



# CHIMERIX

DEUTSCHE BANK 43<sup>RD</sup> ANNUAL HEALTHCARE  
CONFERENCE

MICHELLE BERREY, MD, MPH  
PRESIDENT AND CEO  
MAY 9, 2018

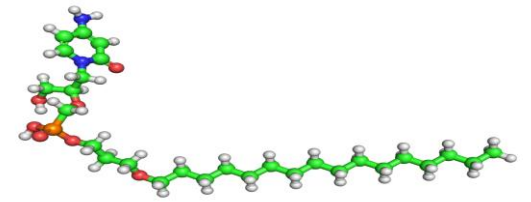
# Forward-Looking Statements

*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 March 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

- Experienced and committed management team with successful track records developing significant antiviral drugs and first-in-indication commercial launches
- Brincidofovir: first broad-spectrum antiviral in development
  - Oral BCV: in late-stage development for treatment of smallpox and adenovirus
  - New IV BCV: may support longer duration of dosing for prevention of serious viral infections in transplant recipients, and treatment of viral diseases including CNS infections
- Proprietary lipid-conjugate technology has led to two clinical-stage compounds
  - Brincidofovir (CMX001, BCV) and CMX157, licensed to ContraVir
- CMX521: newest investigational nucleoside for norovirus in Phase 1
- Chimerix remains well-capitalized to achieve planned milestones with \$209M at the end of 1Q 2018
- Patent protection into 2034 for brincidofovir, and 2036 for CMX521

# Lead Compound: Brincidofovir (BCV, CMX001)



- Broad-spectrum antiviral with high *in vitro* potency against all herpes viruses, adenovirus subtypes, other DNA viruses that cause human disease
- Oral suspension, oral tablets, and IV formulations in development
  - Both formulations deliver BCV to blood and cells known to carry DNA viruses
  - Cleavage of lipid side-chain occurs in the cell, delivering the active antiviral directly to the site of viral replication
  - Not associated with kidney toxicity or hematologic toxicity<sup>1,2</sup>
- Potential indications:
  - Treatment of serious AdV infection and disease
  - Treatment of smallpox
  - Prevention of serious viral infections in stem cell transplant recipients (HCT)
  - Treatment of BK virus in kidney and HCT transplant recipients

***BCV is the only broad spectrum antiviral with demonstrated potency against a variety of DNA viruses, a high barrier to resistance, no kidney or hematologic toxicity, and patent protection until 2034***



# Brincidofovir: Potent Broad Spectrum Antiviral

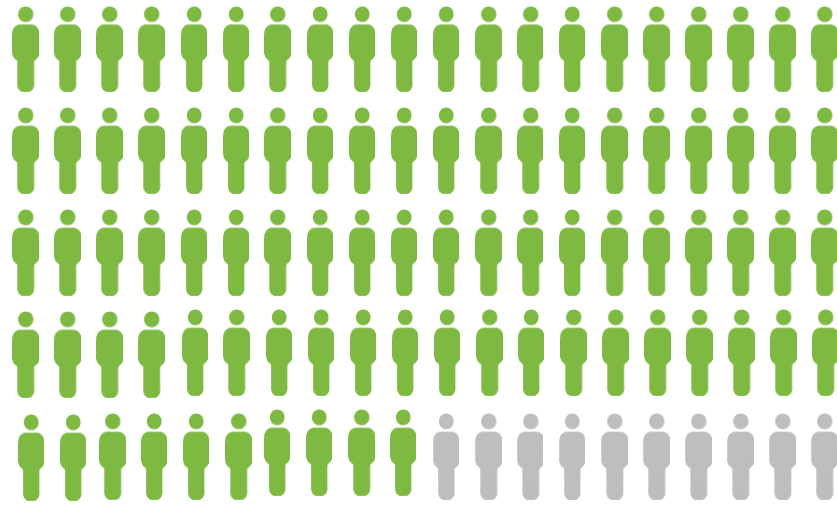
Viral Family	Virus	BCV	Cidofovir	Maribavir	Letermovir	Ganciclovir*	Foscarnet	Acyclovir
Herpes	Cytomegalovirus	0.001	0.4	0.31	0.005	3.8	50-800	>200
	Epstein-Barr Virus	0.03	65.6	0.63	>10	0.9	<500	6.2
	Human Herpesvirus 6	0.003	2.7	Inactive	>10	5.8	16	10
	Human Herpesvirus 8	0.02	2.6	Inactive	—	8.9	177	>100
	Herpes Simplex Virus 1	0.01	3.0	Inactive	>10	0.7	92-95	3.8
	Herpes Simplex Virus 2	0.02	6.5	Inactive	>10	2.5	91-96	4.4
	Varicella Zoster Virus	0.0004	0.5	Inactive	>10	1.3	39.8	3.6
Adenovirus	Adenovirus (AdV-B7)	0.02	1.3	—	>10	4.5-33	Inactive	>100
Polyoma	BK Virus (BKV)	0.13	115	—	—	>200	Inactive	>200
	JC Virus (JCV)	0.045	>0.1	—	—	—	Inactive	—
Papilloma	Human Papillomavirus	17	716	—	—	Inactive	—	Inactive
Pox	Variola	0.1	27	—	—	—	—	—
	Vaccinia	0.8	46	—	—	>392	Inactive	>144

Potency expressed as EC<sub>50</sub> = concentration in μM required to reduce viral replication by 50% *in vitro*; “—” indicates no data.

\*Valganciclovir is rapidly converted to ganciclovir *in vivo*; ganciclovir is the relevant compound for cell activity studies.

Source: Data are compiled from multiple sources and include multiple materials and methodologies.

