



# CHIMERIX

J.P. MORGAN HEALTHCARE CONFERENCE

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**PRESIDENT AND CEO**  
**JANUARY 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 September 30, 2017 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.*

## 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
- Lack of GI side-effects with multiple doses of **IV BCV** supports progression to Phase 2 patient studies in 2018, leading to potential studies in prevention and treatment of multiple viruses including AdV, CMV, and BKV in 2019
- Regulatory submissions for marketing approval of **oral BCV for smallpox** are planned for 2019
- **CMX521**, the first direct-acting antiviral specific for norovirus, is now in clinical stage development
- We have patent protection through 2034 and sufficient capital to progress oral BCV to value-generating data and/or procurement contracts

# Data-Rich 2018 and 2019 Ahead of Regulatory Decisions

Compound	Indication	1H 2018	2H 2018	2019
Oral BCV	Adenovirus	❖ Enrolling AdAPT	❖ Enrolling AdAPT Adult	❖ <b>AdAPT Data</b>
	Smallpox	❖ Pivotal mouse study	❖ Pivotal mouse study ❖ Supportive rabbit study	❖ MAA submission ❖ NDA submission
IV BCV	Adenovirus and CMV	❖ Initiate Phase 2 in patients	❖ Phase 2 in patients	❖ 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: Developing Solutions for Immunocompromised Patients

- Experienced and committed management team with successful track records developing significant antiviral drugs and first-in-indication commercial launches
- Lead compound brincidofovir has broad-spectrum antiviral activity
  - Short-course oral BCV in late-stage development for treatment of smallpox and adenovirus
  - New IV BCV formulation for prevention of serious viral infections in transplant recipients and treatment of viral diseases in the growing immunocompromised patient population
- Proprietary lipid-conjugate technology has led to two clinical-stage compounds
  - Brincidofovir (CMX001, BCV) and CMX157, licensed to ContraVir
- CMX521: newest investigational compound for norovirus
  - Developed from Chimerix Chemical Library
  - First clinical dosing began in December 2017

# Brincidofovir: Broad Spectrum Antiviral For dsDNA Viruses

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

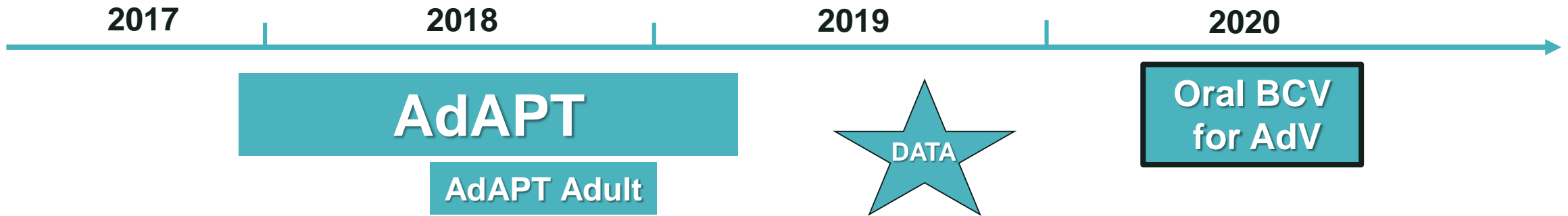
Potency expressed as EC<sub>50</sub> = concentration in µM required to reduce viral replication by 50% *in vitro*; “—” indicates no data.

\*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.



