



# CHIMERIX

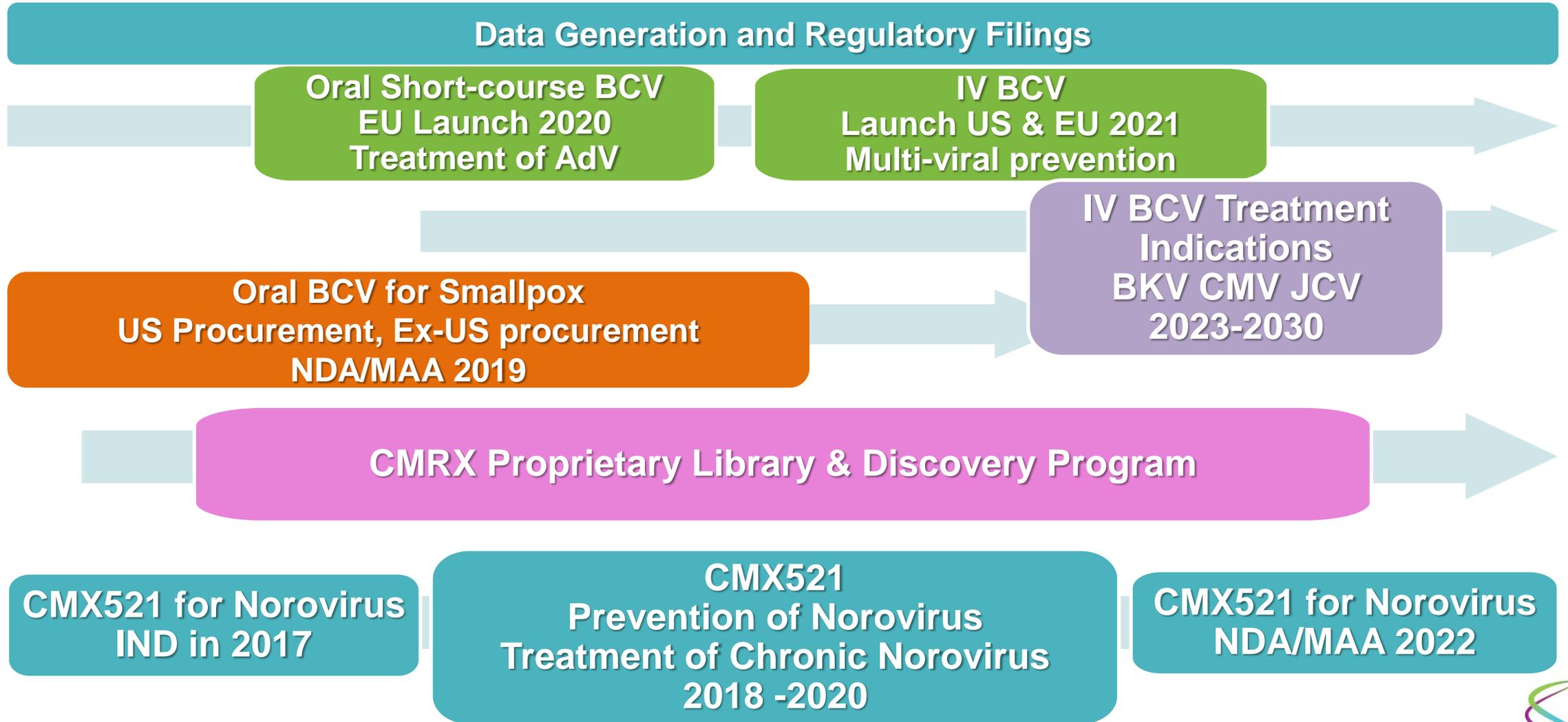
DISCOVERING, DEVELOPING, AND COMMERCIALIZING NOVEL MEDICINES THAT  
IMPROVE OUTCOMES FOR IMMUNOCOMPROMISED PATIENTS

**Garrett Nichols, MD, MS**  
**Chief Medical Officer**  
**March 7, 2017**

# 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. 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 year ended December 31, 2016 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.*