# Stem Cell Transplant (HCT) Recipients are at High Risk of Viral Disease and Mortality

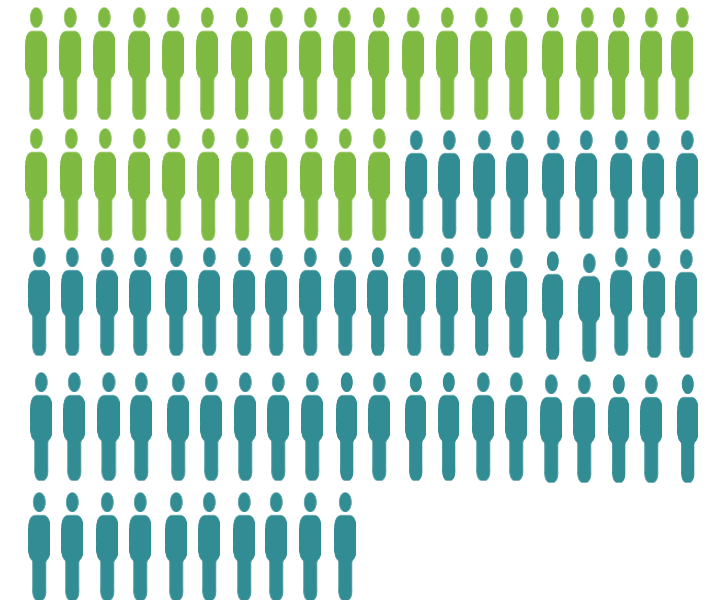


90%

2/3 have two or  
more DNA viruses

66%

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



# Why Are We Excited About 2018?

- AdAPT trial of short-course **oral BCV for adenovirus** enrolling and data expected in 2019; if positive, data should support first regulatory approval
  - AdVance data support the choice of the virologic primary endpoint and demonstrate clinical impact of viral burden
- Lack of GI side-effects with multiple doses of **IV BCV** supports progression to Phase 2 patient studies in 2018
  - Multi-viral prevention remains an unmet need in high-risk HCT, and longer duration of protection may be supported by the improved tolerability of IV BCV
  - Dose-ranging studies for multiple DNA viruses including BKV, CMV, HHV-6 under discussion

# AdAPT Underway – Data Expected in 2019



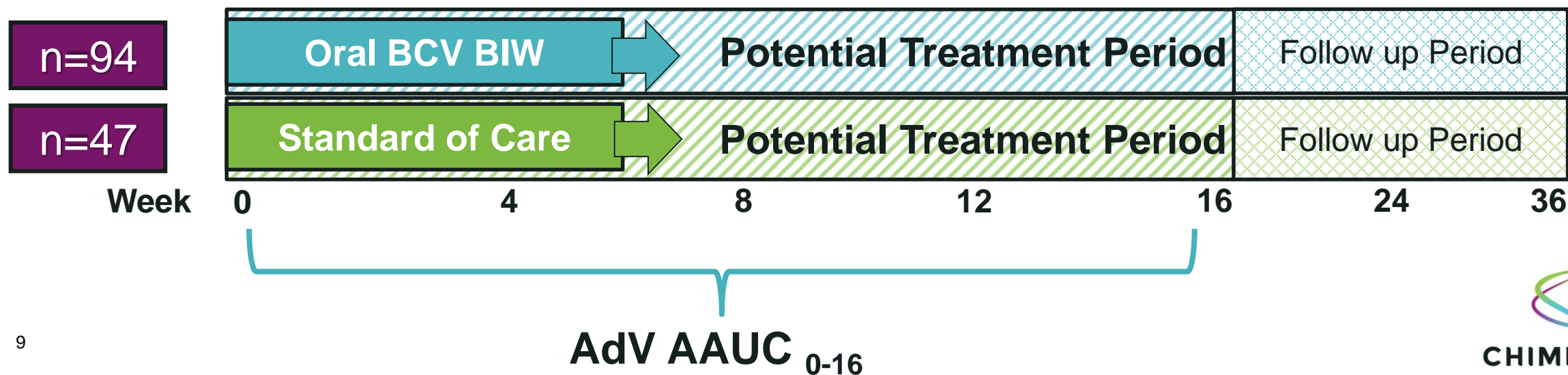
- Study being conducted in US, UK and EU
- Short-course oral treatment for acute life-threatening adenovirus infections
  - Potent antiviral with high barrier to resistance
  - Rapid reduction of AdV viral load in blood and other compartments
  - Short-course treatment minimizes risk of side effects

All timelines are estimated



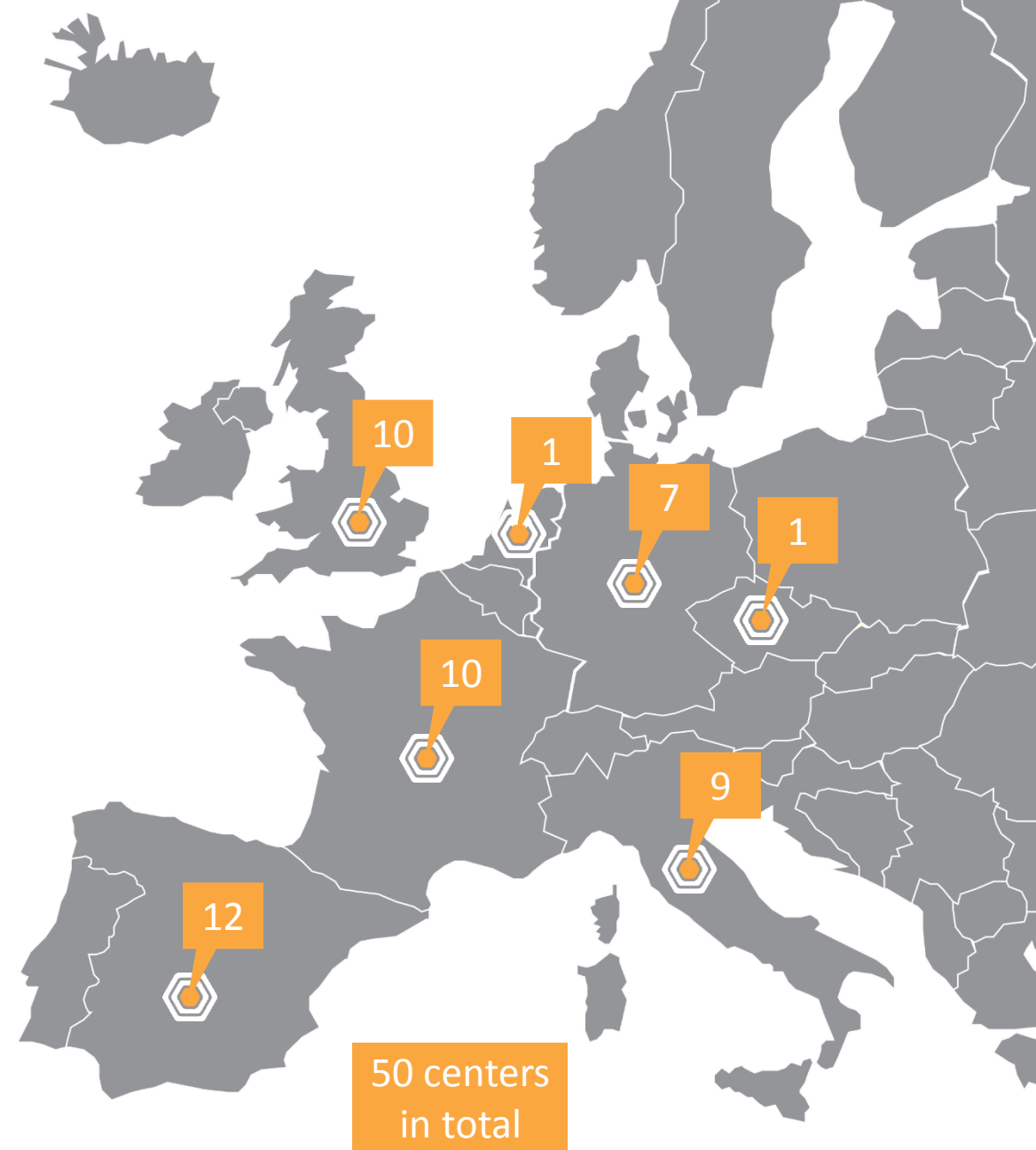
# AdAPT: Adenovirus after Allogeneic Pediatric Transplantation

