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# Jefferies Global Healthcare Conference

June 6<sup>th</sup>, 2017

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## 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. 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

# BioCryst's 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 – Oral (Prophylactic HAE)	→			→			
BCX7353 – Oral Liquid Formulation (Acute HAE)	→			→			
Second generation kallikrein inhibitors (HAE & Other Indications)	→						
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 and Green Cross

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

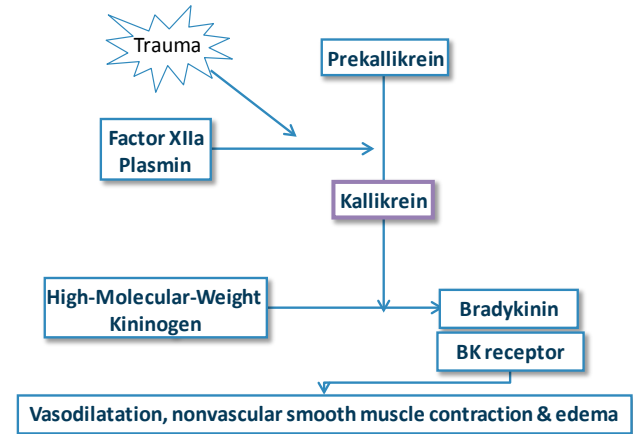


Unpredictable, debilitating, potentially life-threatening swelling attacks

- 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



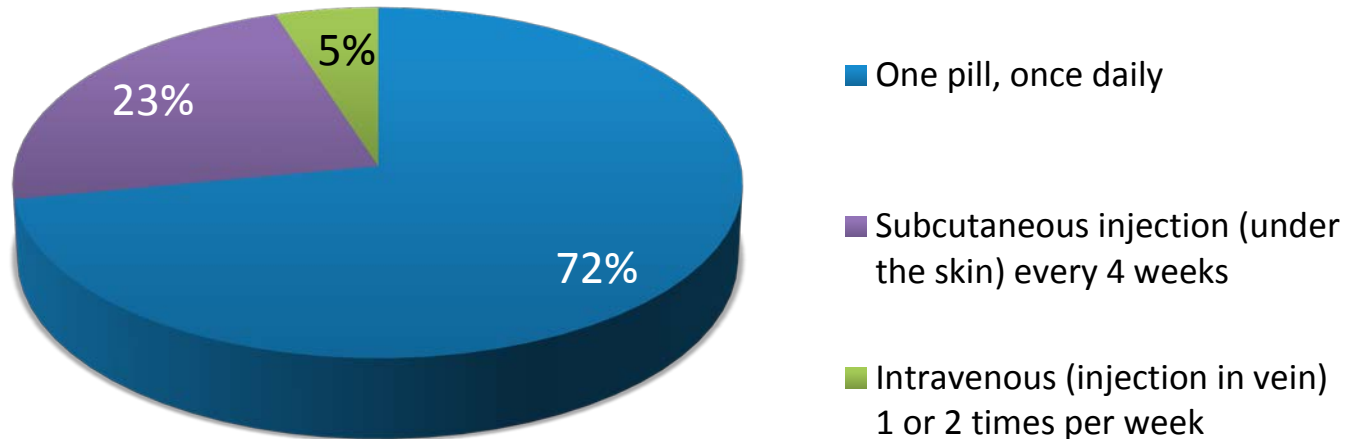
Contact activation pathway is unbalanced based on genetic deficiency of C1 inhibitor (C1-INH)