# Value Drivers for Chimerix



# Chimerix Pipeline

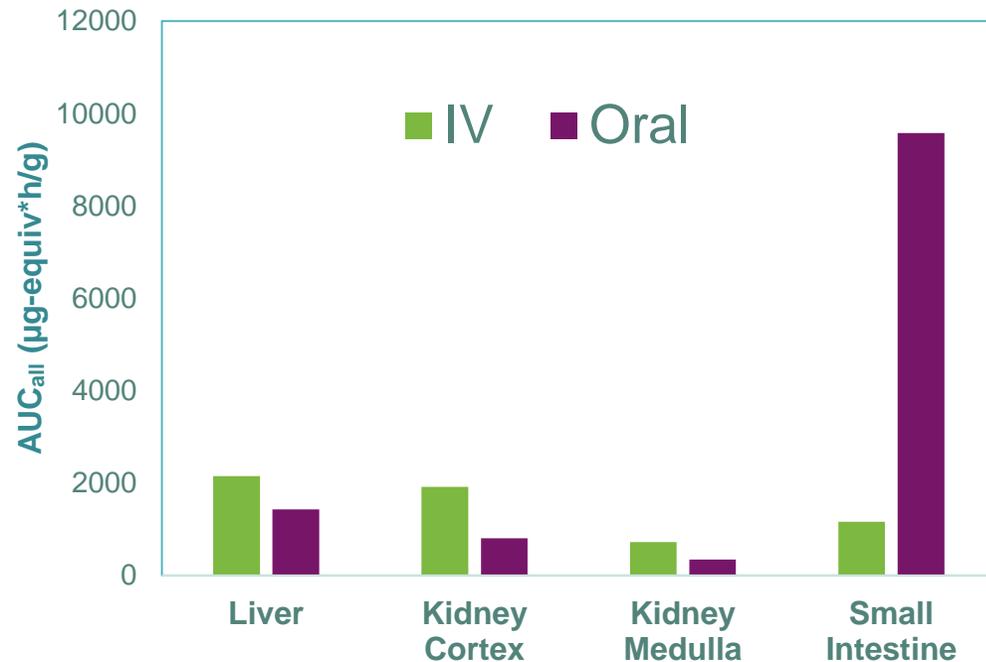
	Program	Discovery	Pre-clinical	Phase 1	Phase 2	Phase 3	Anticipated Approval
Short-course Oral BCV	AdV Treatment	Study 999 in EU (+/- US) to start in 2H 2017					2020
	Smallpox	Data from second animal efficacy model in 2017					2019
IV BCV	Multi-viral Prevention	Data from MAD in 2017		Ph 2/3 in Peds HCT			2021
	BKV Treatment	Initiate Phase 2b late 2017		Ph 2/3 in Kidney Tx			2023
	CMV Treatment	Initiate Phase 2b late 2017					
CMX521	Norovirus	IND 2H 2017		FTIH 4Q2017	POC Challenge Study		2022
CMX157	HBV Treatment	*Licensed to ContraVir					
Business Development		Ongoing Diligence					

# 2016 Brincidofovir Learnings

1. Gastrointestinal toxicity of oral brinci was related to GI “over-exposure” and duration
2. High brinci plasma exposures delivered via the intravenous route in animal studies did not result in the gut injury observed with oral brinci dosing
3. IV brinci provides higher drug levels in plasma and difficult-to-reach compartments in animals – allows exploration of treatment indications not possible with oral dosing
4. Oral brinci was associated with rapid AdV clearance in AdVise
5. Rapid clearance of AdV was associated with a decrease in overall and AdV-associated mortality in AdVise

# Key Learning #1: Oral BCV GI Toxicity is Related to GI “Over-exposure” and Duration

Total Drug Exposure ( $AUC_{all}$ ) in Clearance Organs (rats)



- Oral BCV in rats resulted in significantly higher exposures in the intestine vs other organs, *providing explanation for GI toxicity*
- In rats, IV BCV delivered comparable drug exposure to key organs, *including the liver, kidney, and small intestine*
- IV BCV without GI tox could support longer duration of therapy

***IV BCV is expected to prevent “over-exposure” of gut***

# Learning #2: IV BCV Delivers High Exposures without GI Tox

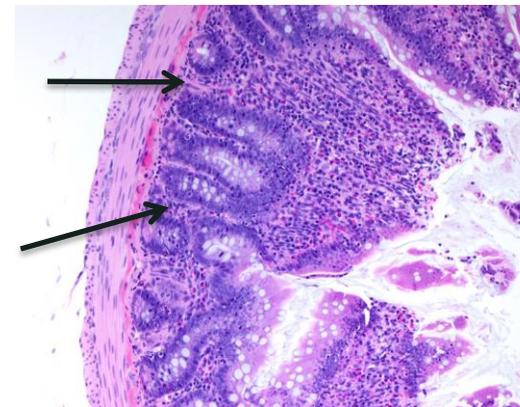
## 28-day rat studies of IV BCV:

- **No in-life clinical findings** at highest dose: IV BCV 15 mg/kg
- **No** animals had diarrhea
- **All** animals gained expected weight during study
- **No** liver enzymes elevations
- **Minimal GI findings** in intestines at final pathology



