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# Barclays 2017 Global Healthcare Conference

March 14<sup>th</sup>, 2017

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**Jon Stonehouse**, President & Chief Executive Officer



# Forward-looking statement

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BioCryst's presentation may contain forward-looking statements, including statements regarding future results, unaudited and forward-looking financial information and company performance or achievements. Although product candidates, including BCX7353, may demonstrate promising results in early preclinical studies and clinical trials, there can be no assurance that any candidate will prove to be safe and effective in subsequent studies or trials. In addition, there can be no assurance that the results of development will lead to an NDA submission or approval or that any product will be commercially successful. These statements are subject to known and unknown risks and uncertainties which may cause our actual results, performance or achievements to be materially different from any future results or performances expressed or implied in this presentation. You should not place undue reliance on the forward-looking statements.

For additional information, including important risk factors, please refer to BioCryst's documents filed with the SEC and located at

<http://investor.shareholder.com/biocryst/sec.cfm>

# BioCryst's strategy is to develop oral drugs for rare diseases

## Drug discovery through structure-based design

- BCX7353 and 2<sup>nd</sup> Gens
- Lead optimization underway for two additional rare disease targets

## Significant supporting capital from antiviral programs

- RAPIVAB® (peramivir injection) and Galidesivir
- Externally funded
- Stockpiling and voucher potential

**Oral  
Drugs For  
Rare  
Diseases**

**Help patients lead normal lives**

# Pipeline

	Lead optimization	Pre-clinical	Ph 1	Ph 2	Ph 3	Filed	Approved
<b>STRATEGY: Develop oral therapies for life-threatening, rare diseases</b>							
BCX7353 (HAE)							
Next generation kallikrein inhibitors							
Rare disease 1							
Rare disease 2							
<b>SUPPORTING ASSETS: Externally funded, potential for significant capital infusions</b>							
RAPIVAB® (peramivir injection)*							
Galidesivir (broad spectrum antiviral) I.M.							
Galidesivir (broad spectrum antiviral) I.V.							

\*licensed to Seqirus, Shionogi, & Green Cross in various geographies—additional filings anticipated

# First target in strategy: Hereditary angioedema (HAE) is a high-need, high-value disease

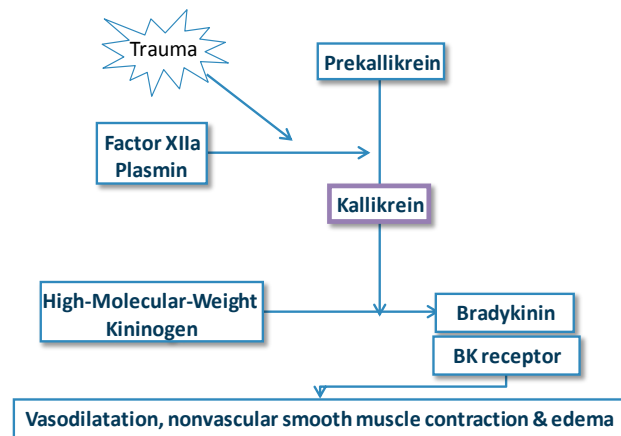


Unpredictable, debilitating, potentially life-threatening swelling attacks

- Rare (estimated global prevalence of 1:50K)
- Growing US market (\$1.2B, 30% growth in 2015)
- Significant global upside as paradigm shifts to attack prevention

High-value, growing market on track to exceed \$2.0B globally

Images obtained from [www.haeimages.com](http://www.haeimages.com)  
Market estimates based on analyst reports, earnings reports, and market data



Contact activation pathway is unbalanced based on genetic deficiency of C1 inhibitor (C1-INH)

- Plasma-derived C1-INH (chronic and acute, infusion)
- Androgen steroids (chronic, oral)
- Bradykinin inhibitor (acute, injection)
- Kallikrein inhibitor (acute, injection)

Current standard of care therapies are injected/infused

# APeX-1 Interim analysis summary

- In 28 HAE patients with frequent attacks (~ 1/ week), BCX7353 350 mg QD for 28 days showed statistically significant and clinically meaningful reductions in angioedema attacks
- Treatment effect was statistically robust

Endpoint	Analysis Population	Reduction compared to placebo - attacks/week (%)	p value
Weekly attack rate (weeks 2-4)	PP	0.572 (63%)	0.006
	ITT	0.474 (52%)	0.035

- > 80% reduction in unequivocal angioedema attacks, characterized by either peripheral symptoms only or a combination of peripheral and abdominal symptoms (“mixed”)
- Some abdominal symptoms reported as angioedema attacks may in fact have been GI-related AEs
- BCX7353 was generally safe and well tolerated: common cold and diarrhea were the most common AEs
- Blood levels of BCX7353 exceeded the proposed target range for efficacy
- Interim analysis results support evaluation of lower doses of BCX7353