- **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>)
- **Small study**: N=141 (2:1 randomization)

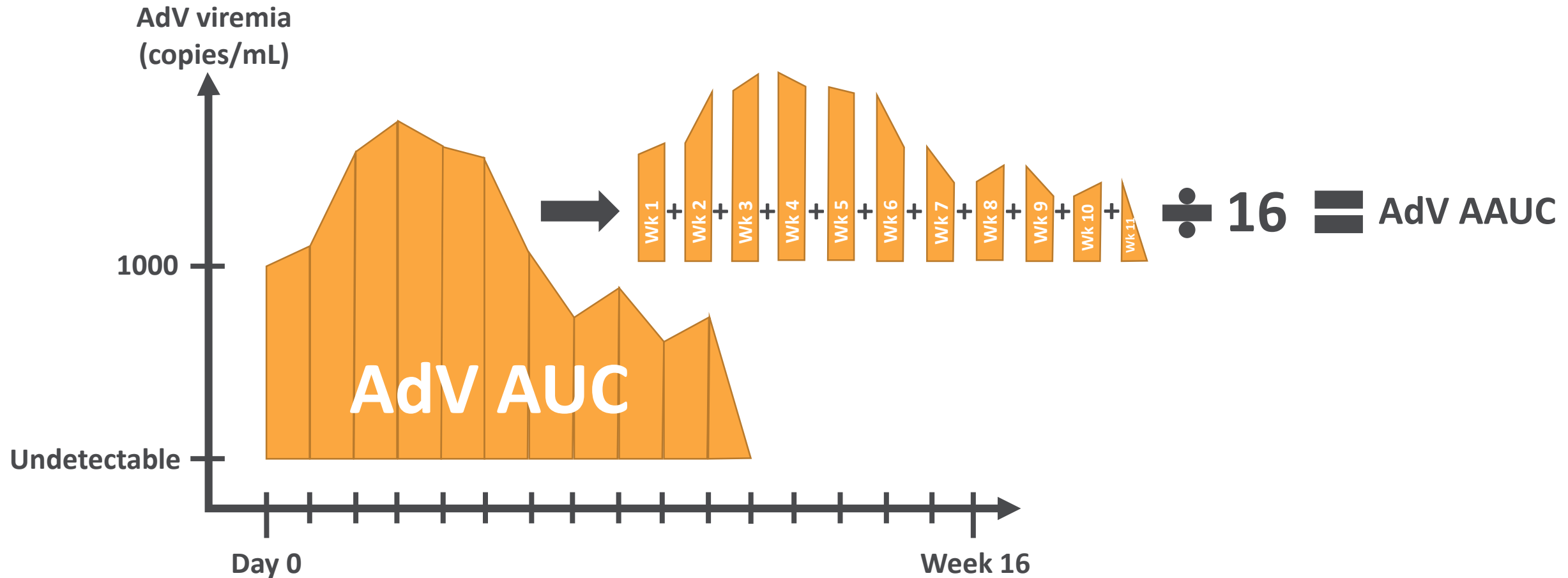


# The AdVance Study

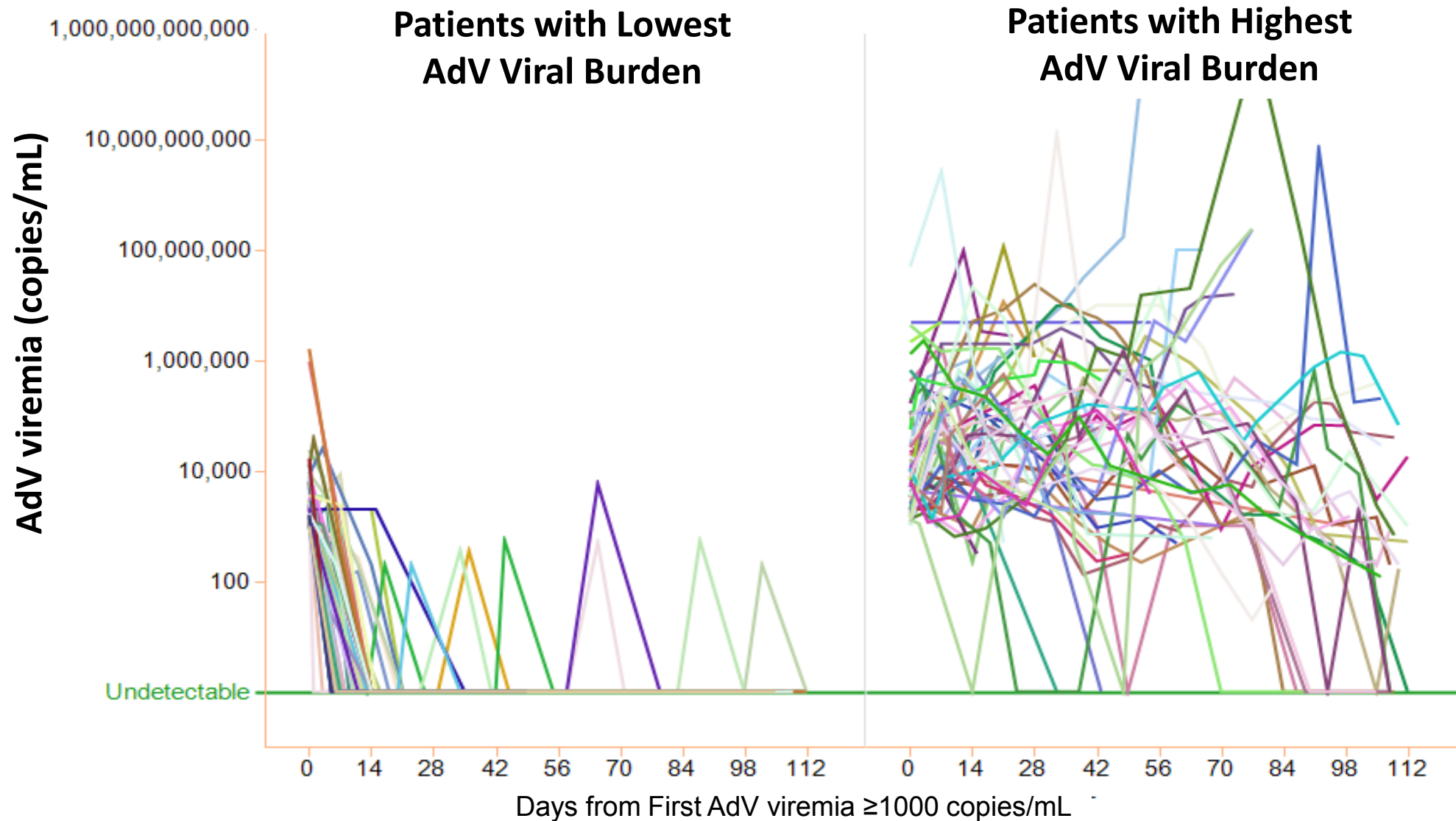
- AdVance is the largest multicenter, multinational study of the incidence, management, and clinical outcomes of AdV infection in allo-HCT recipients
- AdVance represents current standard of care
  - Data were collected from allo-HCT transplants that occurred between January 2013 and September 2015 at 50 participating centers