### Rat intestine after oral BCV

- Significant loss of epithelium in intestinal villi

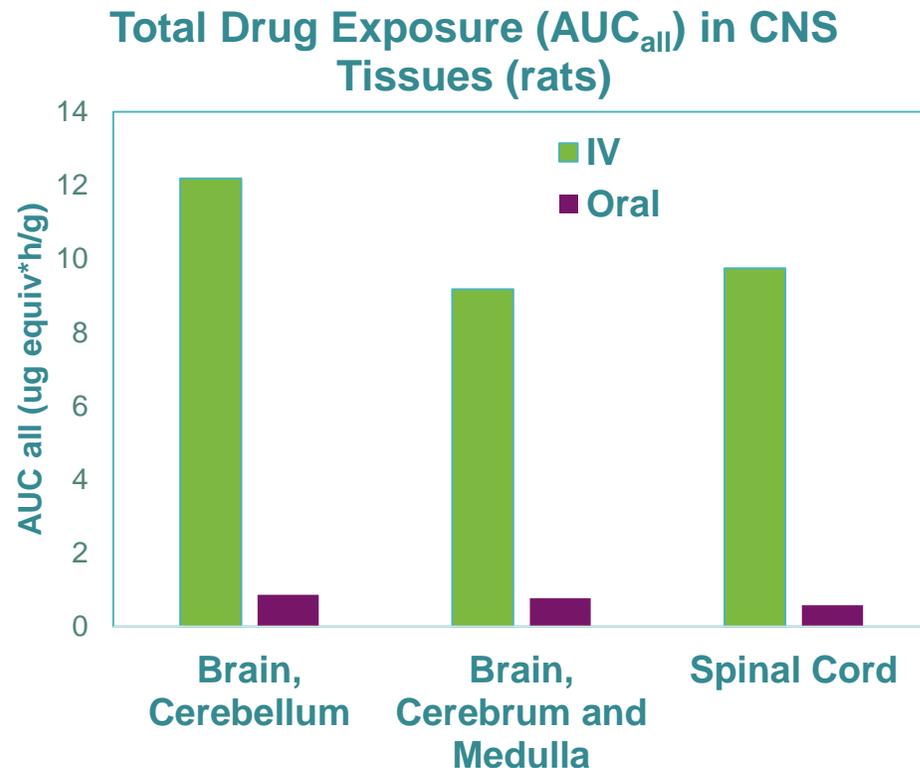


### Rat intestine after IV BCV

- Minimal single-cell effects noted for IV BCV

*IV BCV for 28 days avoided gut injury observed with oral BCV*

# Learning #3: IV BCV Raises the Exposure Ceiling, Delivers More Drug to Plasma and to Difficult-to-Reach Compartments

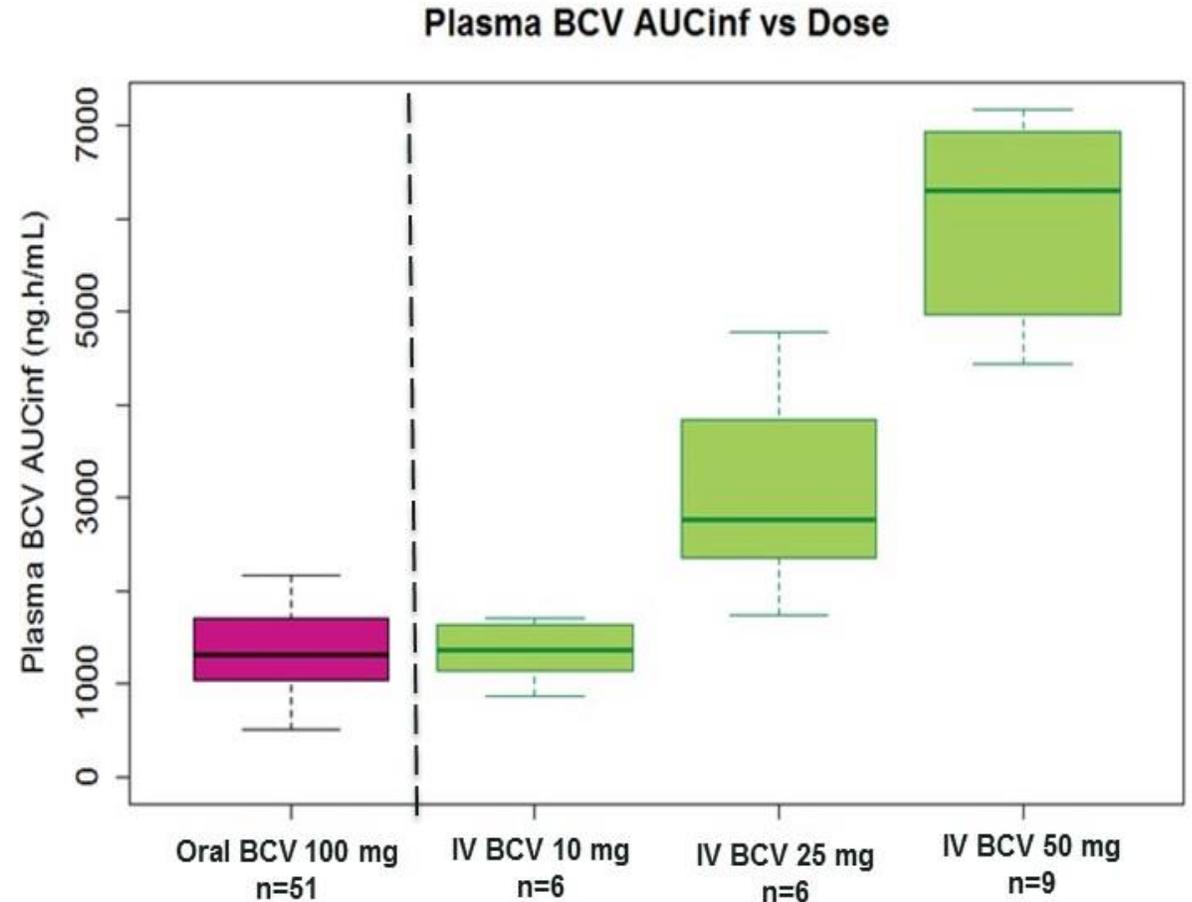


- IV BCV provides higher exposures which may be needed for some treatment indications (BK nephropathy, CMV disease)
- Higher CNS exposures with IV BCV could support testing for viral infections in the brain, e.g.:
  - Herpes encephalitis
  - HHV-6 encephalitis
  - JC virus/PML in transplant recipients or patients with Multiple Sclerosis

***IV BCV enables exploration of treatment indications not possible with oral BCV***

# Ongoing IV BCV Single Ascending Dose Study: Drug Levels

- IV BCV/placebo 10 mg, 25 mg, & 50 mg cohorts have completed dosing in healthy subjects
- IV BCV 10 mg provides similar exposure as oral BCV 100 mg
- Drug exposure was linear as dose was increased
- IV BCV 50 mg provided plasma drug exposures higher than achieved with oral BCV, and above the range of exposures targeted for treatment indications such as CMV and BK nephropathy