# APeX-1 Interim analysis: Rate of overall confirmed attacks

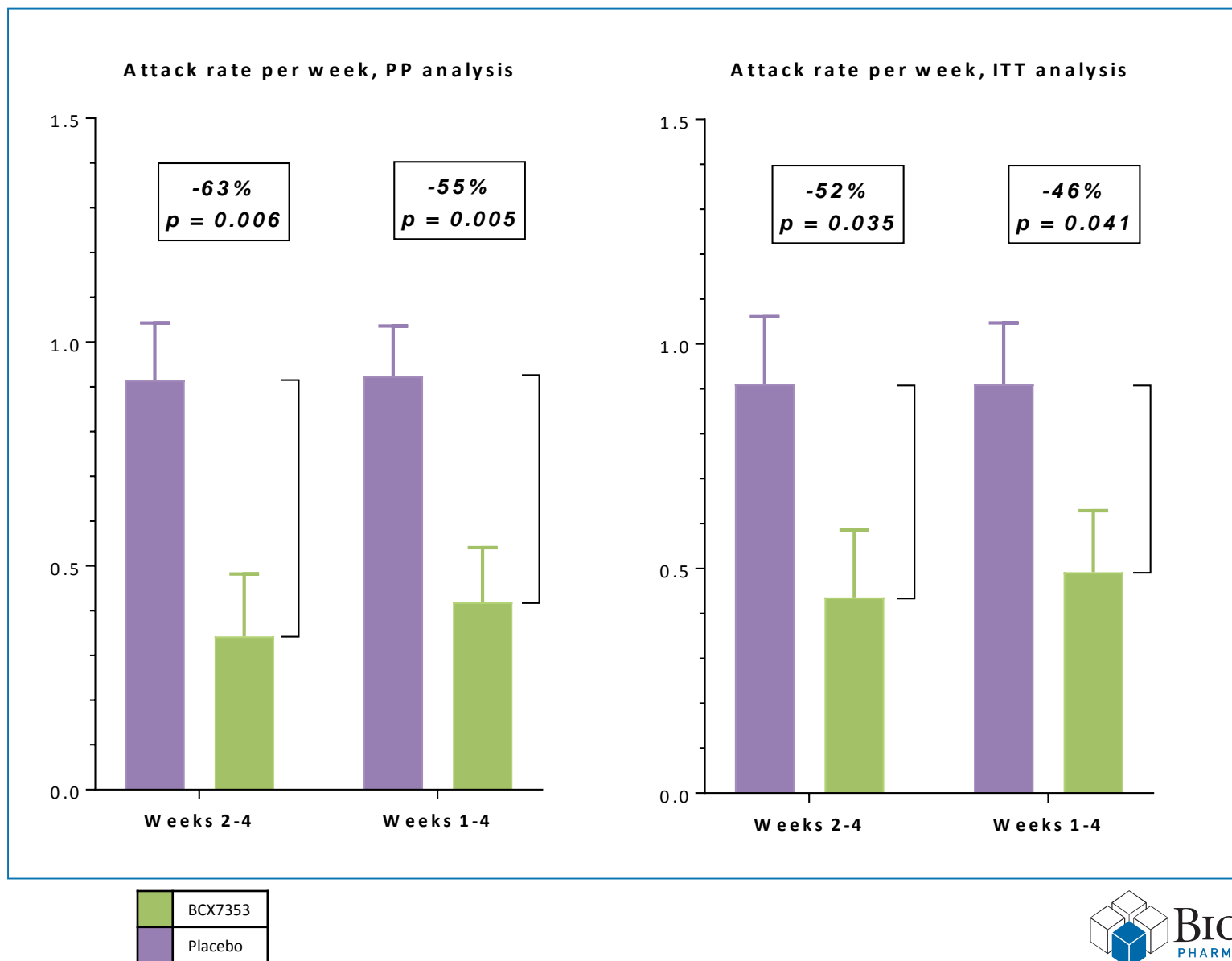
Treatment	n	LS mean <sup>1</sup> Attacks per Week	Difference vs Placebo	Percentage Reduction vs Placebo	p-Value vs Placebo
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Effective dosing period (Week 2-4) – PP Population					
BCX7353 350 mg	11	0.343	-0.572	63%	0.006
Placebo	13	0.915			

Effective dosing period (Week 2-4) – ITT Population					
BCX7353 350 mg	14	0.436	-0.474	52%	0.035
Placebo	14	0.911			

<sup>1</sup> Least squares mean calculated using an ANCOVA model with qualifying attack rate as covariate

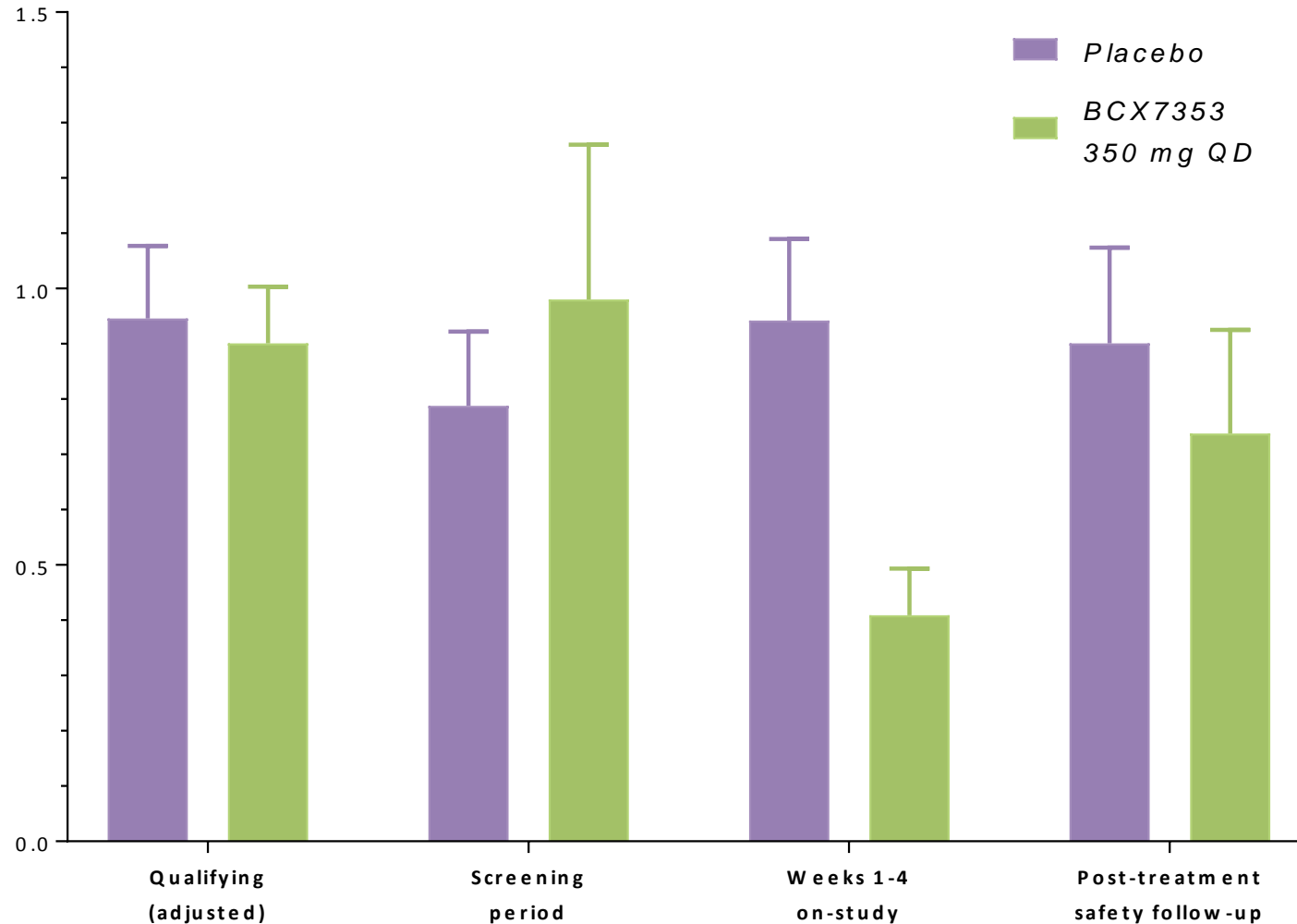
# APeX-1 Interim analysis: Overall angioedema attack rate