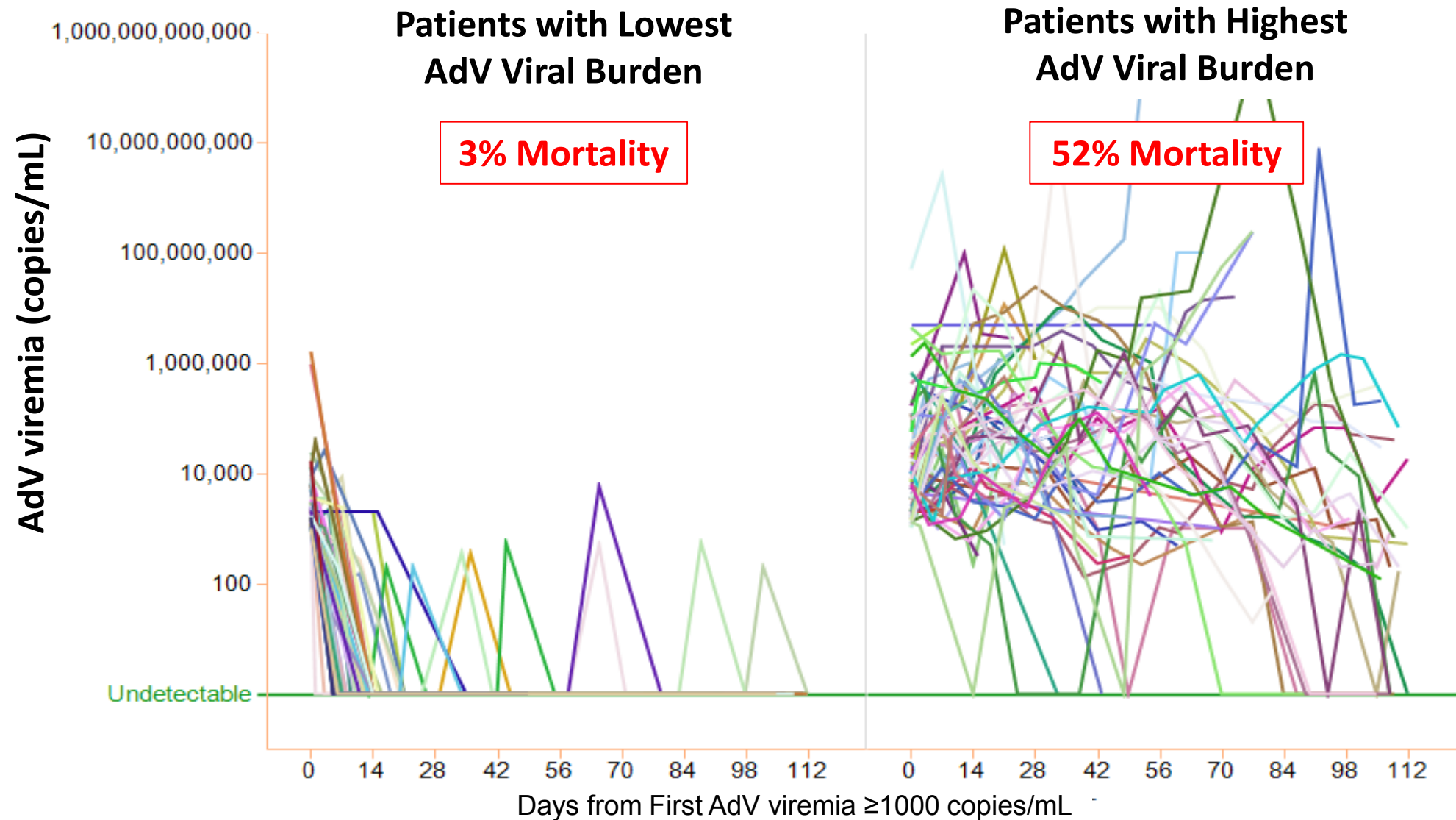
# Calculating AdV Average Viral Burden = AdV AAUC<sub>0-16</sub>