# IV BCV Single Ascending Dose: Preliminary Safety & Tolerability

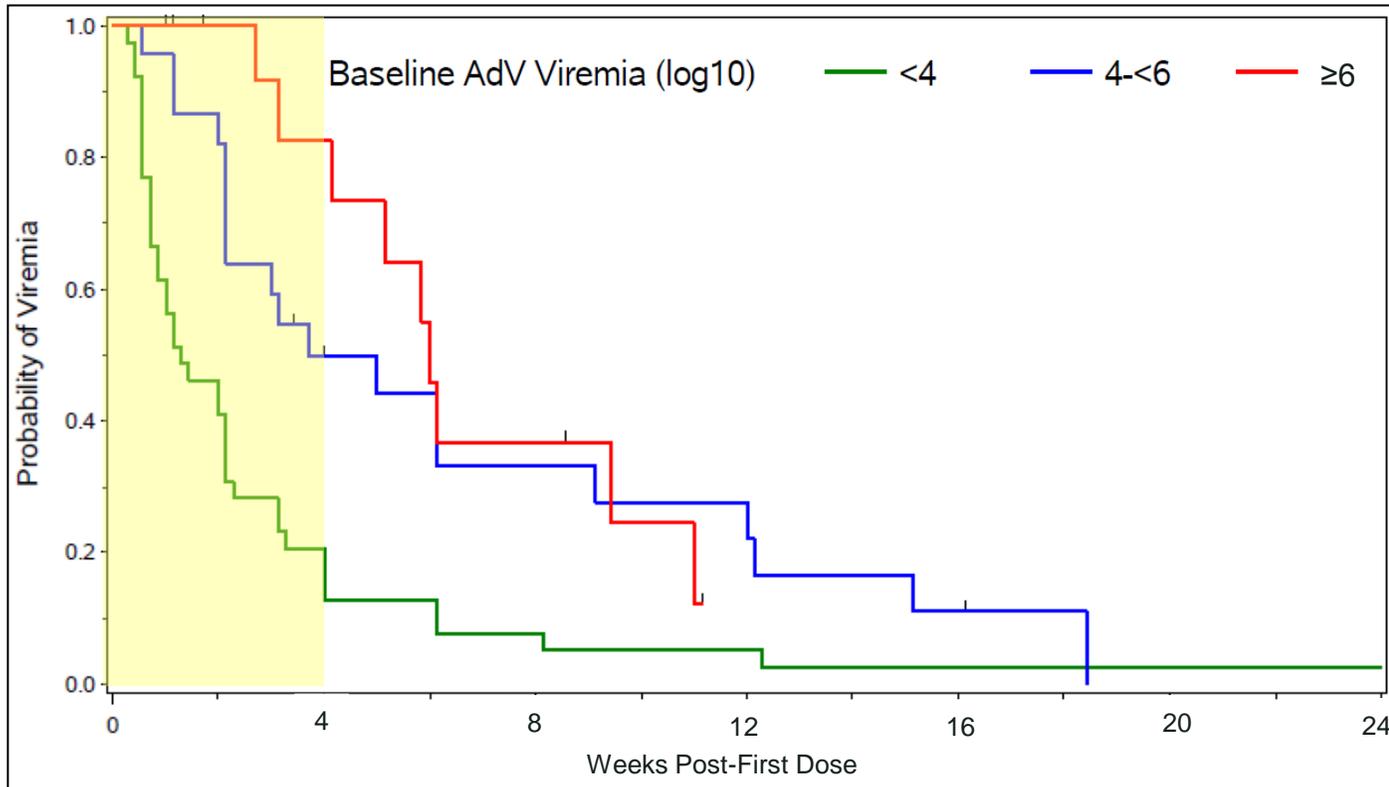
- Cohorts 1-3 IV BCV/placebo doses have been generally safe and well-tolerated:
  - Grade 1-2 lab abnormalities in Cohorts 1, 2 & 3, none clinically significant
    - No myelotoxicity or nephrotoxicity
  - Study-drug related Adverse Events were mild, and limited to Cohort 3
    - 3 subjects with IV site bruising/discomfort
    - 2 subjects with headache (resolved spontaneously)
    - 1 subject with loose stools (resolved spontaneously)

***Observed GI tolerability of single dose IV BCV through Cohort 3 in humans is improved compared to single dose oral BCV***



# Learning #4: Early Intervention Resulted in Undetectable AdV Viral Loads in the First 4 Weeks of Dosing in AdVise

Time to AdV plasma clearance (pediatrics)



- Pediatric pts with lower AdV viral loads at baseline (<10,000 or 4 log<sub>10</sub> c/mL) cleared within a median 8 days of BCV
- Pediatric pts with AdV <5 log<sub>10</sub> c/mL (<100,000): 72% cleared within 4 wks
- Study 999 will enroll at transplant centers that screen for AdV, more who are likely to detect and treat AdV viremia while viral loads are ~5 log<sub>10</sub> or lower

**Short-course oral BCV should result in clearance of AdV in majority of patients**

# Learning #5: Virologic Response Is Associated with a Decrease in Overall Mortality and AdV-Associated Mortality in AdVise