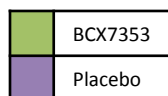
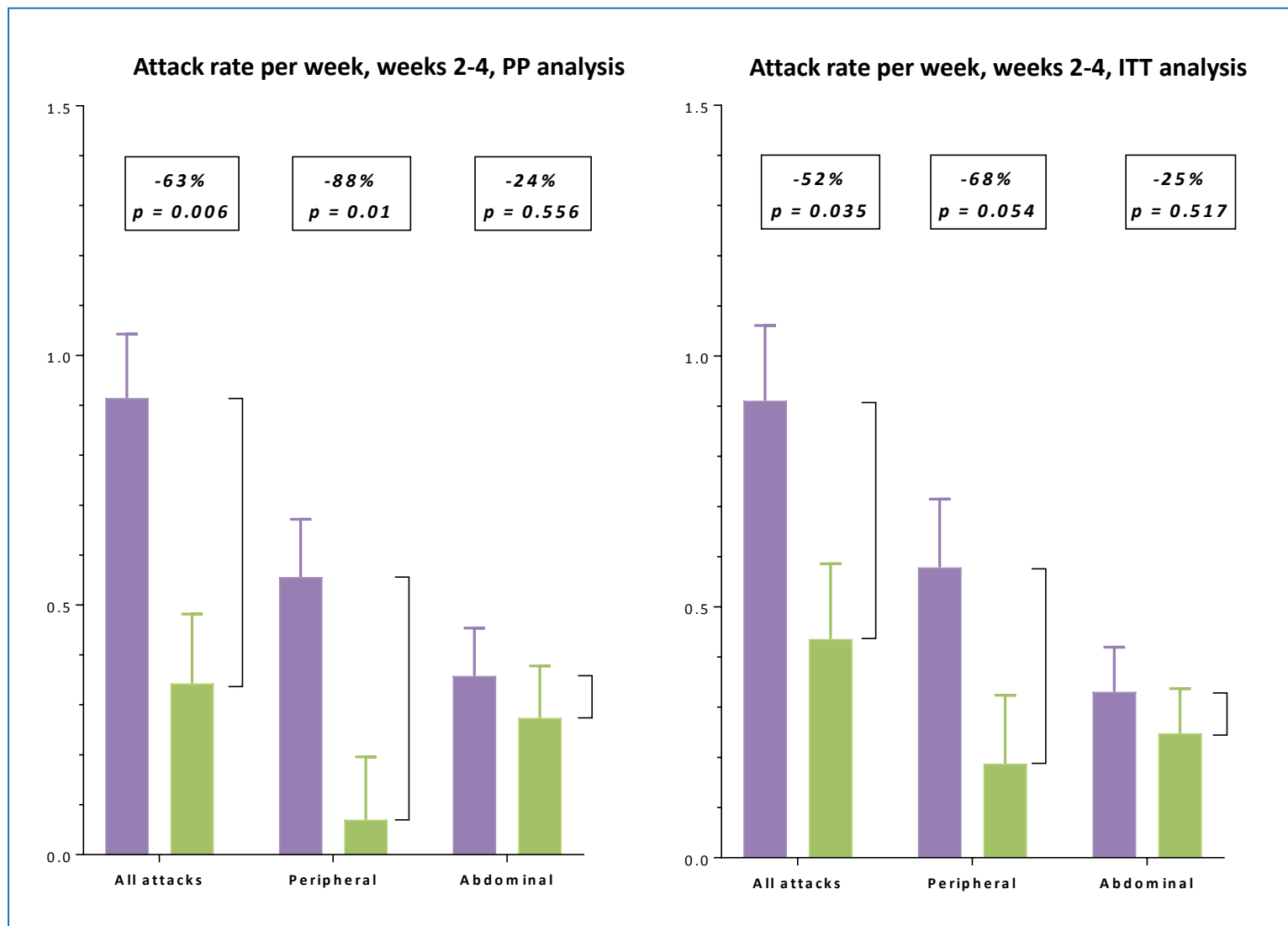
# Qualifying, screening period, on-study and safety follow-up attack rates – PP analysis

Attack rate per week before, during and after study, PP analysis



Qualifying attack rate data collected retrospectively by audit of medical or subject diary records and adjusted by combining attacks recorded on consecutive days as one attack.

# APeX-1 Interim analysis: Angioedema attack rates by pre-specified anatomical location



# APeX-1 Interim analysis: Angioedema attacks by anatomical category

	Peripheral		Mixed		Abdominal	
Effective dosing period (Week 2-4) – Per Protocol Population						
	Attacks	Subjects	Attacks	Subjects	Attacks	Subjects
BCX7353	2	2	2	1	7	5
Placebo	22	9	12	7	2	1
% Change vs Placebo	-91%		-83%		+250%	

Effective dosing period (Week 2-4) – ITT Population						
BCX7353	6	3	3	2	7	5
Placebo	25	10	12	7	2	1
% Change vs Placebo	-76%		-75%		+250%	

Clear imbalance in attack reduction by location. Subjects may not have been able to distinguish between BCX7353- related GI events and early signs of an abdominal attack.