# High and Persistent AdV Viral Loads $\rightarrow$ Increased AdV AAUC<sub>0-16</sub>

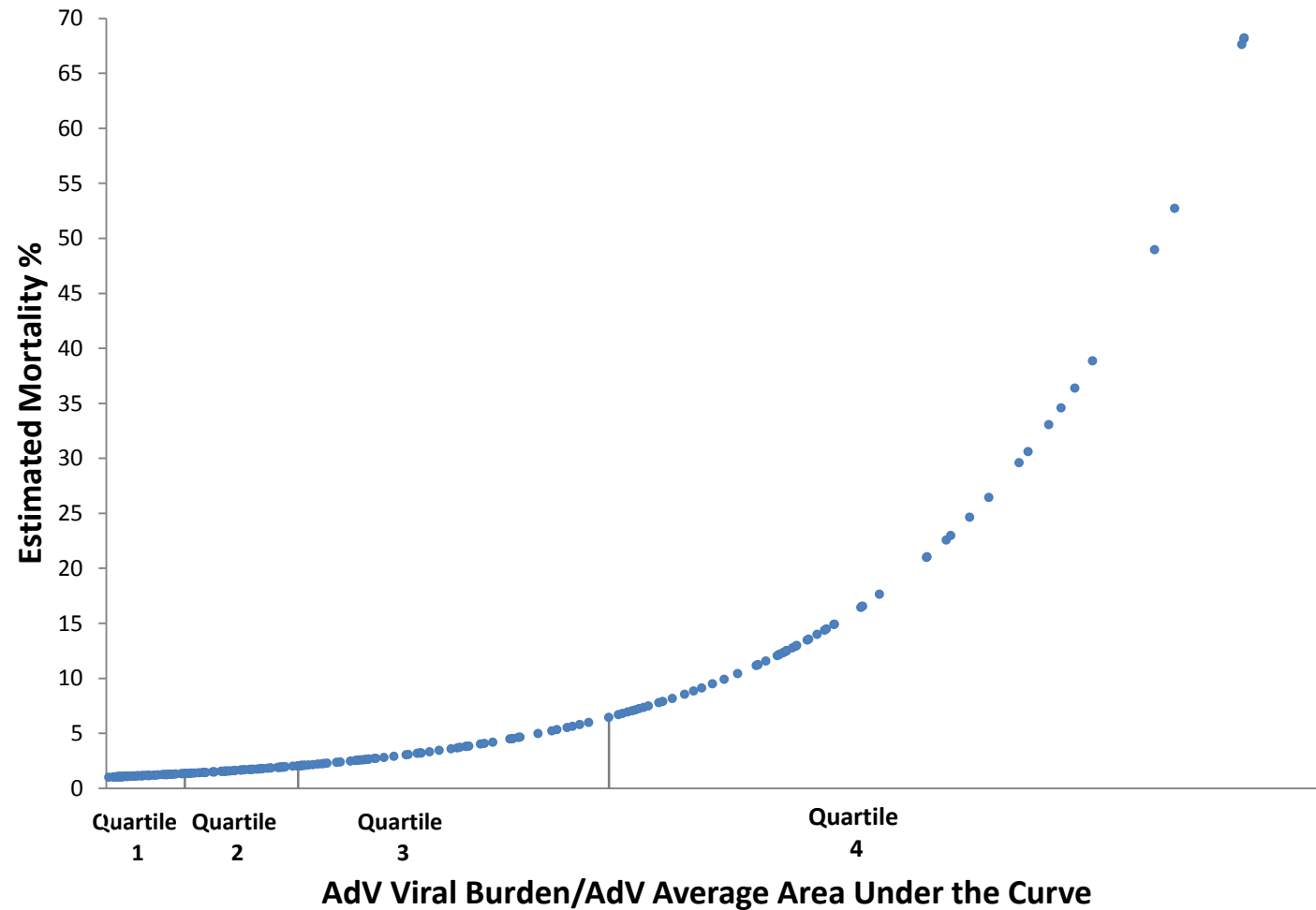


# Higher AdV AAUC<sub>0-16</sub> Correlates with Higher Mortality



# Higher AdV Viral Burden Correlates with Higher Mortality

- Each dot on curve represents an individual, with their AdV AAUC plotted against their estimated mortality
- Important to note: patients received current standard of care
- Each tenfold increase in AdV  $AAUC_{0-16}$  doubles the risk of mortality
- Implication: better control of AdV viremia should decrease mortality due to AdV