- 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

# Patients with HAE overwhelmingly prefer convenient oral therapy

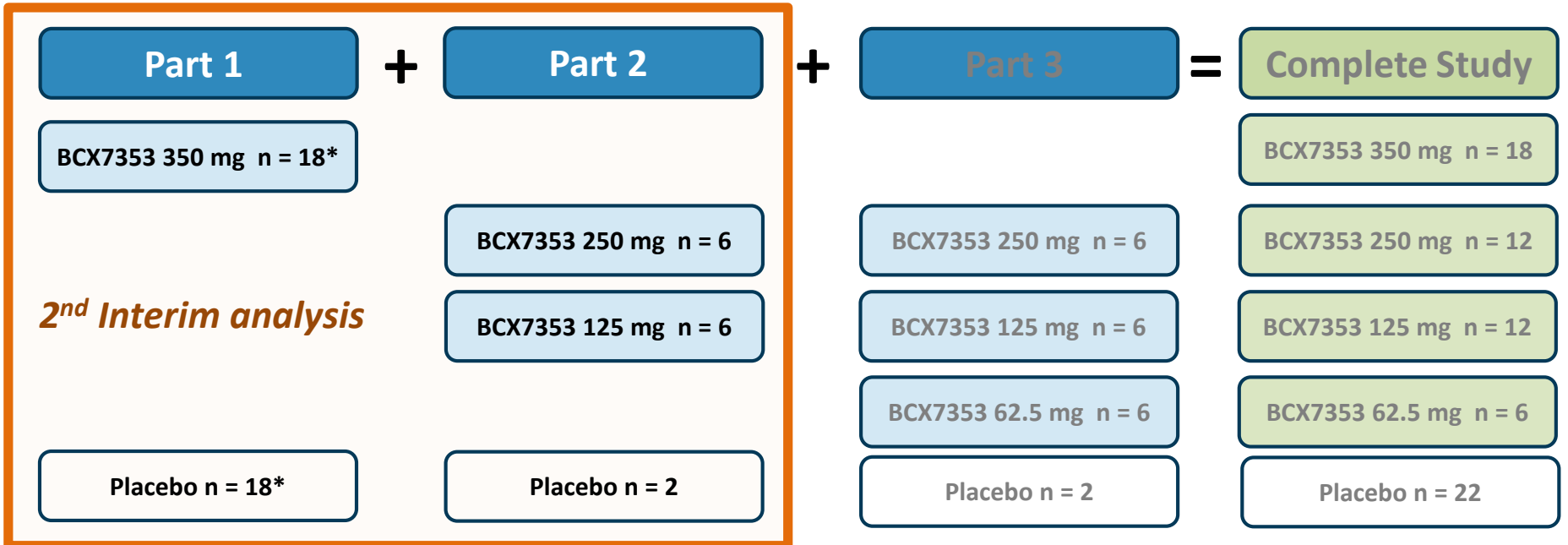
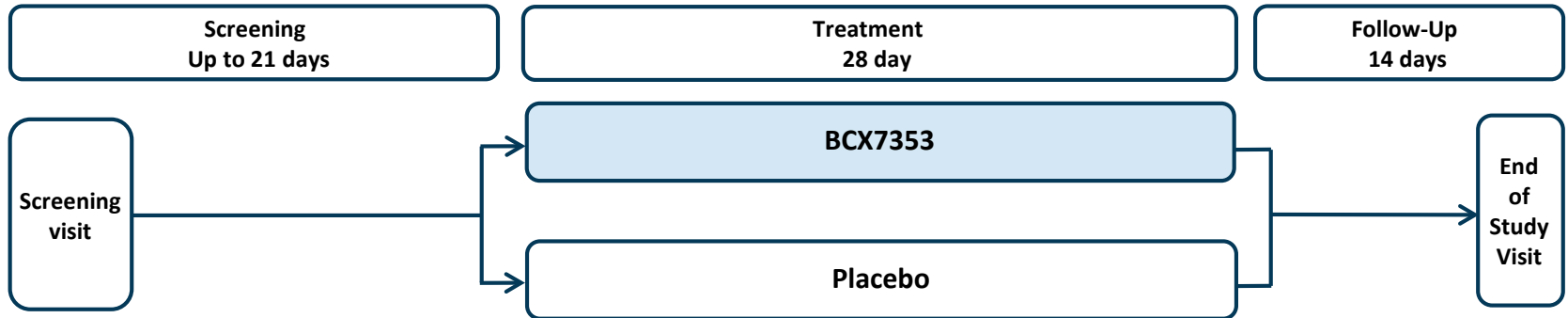
Preferred route of administration among US HAE patients currently taking prophylactic therapy (N=83)



Question: Which medication would you prefer assuming each is equally safe and effective and costs the same amount per year?

# APeX-1: Trial design

## Study Design



*\*1<sup>st</sup> Interim analysis evaluated 14 subjects in each arm in Part 1*

# APeX-1 second interim analysis population

	BCX7353			
	125 mg	250 mg	350 mg	Placebo
Randomized and treated	7	6	18	20
Intent to Treat (ITT) population	7	6	18	20
Per Protocol (PP) population	6	5	14	19
Excluded from PP population				
<i>HAE Type 1 or 2 not confirmed</i>			1	1
<i>&lt;28 days of dosing with study drug</i>	1		3	
<i>Non compliance with diary completion</i>		1		
Study drug compliance, mean % (SD)	98% (5)	99% (1)	98% (8)	98% (6)
Age – years, mean (SD)	48.4 (14.0)	50.7 (12.1)	43.8 (11.6)	46.5 (11.7)
Sex – female, n (%)	5 (71%)	2 (33%)	11 (61%)	12 (60%)
Prior androgen use, n (%)	2 (29%)	5 (83%)	15 (83%)	11 (55%)
Qualifying attack rate, attacks/wk mean (SD)	0.95 (0.26)	0.83 (0.52)	0.84 (0.35)	0.90 (0.46)