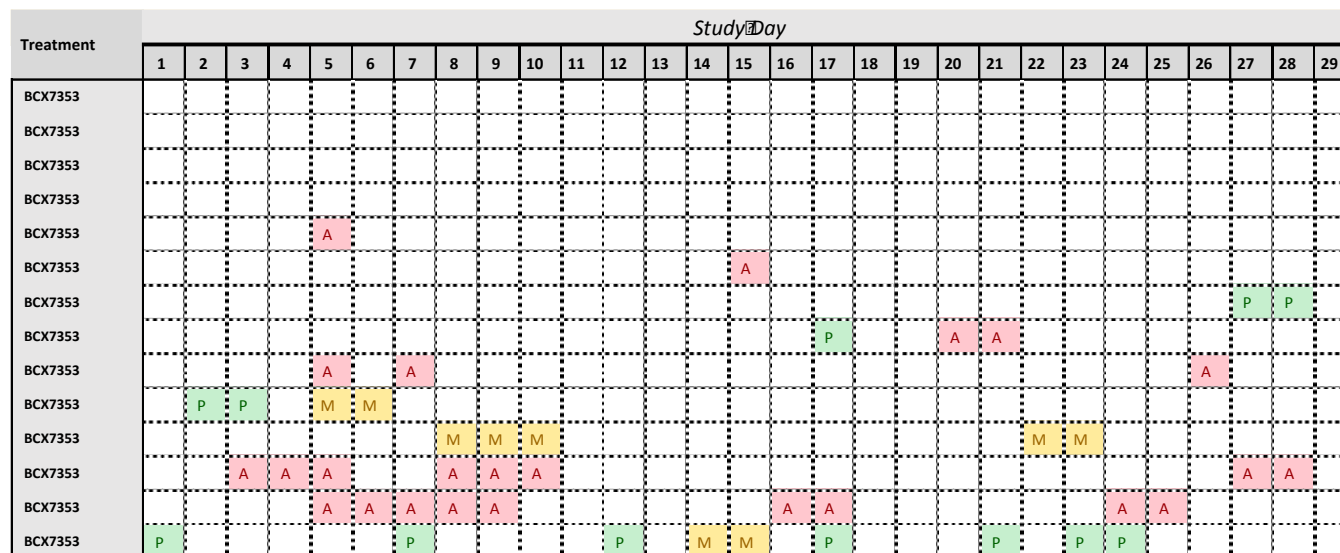
Post- hoc analysis

# APeX-1 Interim analysis: Analysis of gastrointestinal symptoms in the subject diary

AE or symptom	Reported as AE		Reported as attack-related symptoms			
			Mixed peripheral + abdominal attack category <sup>1</sup>		Abdominal-only attack category <sup>1</sup>	
	BCX7353 (n=14)	Placebo (n=14)	BCX7353 (n=14)	Placebo (n=14)	BCX7353 (n=14)	Placebo (n=14)
Abdominal pain	1 (7.1%)	0	1 (7.1%)	5 (35.7%)	7 (50.0%)	3 (21.4%)
Nausea	1 (7.1%)	0	1 (7.1%)	5 (35.7%)	4 (28.6%)	2 (14.3%)
Vomiting	1 (7.1%)	0	0	0	1 (7.1%)	1 (7.1%)

<sup>1</sup> Includes all subject-reported attacks, including those rejected by expert adjudication committee. Multiple reports of the same event in the same subject are only tabulated once

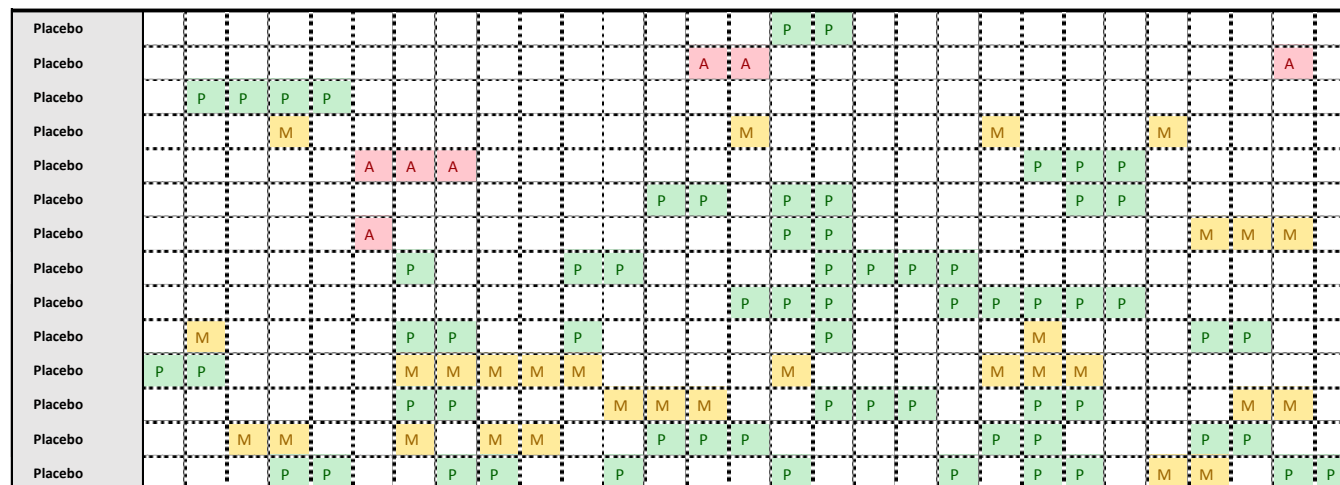
# APeX-1 Interim analysis: Days with any angioedema symptoms recorded in the subject diary, by anatomical category



A Abdominal only

M Mixed

P Peripheral only

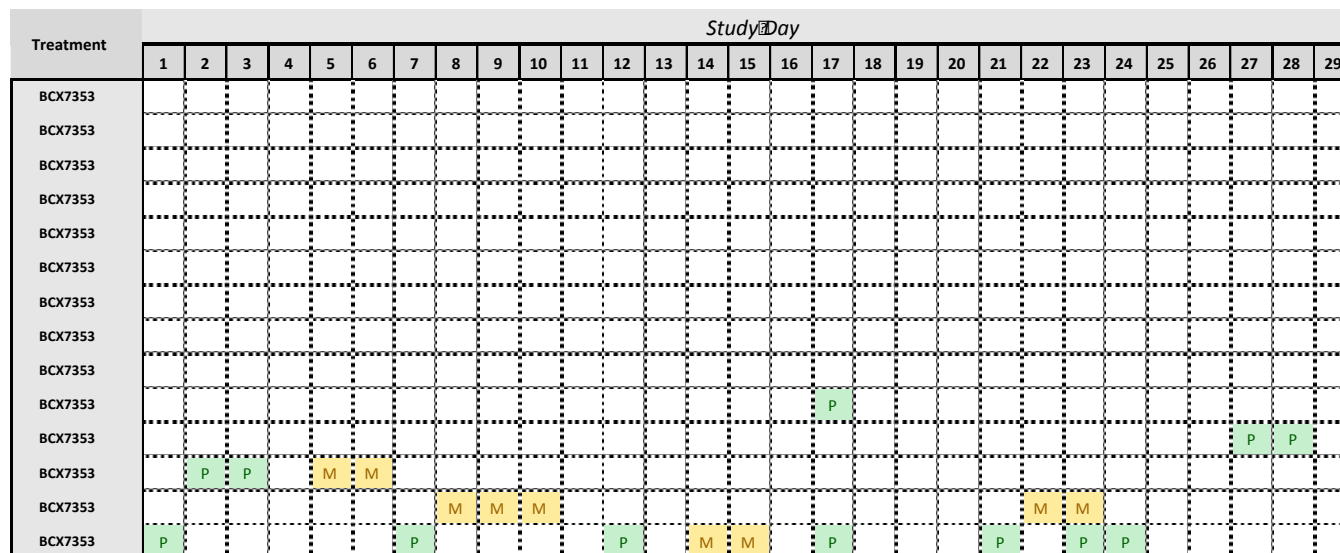


Post-hoc analysis including all days with any symptoms recorded by subjects as attack of HAE.