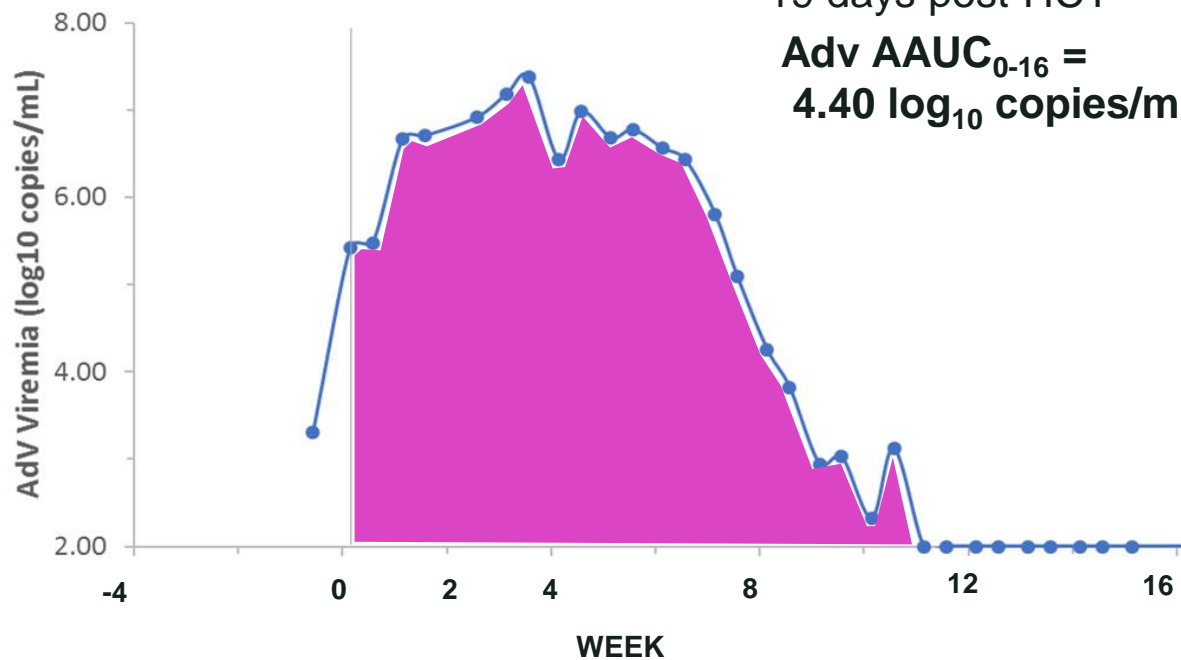


# AdAPT Is Designed for Success

## Local Standard of Care (SoC) from AdVance\*

2 yr old pt  
19 days post-HCT

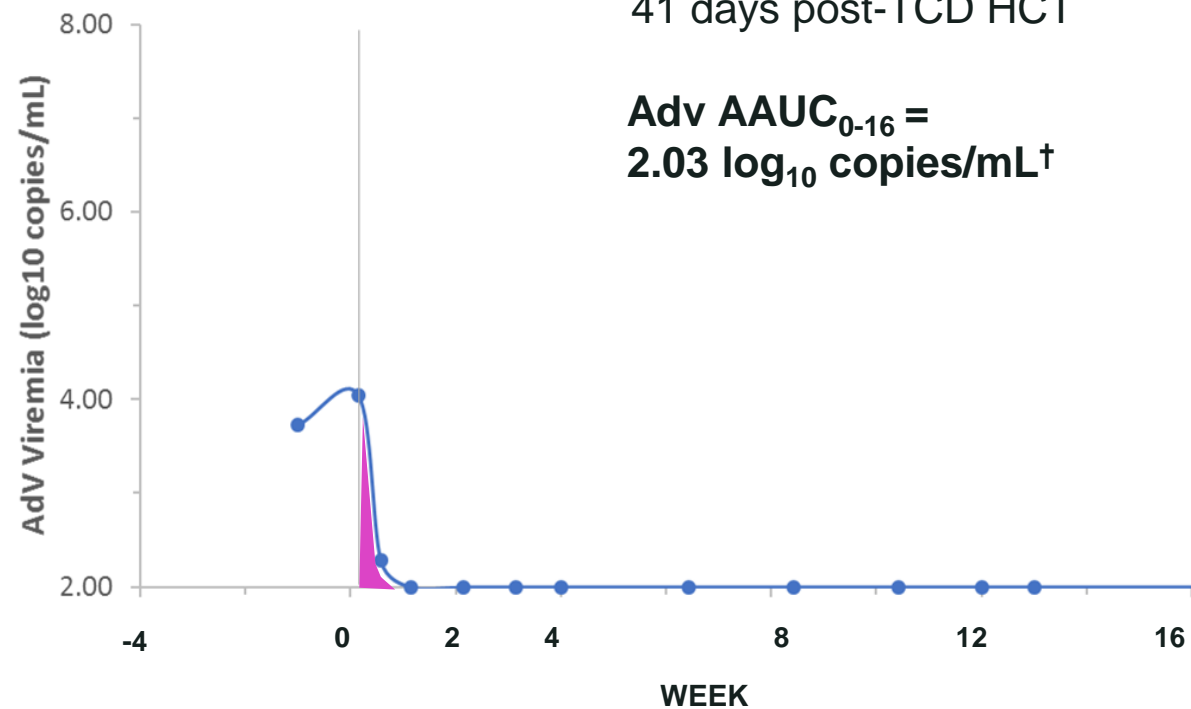
**Adv AAUC<sub>0-16</sub> =  
4.40 log<sub>10</sub> copies/mL†**



## 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†**



**Modeled control – modeled 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

# AdVance: Data Increases Confidence for AdAPT

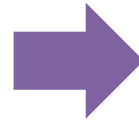
- ⬡ These data increase confidence that AdAPT's primary virologic endpoint is clinically relevant
- ⬡ More rapid control of AdV viremia with BCV should decrease adeno burden (AdV AAUC)
- ⬡ Lower adenovirus burden (AdV AAUC) should decrease AdV-related mortality



# IV BCV: Fulfilling the Potential of Brincidofovir

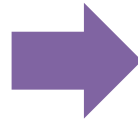
Early development work shows great promise for the IV formulation

IV BCV delivers uniform exposure to key organs



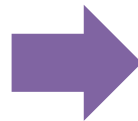
Should allow longer duration of dosing with improved tolerability

IV BCV delivers more drug to difficult-to-reach compartments, especially the brain



Supports evaluation of IV BCV for viral brain infections, such as HHV6 encephalitis or JC virus

IV BCV profile may allow for both treatment and prevention of DNA viral infections

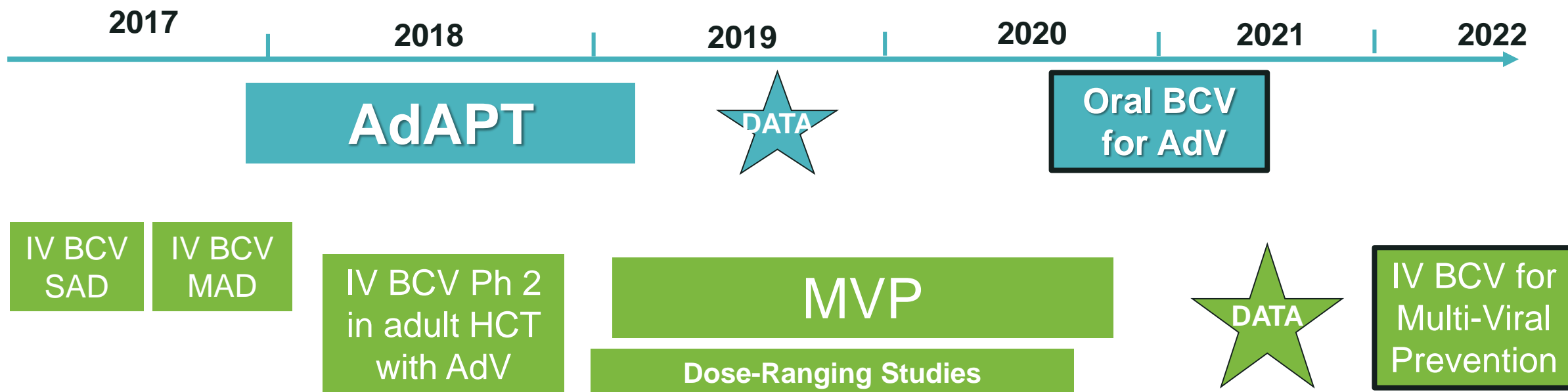


Potential for once-weekly dosing and improved tolerability could allow for broader use in multiple viruses

## IV BCV Multiple Dose Study Demonstrates Improved GI Tolerability

- MAD dosing complete: 10 mg twice weekly, 20 mg once weekly for 2-4 weeks
  - No diarrhea at 10 mg IV twice weekly
    - IV BCV 10 mg provided plasma drug levels equivalent to oral BCV 100 mg which demonstrated antiviral activity in prior studies
  - No dose limiting clinical adverse events
- Phase 2 IV BCV patient studies starting in 1H 2018
  - Demonstrate PK and tolerability of multiple doses in adult HCT recipients
  - Evaluate relationship between dose and AdV decay curves
  - Data expected 2H 2018