# AdAPT Now Enrolling – Data Expected in 2019

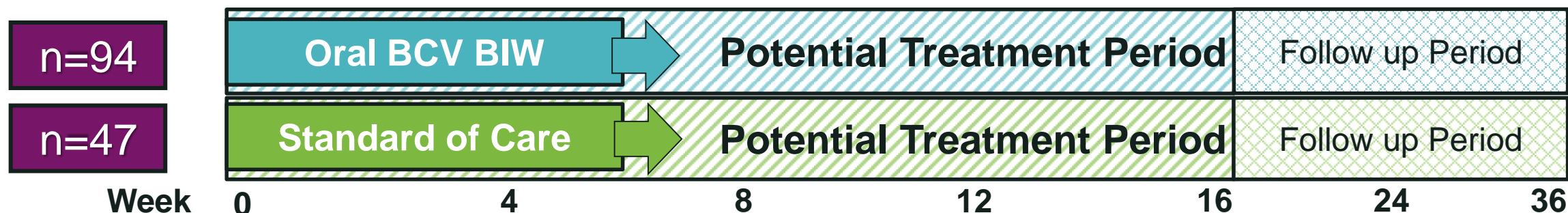


- Study being conducted in US, UK and EU
- Short-course oral treatment for acute life-threatening adenovirus infections
  - Potent antiviral with high barrier to resistance
  - Rapid reduction of AdV viral load in blood and other compartments
  - Short-course treatment minimizes risk of side effects

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 during first 100 days of HCT
- **Short-course therapy**: “Treat-to-clear” paradigm
  - BCV or SoC administered until AdV is cleared from plasma
- **Primary endpoint: AdV viral burden over 16 weeks**
  - Agreed by CHMP and FDA
- **Study size: N=141** to be randomized 2:1 to oral BCV or local standard of care





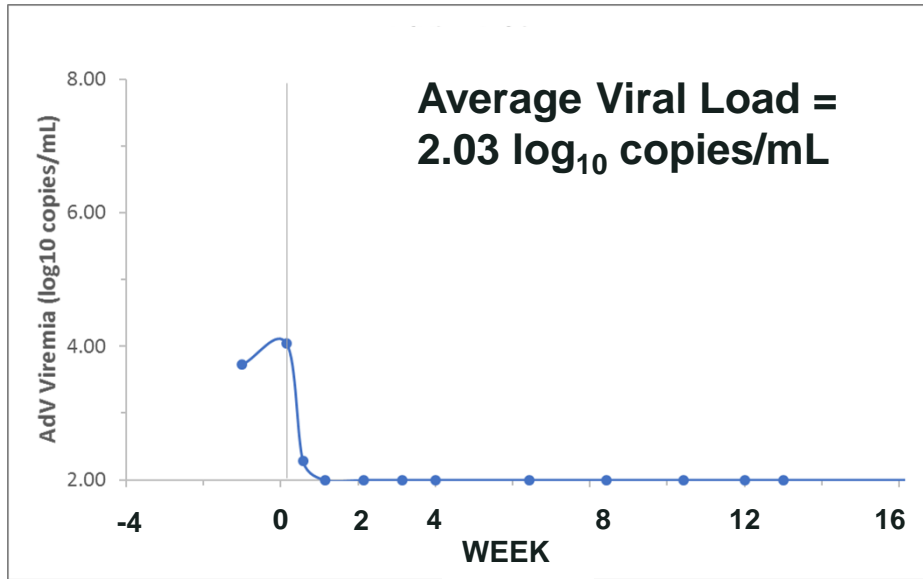
# Maximizing the Probability of Success for AdAPT

- 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 to local 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