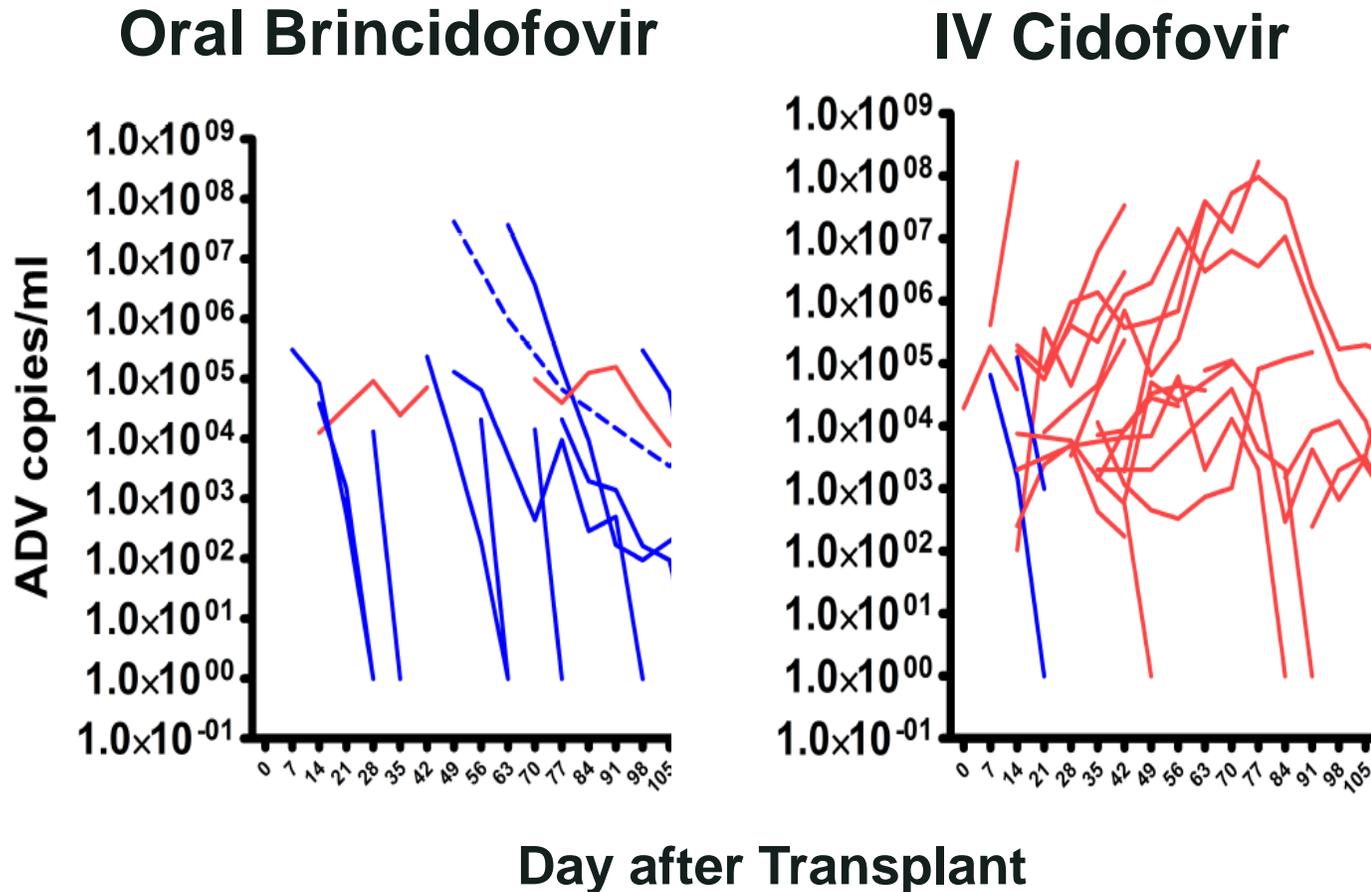
Patients with Disseminated AdV Disease		Mortality		AdV-Associated Mortality
Pediatric	Responder*	7/28 (25%)	} p=0.031	1/28 (4%)
	Non-responder	7/13 (54%)		2/13 (15%)
Adult	Responder*	5/10 (50%)	} p=0.0004	0/10 (0%)
	Non-responder	13/14 (93%)		10/14 (71%)

\* Responders are subjects with baseline AdV viremia still on study at week 6 who had undetectable plasma AdV at week 6; non-responders are subjects who did not achieve the specified cut-off