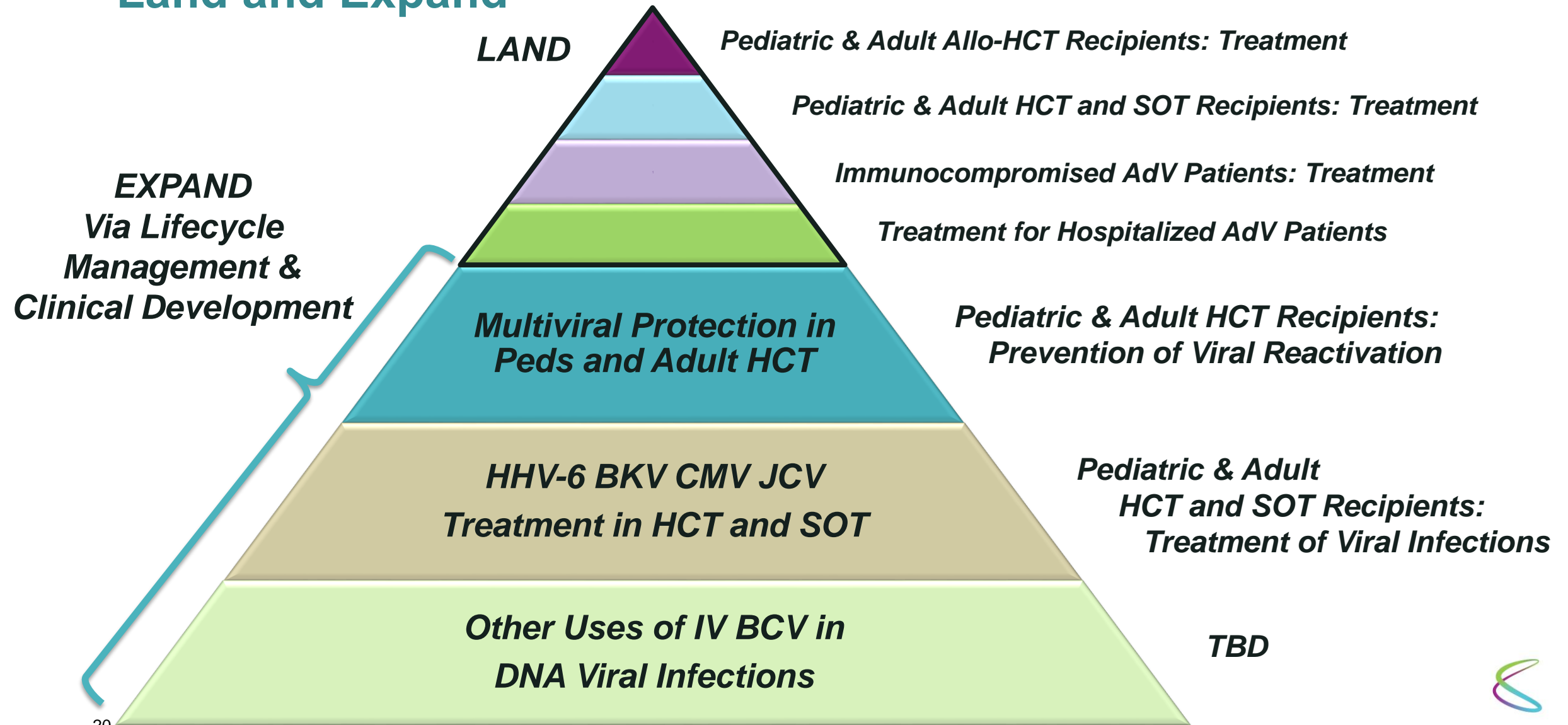
# Anticipated Brincidofovir Milestones and Regulatory Decisions







- Open-label Phase 2 IV BCV studies in adult patients to read out throughout 2018
- IV BCV offers the promise of longer duration dosing for prevention of multi-viral infection
- IV BCV dose-ranging studies in other serious viral infections including BKV, JCV, HHV-6

All timelines are estimated

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



# BCV Market Potential: Growing Transplant and Immunocompromised Patient Populations

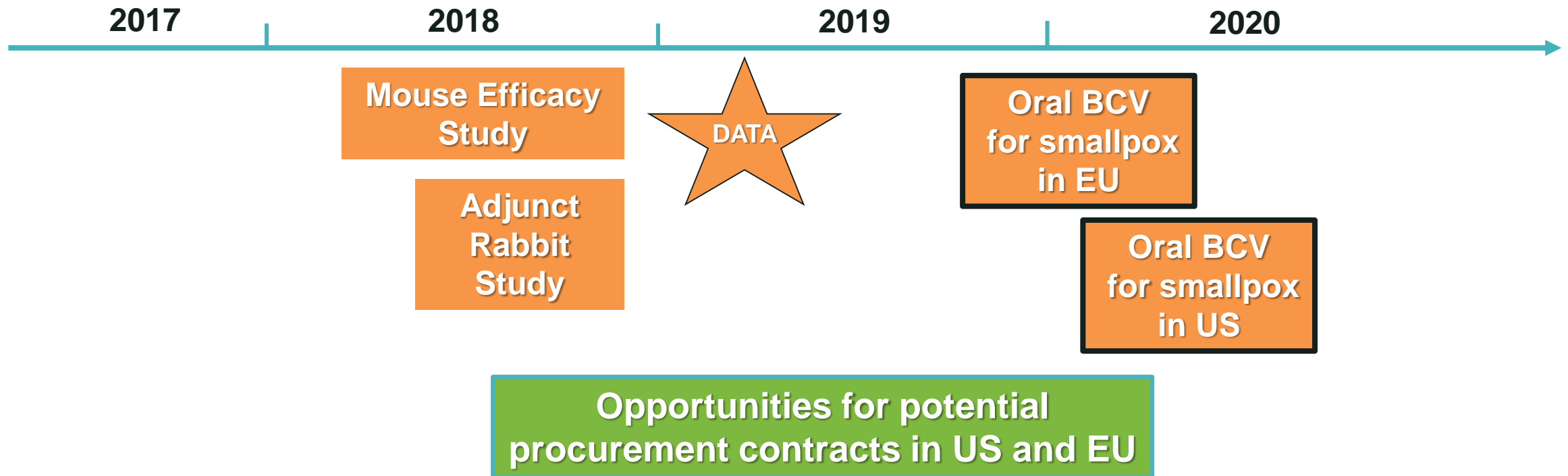
				
TRANSPLANTS PER YEAR	U.S.	European Union (28)	ROW	TOTAL
<b>HCT</b>				
Allogeneic	8,700	16,400	10,154	35,254
Autologous	15,000	21,700	6,515	43,215
<b>HCT TOTALS</b>	<b>23,700</b>	<b>38,100</b>	<b>16,669</b>	<b>78,469</b>
<b>SOT</b>				
Kidney	19,860	20,000	40,700	805,60
Liver	7,800	7,400	10,500	25,700
Other SOT	5,940	4,500	1,400	11,840
<b>SOT TOTALS</b>	<b>33,600</b>	<b>31,900</b>	<b>52,600</b>	<b>118,100</b>
<b>TOTAL TRANSPLANT</b>	<b>57,300</b>	<b>70,000</b>	<b>69,269</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., HSCT in Europe 2014, [nature.com/bmt](http://nature.com/bmt), 2016. ROW HCT: 2013 HCT figures from The WBMT Global Survey presented by Helen Baldomero at WBMT meeting in Riyadh 2017, slide 11 (South East Asia/Western Pacific and Eastern Mediterranean/Africa). TOTAL HCT: US + EU + ROW. EU & TOTAL SOT: Newsletter Transplant – International Figures On Donation And Transplantation 2014; EDQM, volume 20, 2015. ROW SOT: Total - EU - US

# Brincidofovir: Oral Antiviral With Demonstrated Activity Against Smallpox

- Oral BCV has demonstrated 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 to be submitted to FDA as “weight of the evidence” with NDA.
  2. Mouse pox / ectromelia replicates respiratory infection route of human smallpox infection
- Regulatory submissions planned for 2019
- Procurement opportunities being pursued in the US via BARDA, or following approval in Europe/ROW