# Rapid Antiviral Effect of Oral Brincidofovir vs Local SOC\*

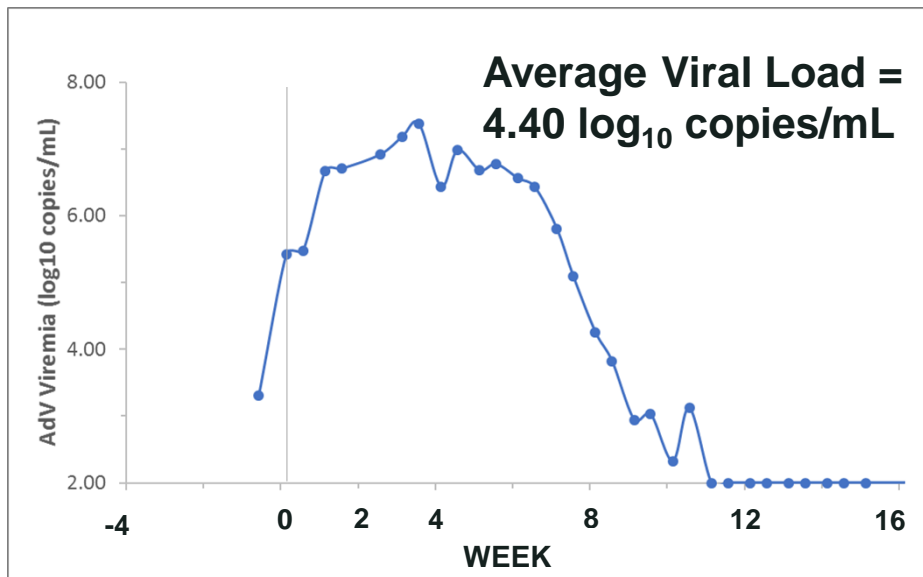
## Oral BCV from Advise

3 yr old pt  
41 days post-TCD  
HCT



## Local Standard of Care (SoC) from Advance

2 yr old pt  
19 days post-HCT



- Detection of AdV in the blood after transplant predicts rapid progression to AdV disease and death in high-risk transplant recipients
- Oral BCV has demonstrated rapid clearance of AdV viremia
- BCV does not require immune reconstitution to provide viral load reductions

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



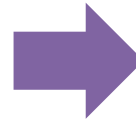
# Regulatory Acceptance of AdV Viral Load as a Surrogate Endpoint for Pivotal Studies

- AdAPT was designed with European regulators; positive data should support full or conditional approval
- FDA has recently announced CMV viremia as an acceptable surrogate endpoint for pivotal CMV studies; viremia without statistically significant mortality sets an important precedent for anticipated discussions on results from AdAPT
- We are working with international experts to build similar substantial evidence in support of AdV viral load as an acceptable surrogate endpoint for pivotal studies
  - European Group for Blood and Marrow Transplant (EBMT) plans to publish ID Working Group position paper with state-of-the-art screening and treatment recommendations for the diagnosis and treatment of adenovirus after HCT
  - AdVance: multiple abstracts planned for EBMT March 2018 that demonstrate the correlation of AdV viral burden with risk of mortality
  - Multiple independent analyses from transplant centers across Europe and the US show a strong correlation of AdV viral load, disease and mortality

## IV BCV: Fulfilling the Potential of Brincidofovir

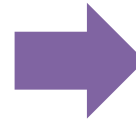
Early development work shows great promise for the IV formulation

IV BCV delivers uniform exposure to key organs



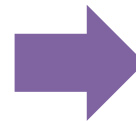
Does not over-expose gut which should allow for long-term tolerability