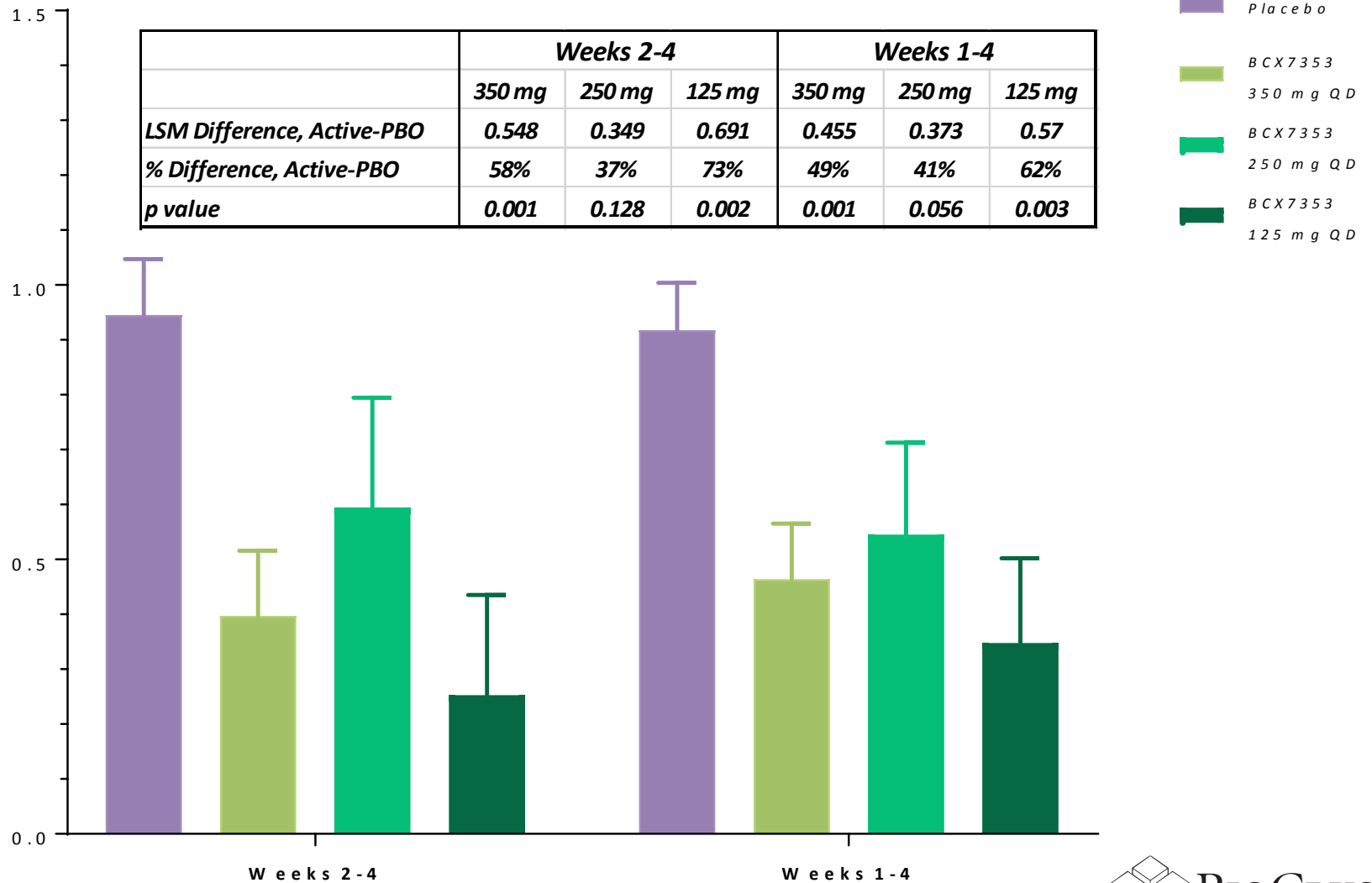
## Rate of overall confirmed attacks: PP population