***Undetectable AdV was associated with nearly double the overall survival***



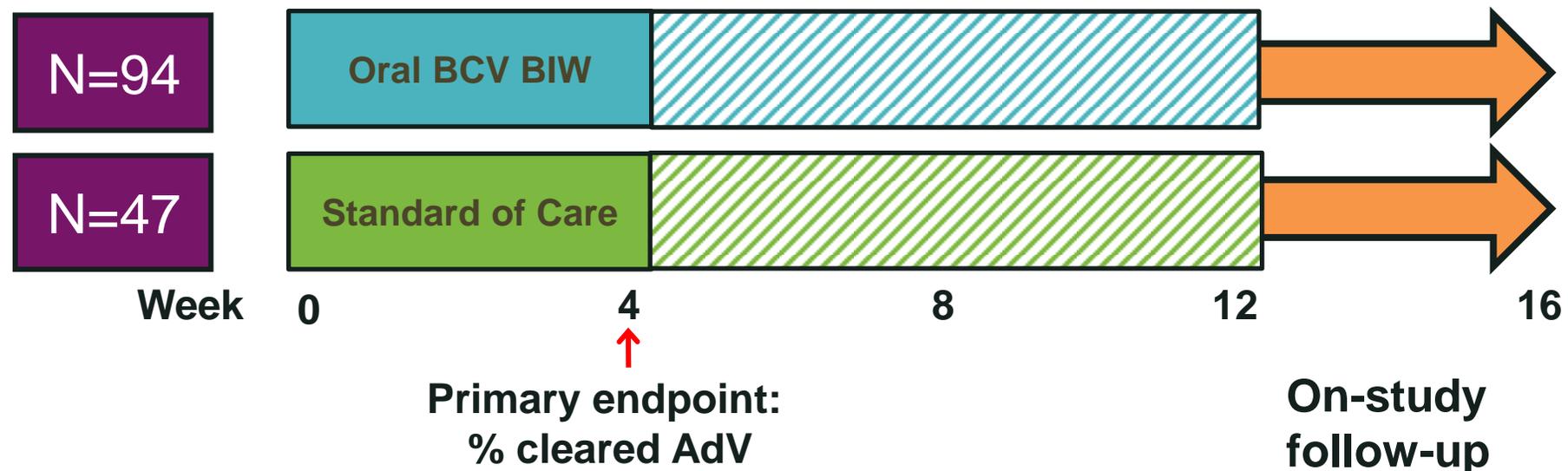
# Greater AdV Viral Load Reduction for Brinci vs Cidofovir in First 100 Days Post-Transplant from UK Consortium



- AdV  $2 \log_{10}$  c/mL decline in 2 wks (solid blue lines) was observed with oral BCV in 13/18 (72%) vs. 2/23 (9%) with IV cidofovir
- Complete response observed in 13 oral BCV patients (80%) vs. 8 patients with cidofovir (35%)
- Differences were greatest in first 100 days post-HCT (before immune reconstitution)

# Proposed Study 999: Short-course Oral BCV for Treatment of AdV in Pediatric HCT in First 100 Days Post-Transplant

- **Small, open label, comparative study of BCV vs. standard of care**
  - Inclusion: pediatric T-cell depleted or cord blood HCT recipients with confirmed > 1000 c/mL AdV DNA in plasma, <100d from HCT
- **Duration: Treat until AdV cleared from plasma** (minimum 4 weeks, maximum 12 weeks)
- **Primary endpoint: % undetectable plasma AdV at Week 4**
  - N~140 (2:1, 90% power) for 70% vs. 40% response rate
  - Superiority of BCV in clearance of AdV from plasma could enable conditional or full EU Approval



# Next Steps for IV and Oral BCV

## Oral BCV

- Short-course dosing for treatment of AdV and smallpox continue in development
- Small comparative study in pediatric HCT recipients at high risk of AdV disease anticipated to begin in 2H 2017, potential for conditional or full approval in the EU based on positive data

## IV BCV

- Single Ascending Dose Study in healthy subjects continues, with one additional cohort nearing completion
- Multiple-ascending dose study in healthy subjects to initiate in 1H 2017
- Phase 2 dose-ranging studies in treatment of CMV and BKV infections anticipated
- Opportunity to explore a broad range of additional indications, esp CNS infections
- Ability to dose for longer durations with lower risk of GI tox allows pursuit of multi-viral prevention

***Our ability to provide BCV in oral and IV formulations enables development across multiple indications and populations, with the potential to address conditions without any approved therapies***



