weight of the evidence” together with adjunct rabbitpox study to be completed in early 2019.
  2. **Mousepox** / ectromelia replicates respiratory infection route of human smallpox infection. Pivotal mousepox study to be completed in 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



# CMRX: Four Active Clinical Programs in 2019

Program	Indication	Pre-clinical	Phase 1	Phase 2	Phase 3	Status	Anticipated Approval
Short-course Oral BCV	AdV Treatment					AdAPT enrolling	2021
	Smallpox Treatment					Animal Rule Pivotal Studies Progressing	2020
IV BCV	POC in BK					Ph 2 in 2019	2022
	Multi-Viral Prevention					Ph 2 initiated	2022

- 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 \$194M at the end of 3Q2018