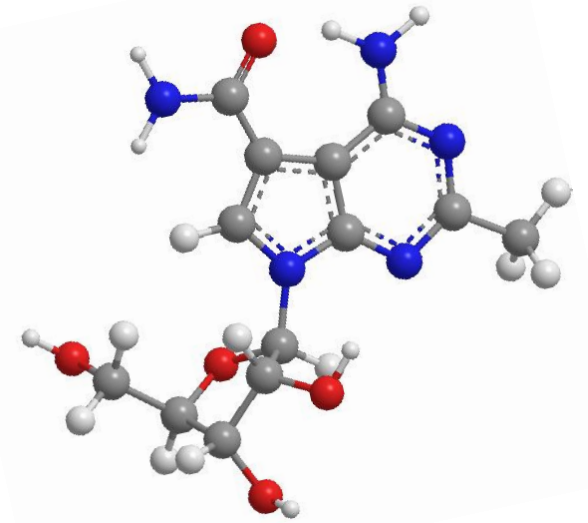
# Brincidofovir for Smallpox: Completing Studies and Proceeding Toward Filing of Marketing Applications



All timelines are estimated

# CMX521: a Small Molecule Antiviral for Norovirus

- Nucleoside with pan-genotype activity
  - Targets region of virus that is common to all strains
- Safety profile looks very promising
  - In vitro and in vivo
- High probability of clinical efficacy for a drug in Phase 1
  - Preferential delivery of drug to target cells
- Patent protection until 2036
- Nothing approved for prevention or treatment





# Two Distinct Segments for Norovirus Opportunity Identified

Worldwide: ~700 MM cases of norovirus each year (~20 MM in U.S.)

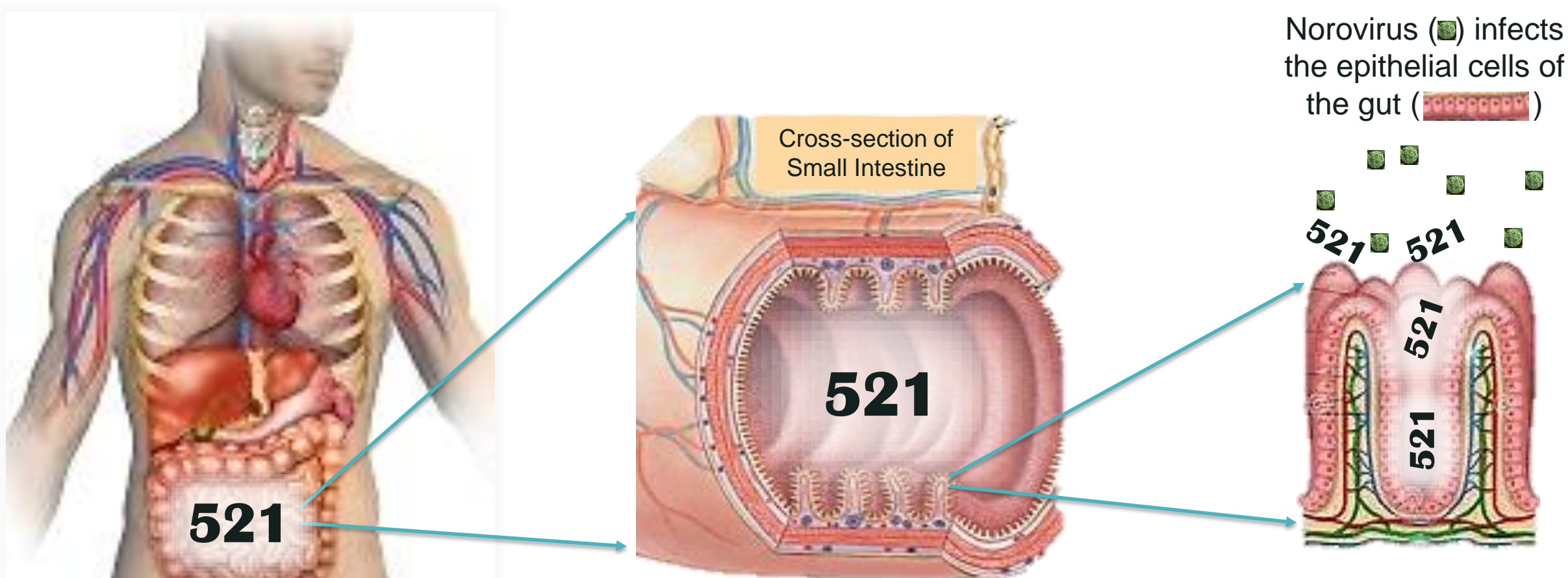
## ■ Treatment of Chronic Norovirus Infection

- Allogeneic stem cell transplant recipients
- Solid Organ transplant recipients
- Other immunocompromised patients
- Asymptomatic shedders
  - Put others at-risk in public settings
  - Food handlers, hospital or healthcare worker

## ■ Prevention of Acute Norovirus Infection

- At-risk individuals who have been exposed to a *confirmed* case of norovirus, e.g. family members, hospital or healthcare workers, co-workers, students
- Individuals who may be at-risk due to a local outbreak without confirmed exposure
- Individuals who elect to or need to be protected from a potential outbreak

# CMX521 Preferentially Delivered to Target Cells with Oral Dosing







- More drug in target sites increases efficacy
- Less drug in non-target sites increases safety

# Data-Rich 2018 and 2019 Ahead of Regulatory Decisions

Compound	Indication	1H 2018	2H 2018	2019
Oral BCV	Adenovirus	❖ Enrolling AdAPT ❖ AdVance Data	❖ Enrolling AdAPT	❖ Enrolling AdAPT ❖ <b>AdAPT Data</b>
	Smallpox	❖ Agree pivotal mouse study	❖ Pivotal mouse study ❖ Pivotal rabbit study	❖ MAA submission ❖ NDA submission
IV BCV	Adenovirus and CMV	❖ Initiate Phase 2 in adult HCT	❖ Phase 2 in adult HCT	❖ Initiate MVP pivotal trial
CMX521	Treatment of Chronic Norovirus	❖ Ph 1 single dose study	❖ Ph 1 multiple dose study	❖ Norovirus: Challenge / Proof-of-Concept trial
	Prevention of Norovirus Outbreaks			

# CMRX: Four Active Clinical Programs in 2018

Program	Indication	Pre-clinical	Phase 1	Phase 2	Phase 3	Status	Anticipated Approval
Short-course Oral BCV	AdV Treatment					AdAPT enrolling	2021
	Smallpox					Animal Rule models progressing	2020
IV BCV	Multi-viral Prevention					Ph 2 in patients 2018	2022
CMX521	Norovirus					SAD/MAD in 2018	2023

- Chimerix remains well-capitalized with \$209M at the end of 1Q2018
- Patent protection into 2034 for brincidofovir, and 2036 for CMX521



Q&A



**CHIMERIX**