Treatment	n	LS mean <sup>1</sup> Attacks per Week	Difference vs Placebo	Percentage Reduction vs Placebo	p-Value vs Placebo
Effective dosing period (Week 2-4) – PP Population					
BCX7353 combined	25	0.402	-0.543	57%	<0.001
BCX7353 125 mg	6	0.253	-0.691	73%	0.002
BCX7353 250 mg	5	0.595	-0.349	37%	0.128
BCX7353 350 mg	14	0.397	-0.548	58%	0.001
Placebo	19	0.945	-	-	-
<i>Part 1 Interim analysis:</i>					
<i>BCX7353 350 mg</i>	<i>11</i>	<i>0.343</i>	<i>-0.572</i>	<i>63%</i>	<i>0.006</i>
<i>Placebo</i>	<i>13</i>	<i>0.915</i>			

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

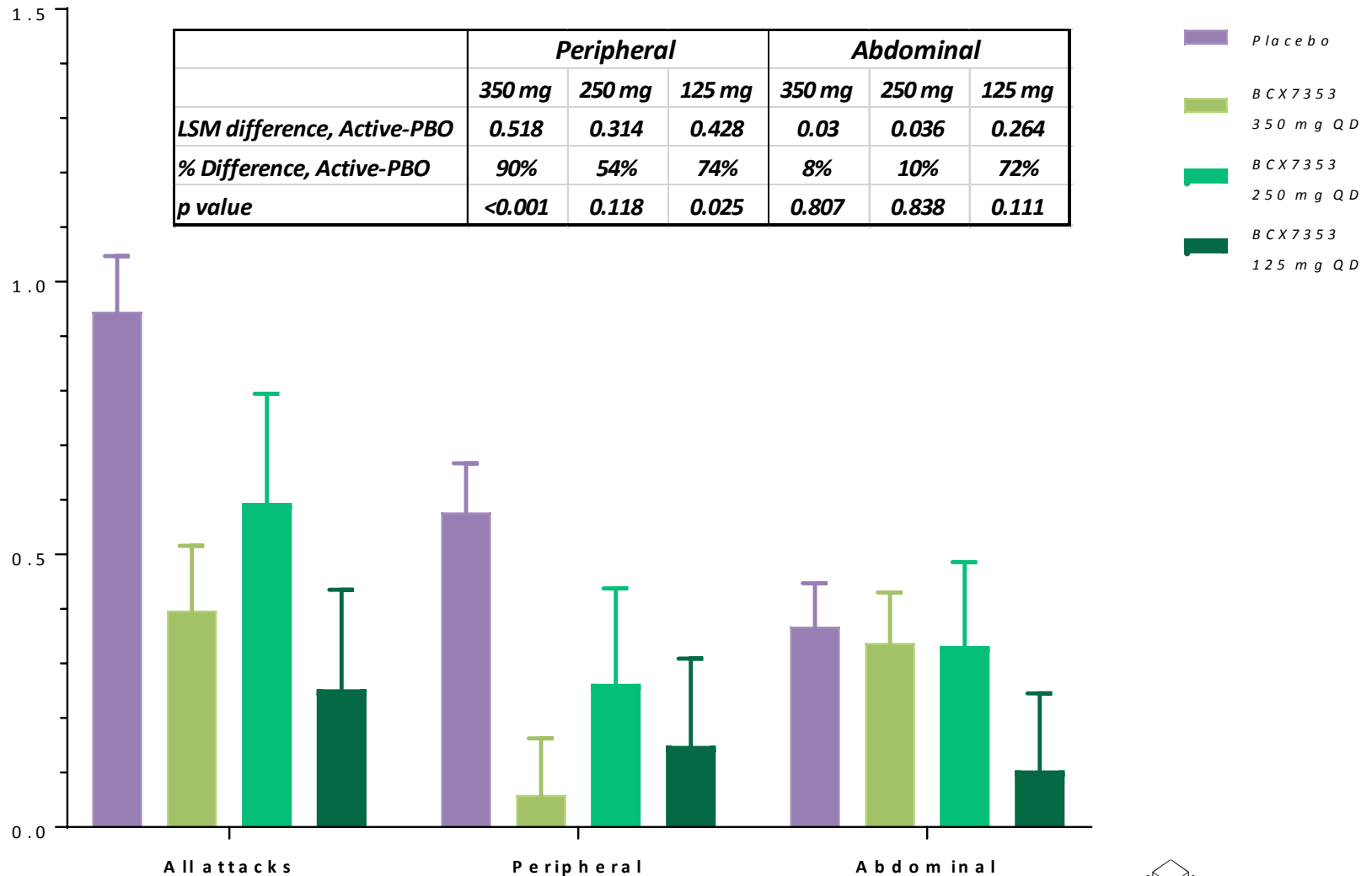
# Overall attack rate, PP analysis, weeks 2-4 and 1-4