# Demonstrating IV BCV's Multi-Viral Prevention

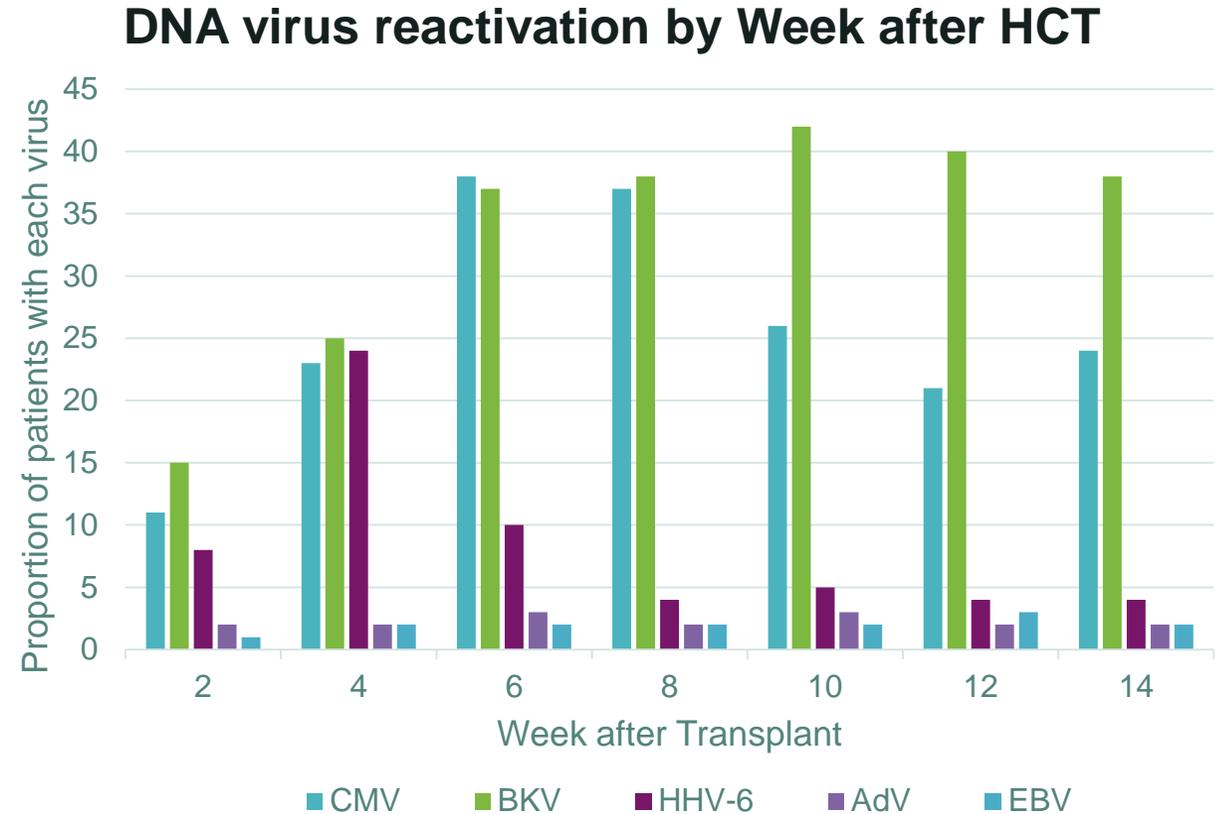
- Pediatric patients are at high risk for multiple DNA virus infections, with adenovirus-related mortality a particular concern
- The lower risk of GI toxicity with IV BCV may allow longer duration of dosing throughout high-risk period
- Proposal: **placebo-controlled trial of IV BCV in pediatric allogeneic HCT recipients**
  - Primary endpoint of prevention of adenovirus allows placebo control
  - Secondary endpoint of prevention of CMV, as high-risk pediatric HCT recipients tend to reactivate AdV earlier than CMV
  - Other secondary endpoints to include other DNA virus prevention and health outcomes
- Benefits:
  - Superiority design allows smaller study than head-to-head trial for CMV

***Details of this study will be forthcoming at our Investor Event***



# Adult and Pediatric HCT Recipients Face Risks Beyond CMV

- Multiple DNA viruses commonly reactivate as early as the first week after transplant
- Of the HCT recipients who reactivated CMV, >75% had at least one other DNA virus identified and were at increased risk of mortality
- 1 in 3 HCT recipients had  $\geq 3$  DNA viral infections detected



***More DNA viruses reactivating = higher risk of death***

# Unmet Need Drives Ongoing Demand for Brincidofovir

- More than 300 patients received oral BCV for life-threatening AdV in 2016

	Pediatrics		Adults		TOTAL
	Asymptomatic	Symptomatic <sup>a</sup>	Asymptomatic	Symptomatic <sup>a</sup>	All
<b>EINDs/NPP</b>	-	<b>344</b>	-	<b>210</b>	<b>566<sup>b</sup></b>
<b>Study 202</b>	<b>24</b>	<b>3</b>	<b>10</b>	<b>2</b>	<b>39</b>
<b>Study 304</b>	<b>51</b>	<b>79</b>	<b>23</b>	<b>48</b>	<b>201</b>
<b>Study 350</b>	<b>10</b>	<b>19</b>	<b>5</b>	<b>23</b>	<b>68<sup>c</sup></b>
<b>Study 351</b>	<b>3</b>	<b>62</b>	<b>1</b>	<b>26</b>	<b>92<sup>d</sup></b>
<b>Total</b>	<b>88</b>	<b>465</b>	<b>39</b>	<b>321</b>	<b>966</b>

<sup>a</sup>Includes local and disseminated AdV disease

<sup>b</sup>Includes 12 pts whose age is not known; assumes that EIND/NPP pts are symptomatic; Includes 9 patients who received open-label BCV

<sup>c</sup>Grimley et al. EBMT 2013; total numbers includes all subjects with AdV identified as a primary or secondary DNA viral infection that could not be classified (N=68)

<sup>d</sup>Ongoing expanded access protocol, n=92 as of 22 Feb 2017



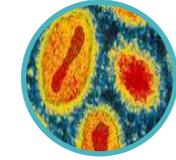
# SMALLPOX

Oral Brincidofovir for Treatment of Smallpox



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# Short-course Oral BCV for Smallpox



- Human safety summary of 3 weeks' exposure to oral brincidofovir submitted to FDA, manuscript published in peer-reviewed journal<sup>1</sup>
- Efficacy to be evaluated via two animal model studies under FDA's Animal Rule
  - Pivotal Rabbitpox Efficacy Study demonstrated 100% survival in animals treated immediately with BCV at the time of confirmed infection
  - Design elements of a pivotal efficacy study in a second animal model of smallpox are being finalized with BARDA
- FDA discussion to follow availability of mouse study data
- BARDA continues to prioritize smallpox for procurement to the Strategic National Stockpile
- We intend to apply for a PRV for smallpox under the 21<sup>st</sup> Century Cures Act

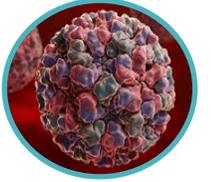


# NOROVIRUS

CMX521 for Norovirus



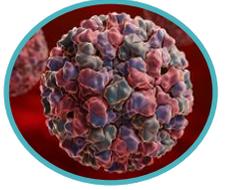
# Norovirus Treatment/Prevention Presents a Significant Opportunity