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 infection

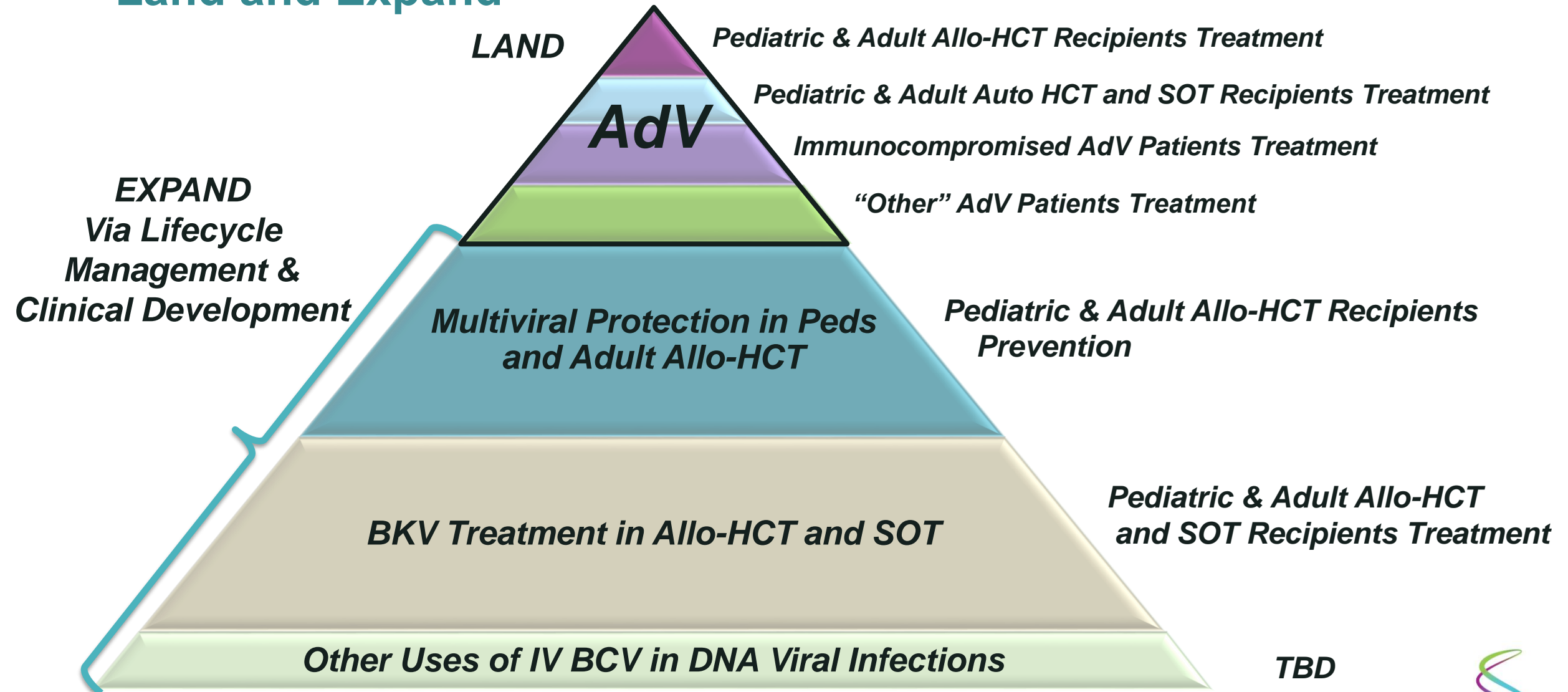


Potential for once-weekly dosing and improved tolerability could allow for broader use in multiple viruses

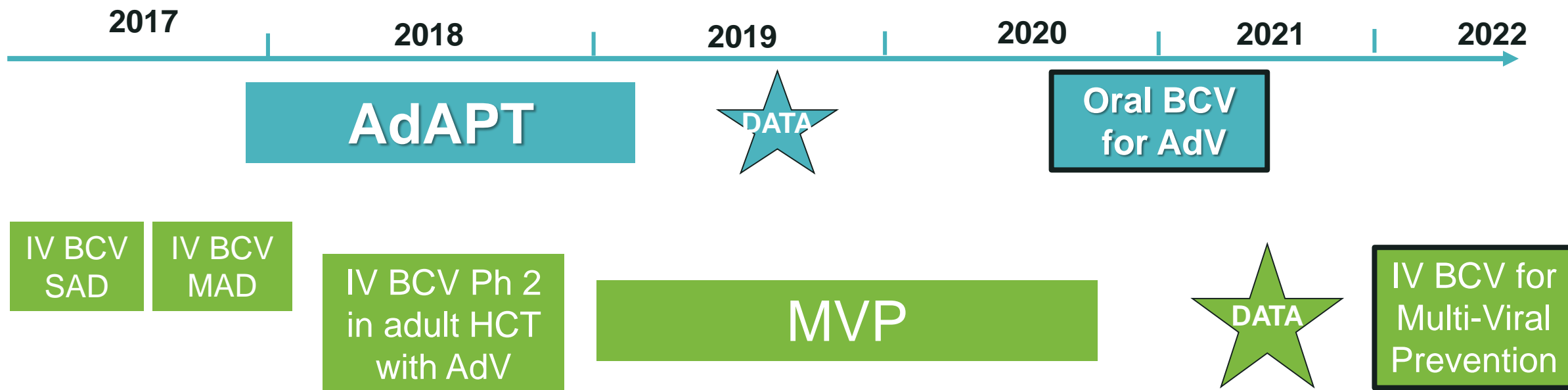
## IV BCV: Multiple-Ascending Dose Study Demonstrates Improved GI Tolerability

- Multiple Ascending Dose (MAD) Study Design:
  - IV BCV 10 mg twice-weekly (BIW), 20 mg once-weekly (QW) for 4 doses
  - No dose-limiting clinical adverse events
  - No diarrhea with IV BCV 10 mg twice-weekly
    - IV BCV 10 mg provided plasma drug levels equivalent to oral BCV 100 mg which demonstrated antiviral activity in prior studies
- 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 change-from-baseline in AdV in blood and stool
  - Data expected 2H 2018 to inform dose & dosing regimen for MVP-Peds study of multi-viral prevention