Analysis of ITT population, adjudicated attacks.

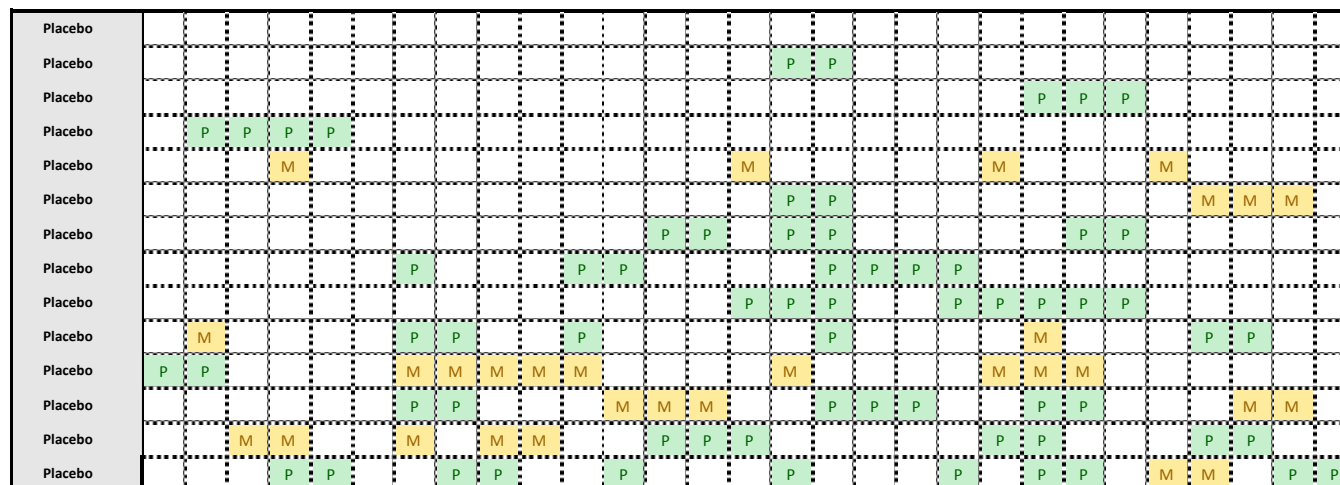
Study subjects (rows) in each treatment group ordered by increasing number of days with symptoms.

**APeX-1 Interim analysis: Days with unequivocal angioedema symptoms recorded in the subject diary, by anatomical category**



**M** Mixed

**P** Peripheral only



Post- hoc analysis excluding any attacks with only abdominal symptoms.

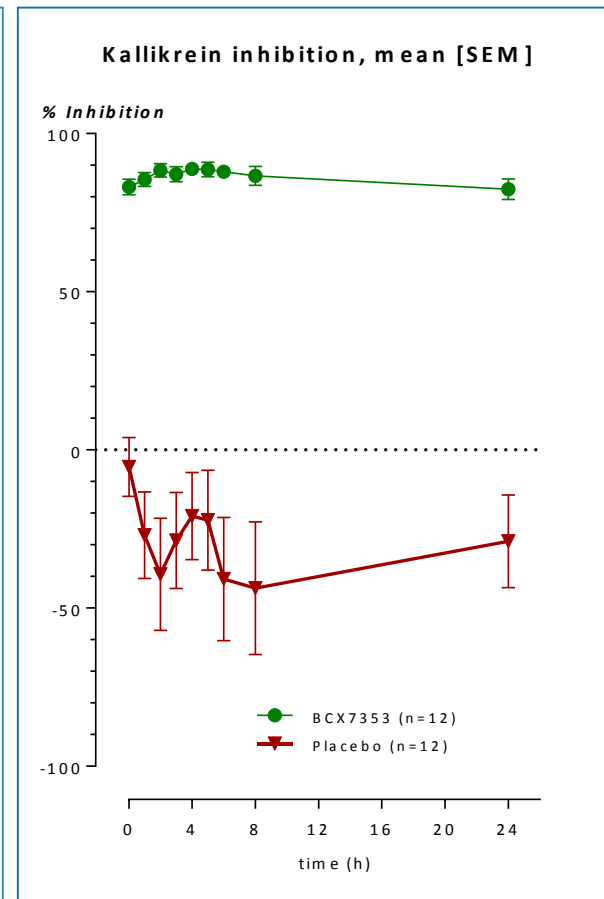
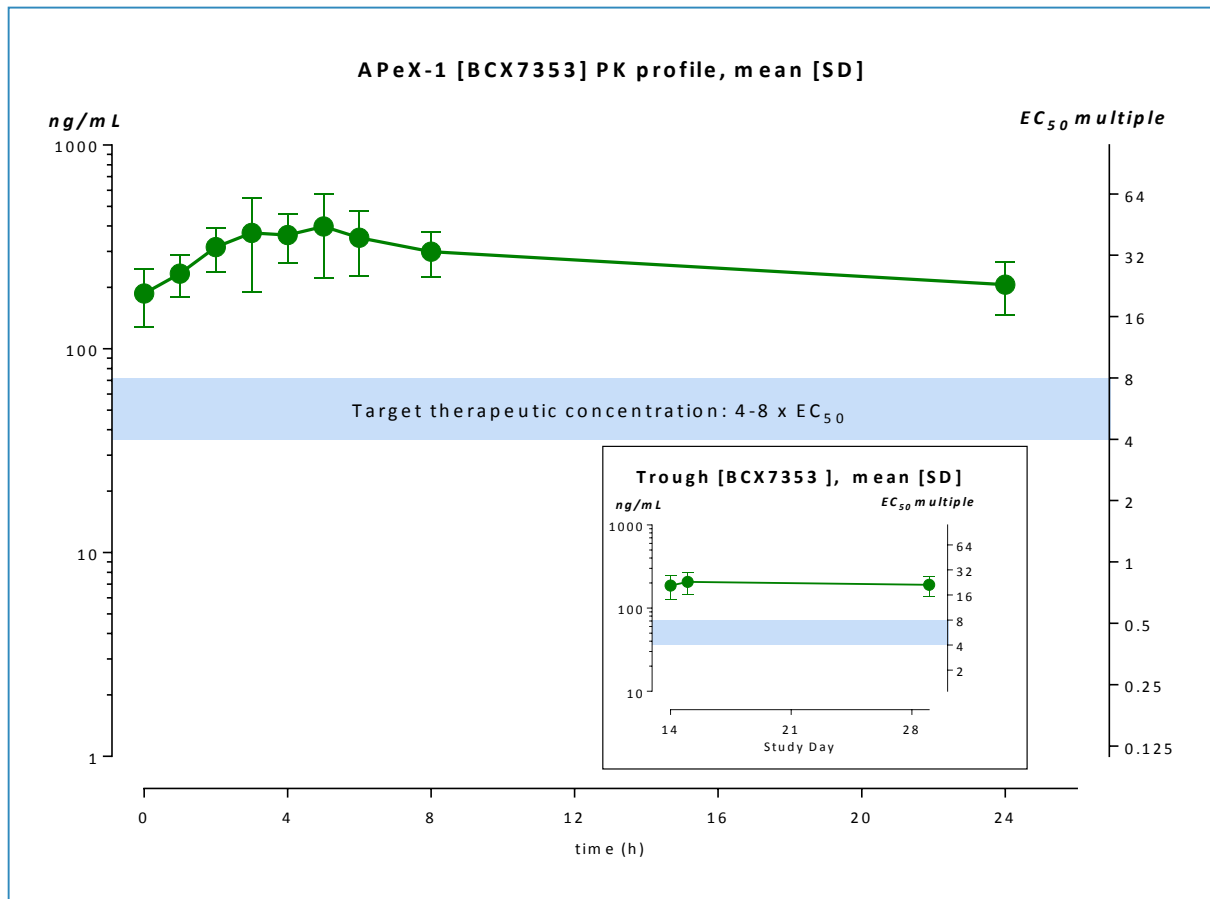
### Analysis of ITT population, adjudicated attacks.