- Norovirus: RNA virus, previously referred to as Norwalk
- Noroviruses are the most common causes of epidemic acute gastroenteritis worldwide
- \$60B each year in healthcare utilization and lost productivity
- >60% of norovirus outbreaks in the US are in healthcare facilities which presents an opportunity for rapid identification and prophylaxis
- Chronic norovirus infection is increasingly recognized and presents a significant unmet need in immunocompromised population
  - Immunosuppressive therapy is a risk factor for chronic norovirus
  - Up to 20% of HCT & SOT recipients experience chronic symptoms of norovirus lasting weeks to years
- There are no approved drugs or vaccines for the treatment and/or prevention of norovirus



# Candidate for Norovirus: CMX521

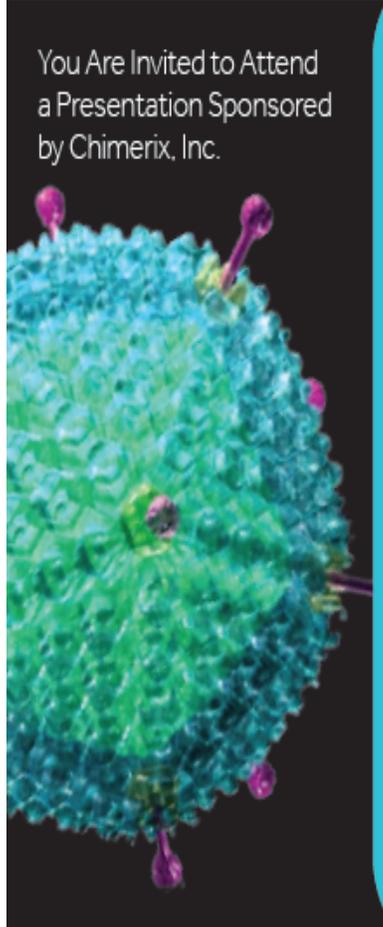


- CMX521: nucleoside that targets highly conserved viral RNA polymerase, enabling broad activity against diverse (likely all) wild-type strains
- High barrier to resistance *in vitro*, with >50 passages required to confer any mutations
- Proof-of-concept has been established in mouse model with oral delivery
- Toxicology studies are progressing in mouse, rat and dog, and suggest a very favorable safety profile
- IND submission and FTIH on track for 2017

	EC50 ( $\mu\text{M}$ )	CC50 ( $\mu\text{M}$ )	SI
<b>CMX521</b>	2.1 (n=33)	114	54

# Educational Efforts Continue to Build

- Multiple activities scheduled for the European BMT Meeting in March
  - KOL Advisory Board
  - Chimerix supported educational presentation on March 27, 2017
- Several oral presentations and abstracts of interest including:
  - Data from the Chimerix long-term registry study of patients from our trials
  - Data from the UK, France, Spain and the Netherlands summarizing their experiences using brinci to treat AdV infections



You Are Invited to Attend  
a Presentation Sponsored  
by Chimerix, Inc.

## Adenovirus Infections Post Hematopoietic Cell Transplantation: Epidemiology, Treatment, and Impact on Clinical Outcomes in the EU

Join our renowned faculty for an informative presentation on the epidemiology, treatment, and clinical outcomes of adenovirus infections after hematopoietic cell transplantation (HCT) in the EU. The faculty will provide updates on the biology and diagnosis of post-HCT adenovirus infections, including risk factors and early intervention techniques. Guidelines for screening and treatment of adenovirus after HCT will be reviewed and examined in light of preliminary data from an ongoing assessment of current practice patterns. Data from the UK on the treatment of adenovirus after HCT in a pediatric population will be shared, followed by an opportunity to ask questions of the faculty panel.

<small>Photo to come</small>	<b>Thomas Lion, MD, PhD</b> Medical Director, Labdia Labordiagnostik GmbH (LabDia) St. Anna Children's Cancer Research Institute (CCRI) Vienna, Austria	<small>Photo to come</small>	<b>Jean-Hugues Dalle, MD, PhD</b> Université Paris Diderot/Hôpital Saint-Louis Paris, France	<small>Photo to come</small>	<b>Prashant Hiwarkar, MBBS, MD</b> Consultant in Paediatric Haematology and BMT Royal Manchester Children's Hospital Manchester, England
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**DATE:** Monday, March 27, 2017  
**TIME:** 12:45 - 14:15

**LOCATION:**  
Palais des Congrès-Marseille Chanot  
Exhibit Hall Floor (between Poster Area  
and Hospitality Suites)

# Chimerix: 2017 Potential Catalysts

1H 2017

- IV BCV: Present final IV BCV clinical data from single ascending dose study, initiate multiple dose study
- CMX521 for Norovirus: IND-enabling studies

2H 2017

- IV BCV: multiple ascending dose clinical data
- Oral BCV: Initiate Study 999, small comparative AdV trial in pediatric HCT recipients for potential approval
- Initiate Dose-Ranging Studies in patients with CMV and BKV
- Data from second animal efficacy model for smallpox
- CMX521: Submit IND and initiate first clinical studies

***\$278 million in capital is sufficient to fund operations through anticipated catalysts in 2017***



**Q&A**

**THANK YOU**



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