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



# Anticipated Brincidofovir Milestones and Regulatory Decisions



- Phase 2 IV BCV data to support dose-selection for MVP pivotal trial
- IV BCV offers the promise of longer term dosing with improved tolerability

All timelines are estimated

# Brincidofovir: Oral Antiviral With Demonstrated Activity Against Smallpox

Oral BCV has demonstrated survival benefit in two animal models of fatal orthopoxvirus infections:

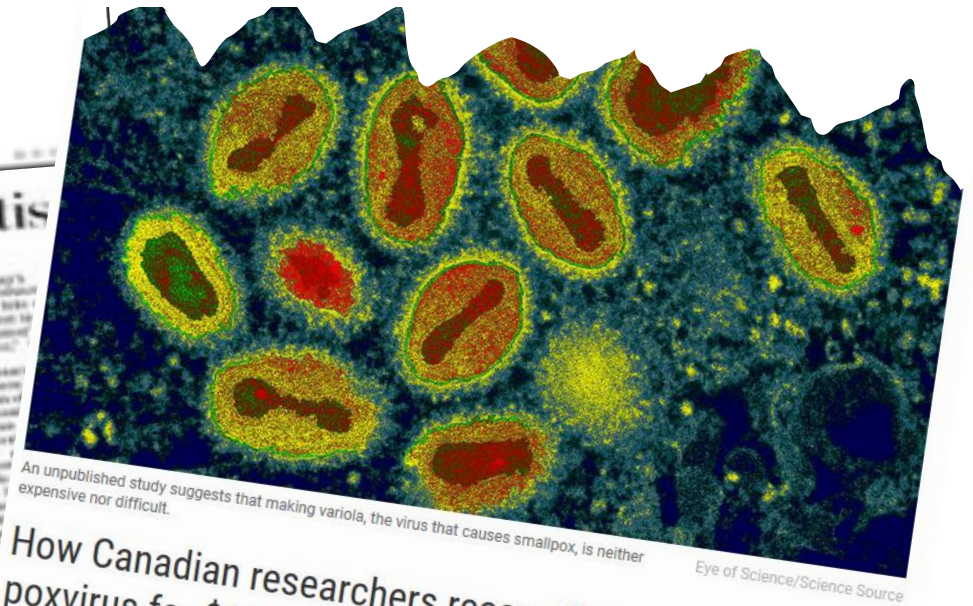
- Rabbitpox virus model replicates human smallpox pathophysiology: asymptomatic infection, illness, and death
  - 100% survival demonstrated in animals that received immediate treatment with brincidofovir
  - Delayed treatment in 24 or 48 hrs resulted 93% survival
- Mouse pox infection (ectromelia) replicates the respiratory infection route of human smallpox infection
  - Pivotal study to be conducted in 2018



# Smallpox: Highest Bioweapon Threat

***“The next epidemic could originate on the computer screen of a terrorist intent on using genetic engineering to create a synthetic version of the smallpox virus...”***

- Bill Gates, Munich, April 2017



An unpublished study suggests that making variola, the virus that causes smallpox, is neither expensive nor difficult.

## How Canadian researchers reconstituted an extinct poxvirus for \$100,000 using mail-order DNA

By Kai Kupferschmidt | Jul. 6, 2017, 5:00 PM



# UN Bioweapons Conference Confirms Global Concern

- Chimerix sponsored a smallpox symposium in December 2017 at UN Biological Weapons Convention in Geneva
  - Threats from synthetic biology, undeclared smallpox stockpiles
  - Role of antivirals as medical countermeasures
- Interest level exceeded expectations
  - Over 100 government agency attachés attended