Study subjects (rows) in each treatment group ordered by increasing number of days with symptoms

# BCX7353 APeX-1 interim analysis: Safety summary

Category	BCX7353 (n=14)	Placebo (n=14)
Number of Subjects with any Serious AE, n (%)	0	0
Number of Subjects with Drug-Related AE of Grade 3 or Grade 4, n (%)	0	0
Number of Subjects with AE Leading to Discontinuation from Study Drug, n (%)	2 (14.3)	0
Non- drug-related, n (%)		
Pre-existing liver disorder (improved from baseline, but persisting)	1 (7.1)	0
Drug-related, n (%)		
Gastroenteritis (unrelated) with liver disorder (related) (elevated ALT 1.9x ULN, GGT 5.4x ULN and ALP 1.6x ULN, with normal AST and bilirubin)	1 (7.1)	0
Treatment-Emergent Adverse Events occurring in ≥2 subjects overall, n (%)		
Nasopharyngitis (common cold)	3 (21.4)	4 (28.6)
Diarrhea	4 (28.6)	2 (14.3)
Flatulence	2 (14.3)	0
Fatigue	2 (14.3)	0
Clinically significant changes in clinical chemistry, hematology or urinalysis, n (%)		
ALT elevation > 3X ULN (ALT 3.9 x ULN, AST 1.8 xULN, GGT10.7 X ULN) <i>Pre-existing colitis, hepatic steatosis (fatty liver), &gt; 20 years androgen use until 3 years prior to study, Baseline increase in liver enzymes</i>	1 (7.1)	0

# Blood drug levels of BCX7353 with once daily oral dosing of 350mg were well above target range



- Trough plasma levels between 11-32 fold of the EC<sub>50</sub> of BCX7353
- Kallikrein inhibition sustained throughout the dosing interval

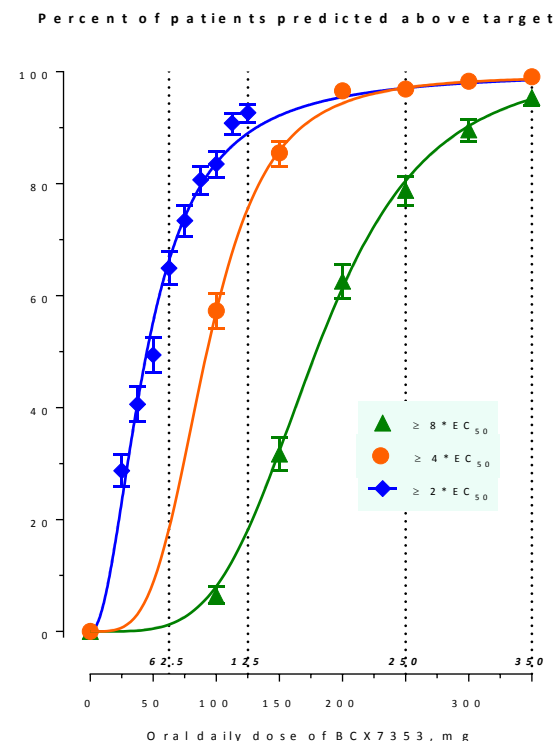
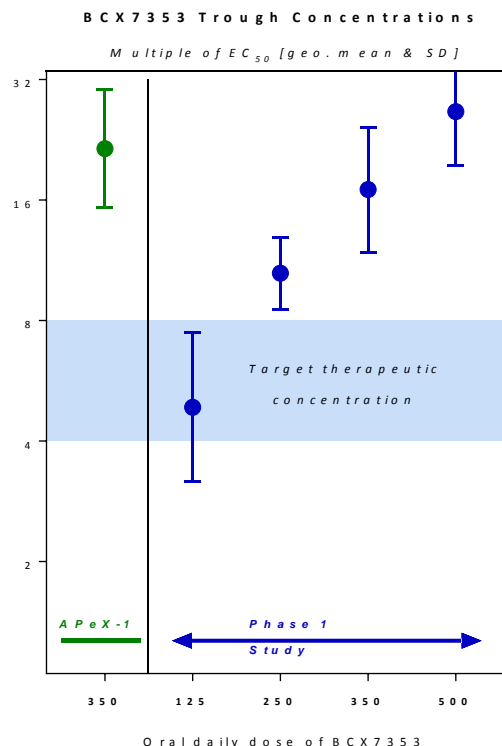
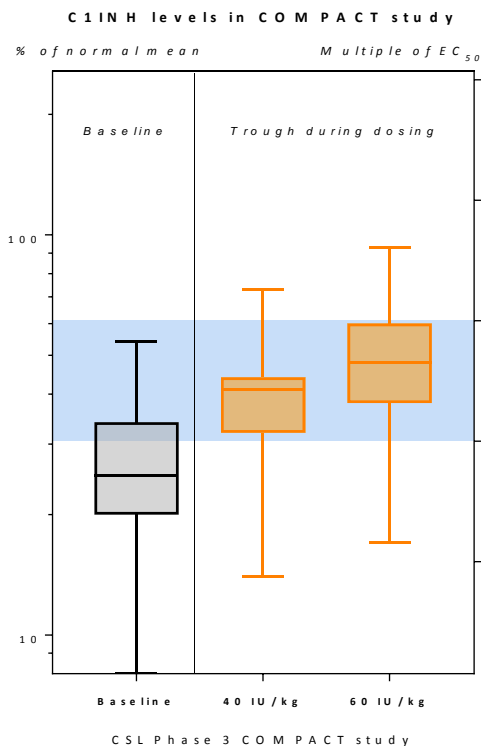