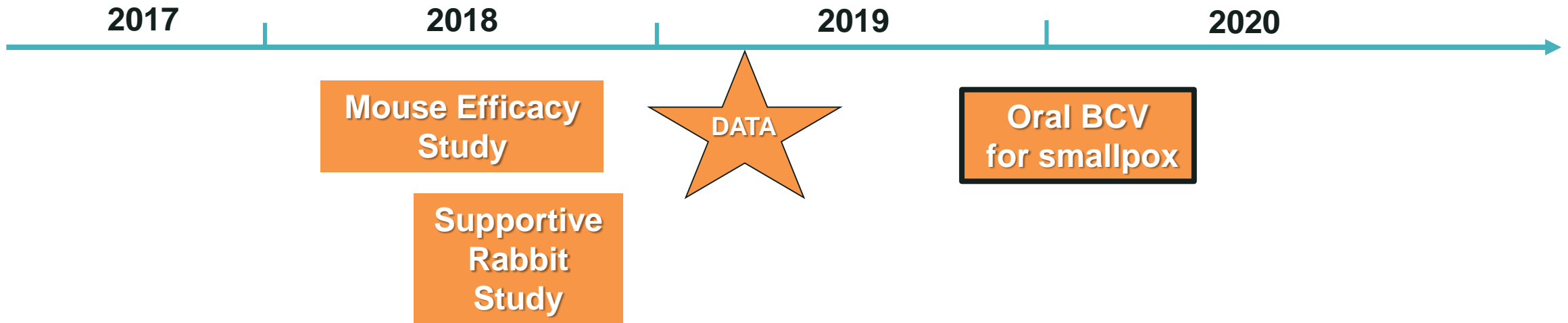




# Expedited EU Submission Supported for Brincidofovir

- EMA marketing approval generally precedes procurement discussions in EU
  - Marketing Approval in EU can be cross-referenced for international procurement contracts outside the EU
- Formal Scientific Advice was requested from the CHMP regarding required elements for a European marketing application for smallpox
  - Animal Efficacy Studies conducted for brincidofovir include a pivotal rabbitpox study which demonstrated 100% survival in animals treated at the time of confirmed infection compared with <50% survival in placebo animals ( $p < 0.001$ )
  - Application would include data from over 50 studies in the supportive mousepox efficacy model
- EMA responded that data from completed studies are sufficient for MAA submission: preparations are underway

# Second Animal Model of Orthopoxvirus for US Submission



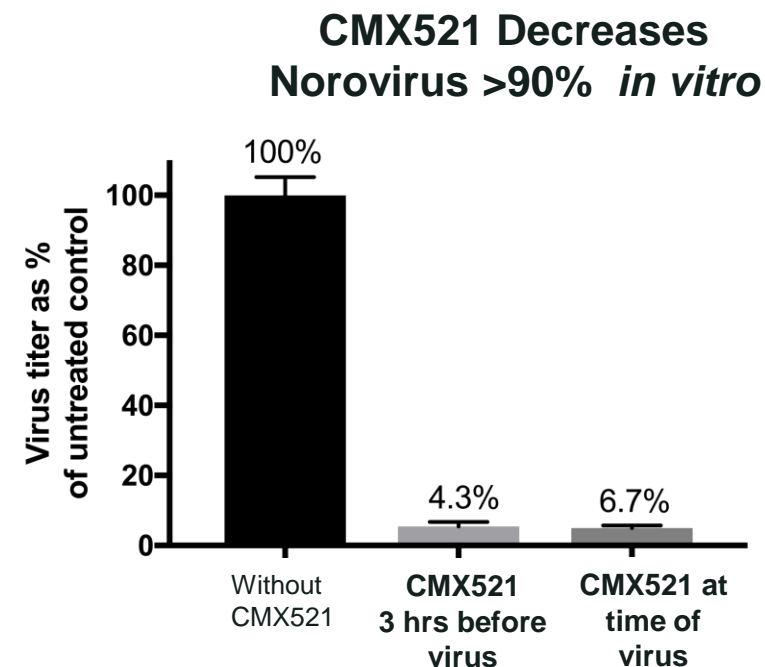
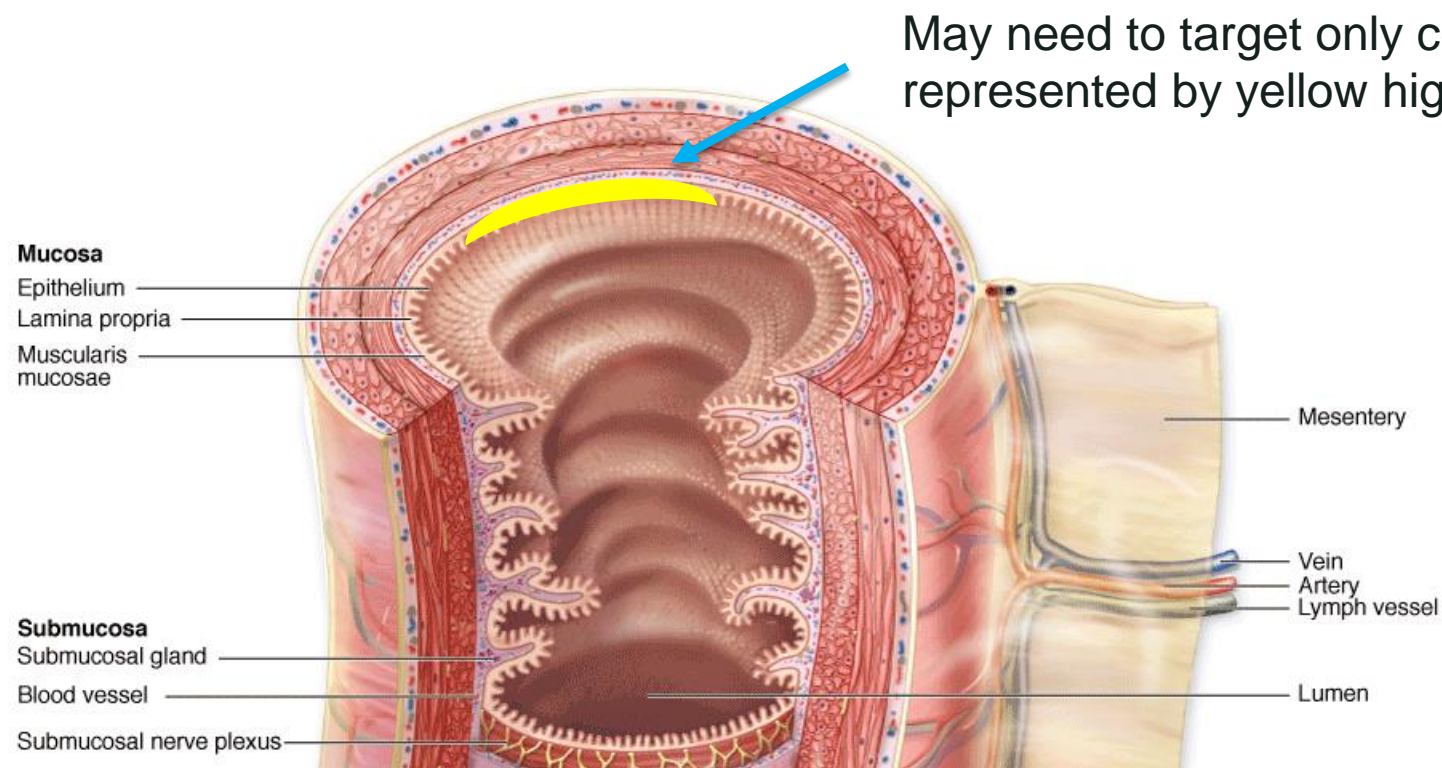
- Plan to initiate pivotal mouse study and supportive rabbit study in 2018
- Data could support filing in US for smallpox in 2019

All timelines are estimated

# CMX521: The First Specific Antiviral for Norovirus

- As a nucleoside selected from the Chimerix Chemical Library, CMX521:
  - targets the polymerase, an enzyme essential for viral replication
  - targets a portion of the virus that remains consistent across diverse strains
  - has demonstrated *in vitro* antiviral activity against all norovirus genotypes tested
- First subject was dosed in December 2017, data anticipated in 2018
  - Intestinal biopsies will determine intracellular drug levels for the target cells
  - Drug levels in intestinal cells that achieve effective *in vitro* concentrations could de-risk program
- ~700 million cases of norovirus each year
- Tremendous economic toll: >\$60 billion/yr

# Treatment Target is the Gut Epithelia



## Norovirus replicates in epithelium of the gut

- Efficacious levels of active antiviral reached at 2-4 hours with  $\leq 10 \mu\text{M}$
- Active antiviral half-life is 24 hours: suggests once-daily dosing