# Exposure comparisons and population PK modeling support evaluation of lower doses of BCX7353

CSL-830 Phase 3 study

BCX7353 APeX-1 & Phase 1

PK Modeling



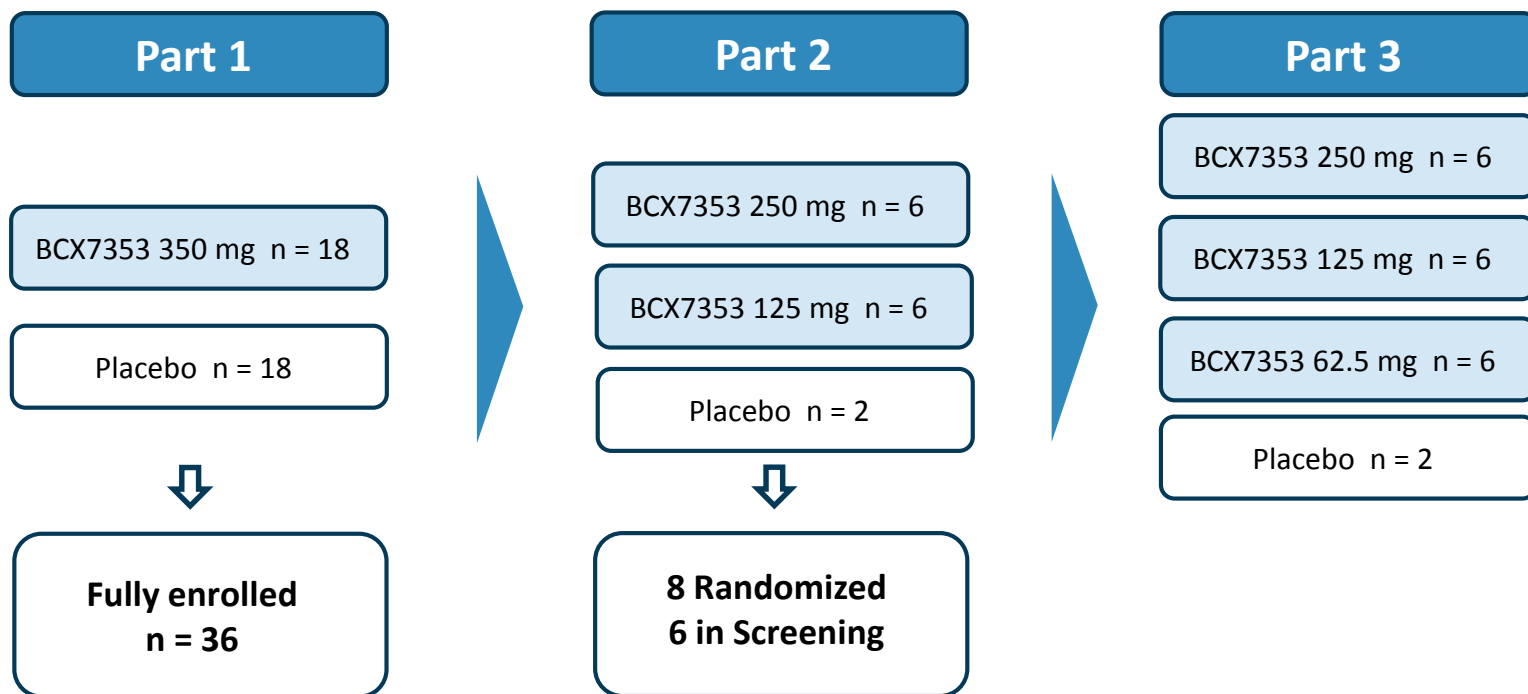
C1INH levels at baseline and after SC dosing with CSL-830<sup>1</sup>

BCX7353 plasma concentrations at 24 hours post-dose

Monte Carlo simulation: 1000 subjects per data point

<sup>1</sup> Zuraw, B. L. *et al.* Presentation at ACAAI 2016. Box plots represent median, 25<sup>th</sup> and 75<sup>th</sup> percentiles, minimum and maximum values. CSL-830 and BCX7353 data are from distinct clinical trials and no head to head study has been conducted.

# APeX-1: Update



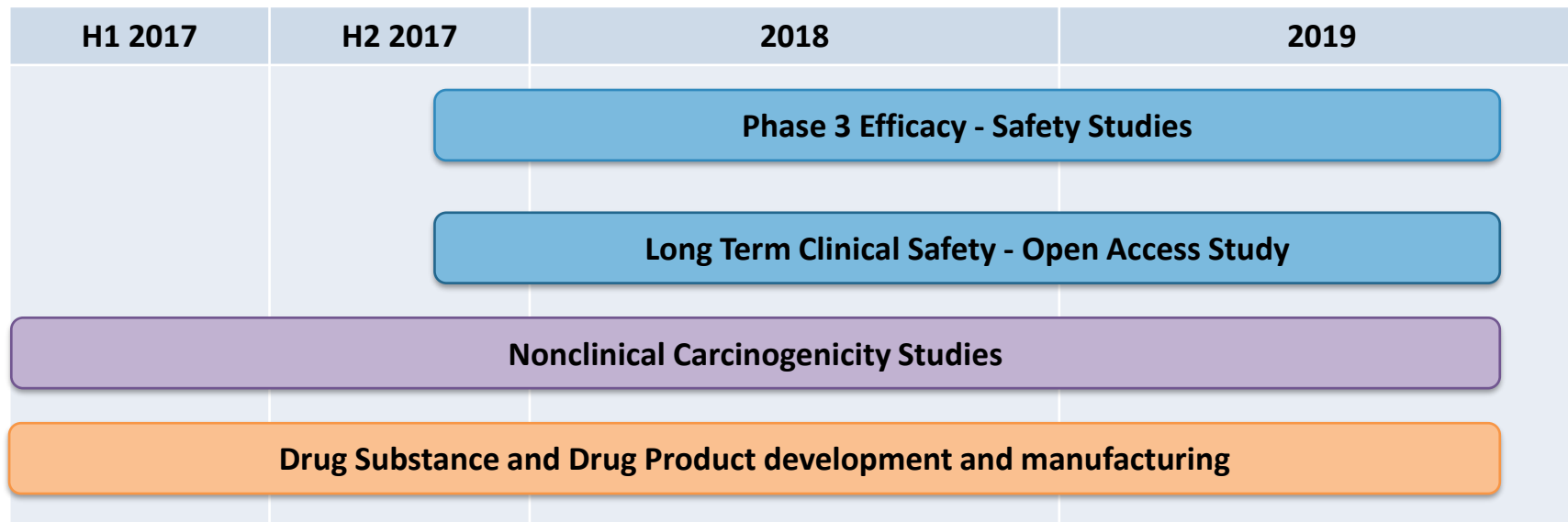
Part 2 data expected 2Q2017

Adding Part 3 with lower dose cohort (62.5 mg) to ensure full evaluation of dose response


Enrolment update reported February 27, 2017.

# BCX7353 Remaining activities after APeX-1

Estimated timing of key activities to support NDA/MAA filing

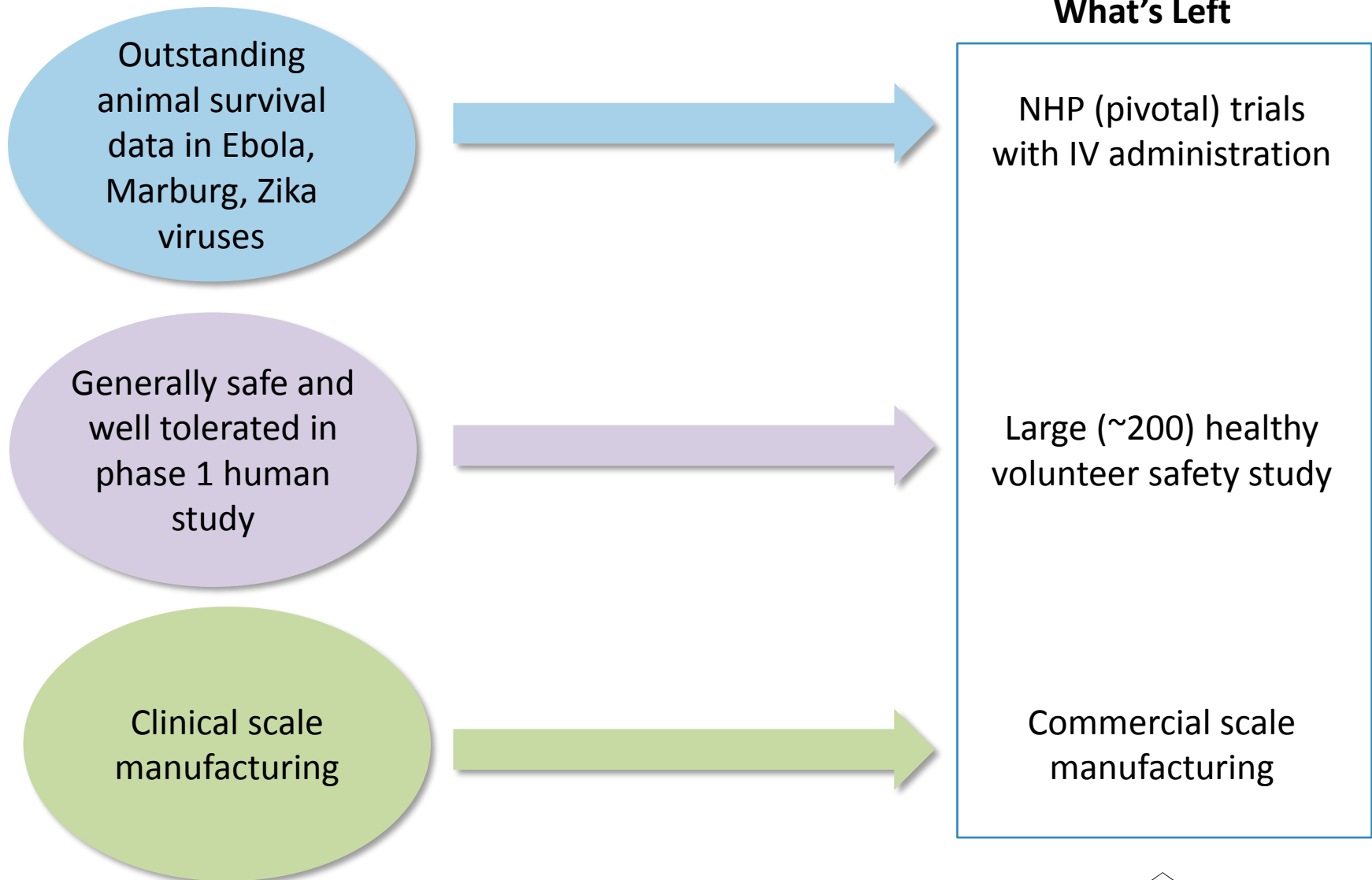


# Antiviral programs are externally funded, generating \$400M to date with the potential for significant future capital infusions

Antiviral Program	Indication	Development funding	Additional capital infusions
	First and only one-dose IV treatment for influenza	Over \$200M US Government funding to support development and approval	<ul style="list-style-type: none"> <li>• Over \$90M in milestones and royalty monetization</li> <li>• Over \$25M in Government stockpiling (Japan/US)</li> </ul>
<b>Galidesivir (BCX4430)</b>	<ul style="list-style-type: none"> <li>• Ebola is lead indication</li> <li>• Broad-spectrum activity observed in Zika, Marburg and several other virus families</li> </ul>	Approximately \$80M US Government contract development funding	<ul style="list-style-type: none"> <li>• Potential for Government stockpiling prior to FDA approval</li> <li>• Potentially eligible for FDA priority review voucher upon approval</li> </ul>

Broad-spectrum activity increases attractiveness of Galidesivir for Government stockpiling

# Galidesivir path to stockpiling and NDA



## Cash position and 2017 guidance (in millions)

Cash & investments at December 31, 2016	\$65
Pro forma 12/31/16 cash + net raise proceeds*	\$107
Senior Credit Facility	\$23
Cash runway without raise proceeds	Into 2018

### Guidance for 2017:

Operating cash utilization	\$30 – 50
Operating expenses <sup>#</sup>	\$53 – 73

<sup>#</sup> Excludes equity-based compensation.

\*Amount is based upon estimated Net Proceeds from \$45 million raise completed on March 9, 2017 (i.e., after deducting all transaction costs). No additional cash inflows are assumed.

# Building a company to generate expanding and sustainable value