# Two Distinct Norovirus Opportunities

## ■ Treatment of Chronic Norovirus

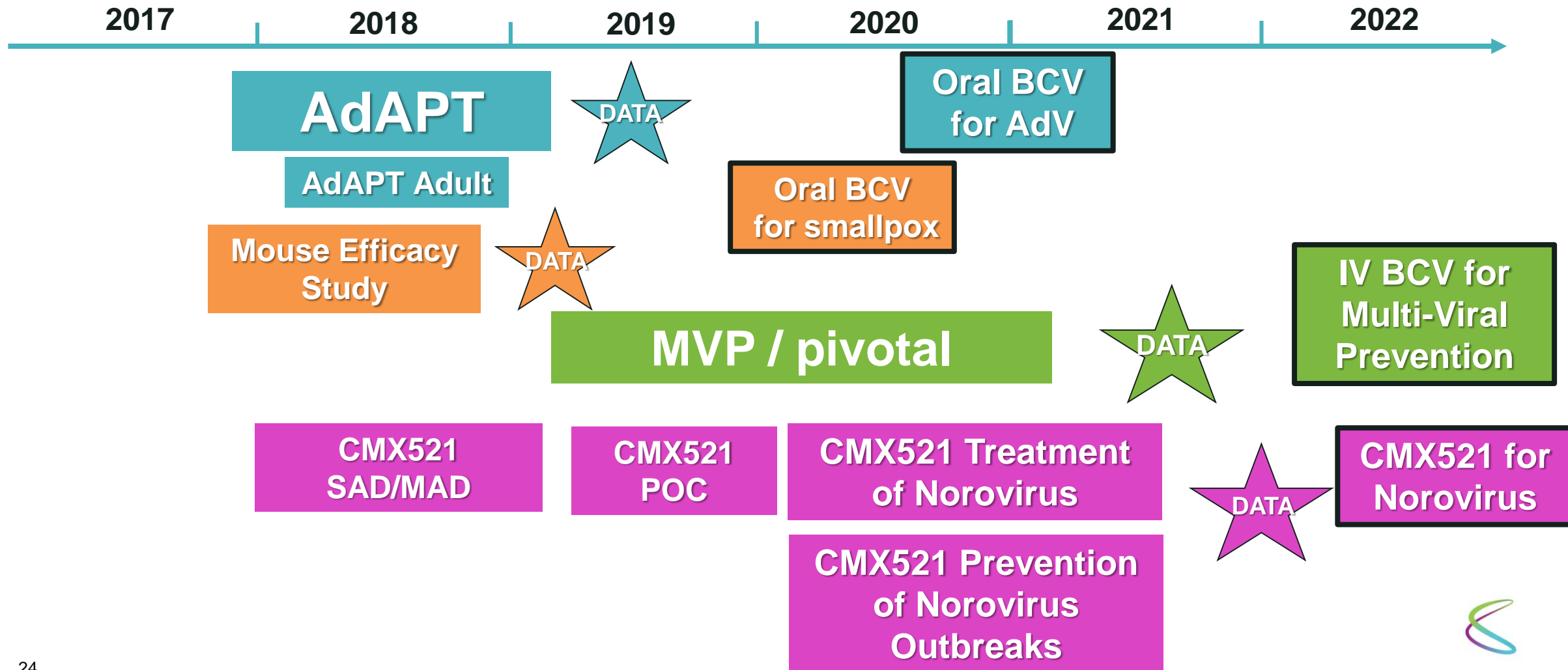
- Increasingly recognized in immunocompromised patients:
  - Stem cell transplant recipients
  - Solid organ transplant recipients
  - Other immunocompromised patients including those on biologics
- Asymptomatic shedders who increase public health risks
  - Food handlers, healthcare workers

## ■ Prevention of Norovirus Outbreaks

- At-risk individuals who have been exposed to a *confirmed* case of norovirus
- 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







# CMRX: Building A Pipeline of Solutions for Patients at Risk of Serious Viral Infections





# 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 \$241M at the end of 3Q 2017
- Patent protection into 2034 for brincidofovir, and 2036 for CMX521