Attack rate per week, PP analysis

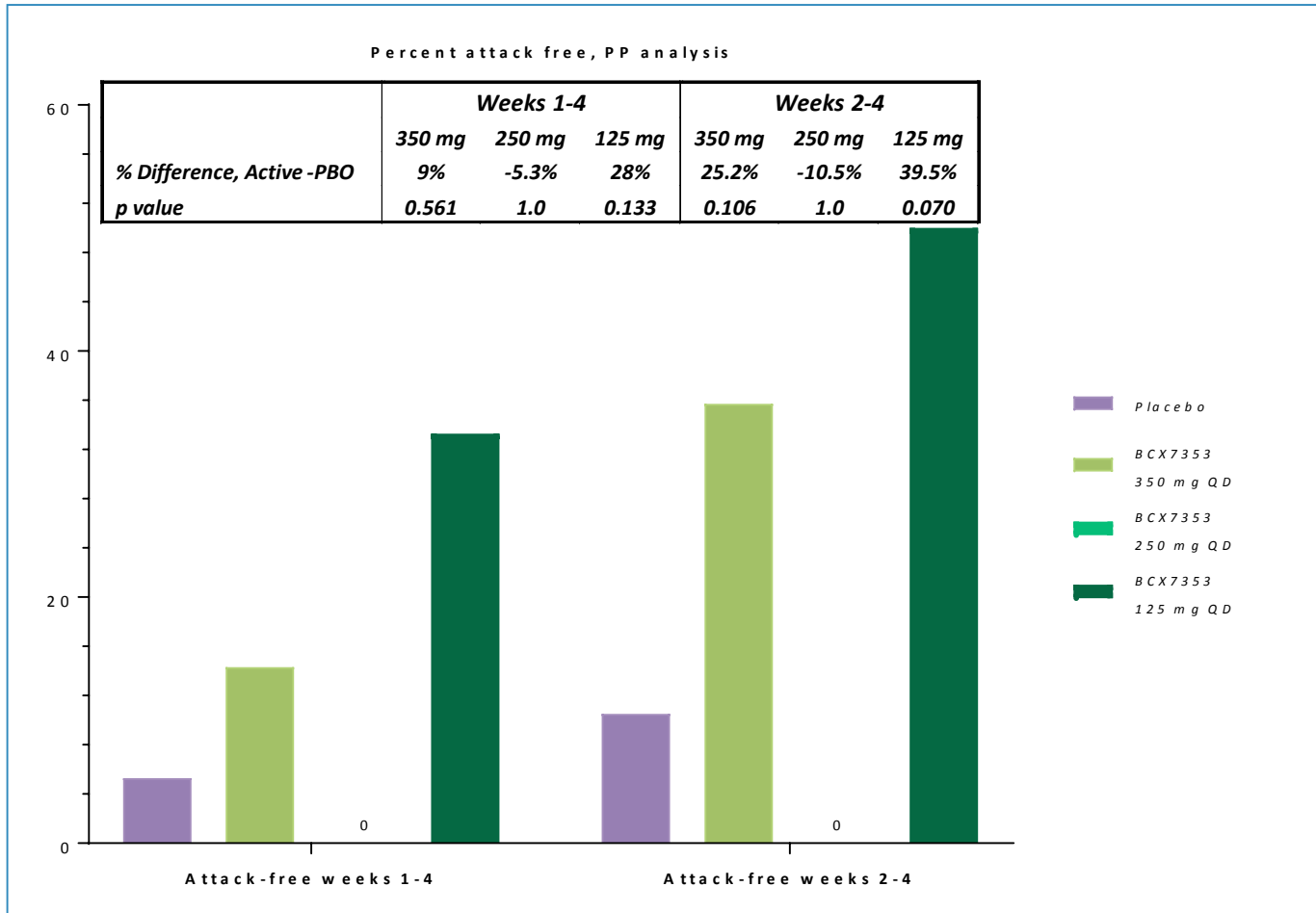


# Attack rates by prespecified anatomical location, PP

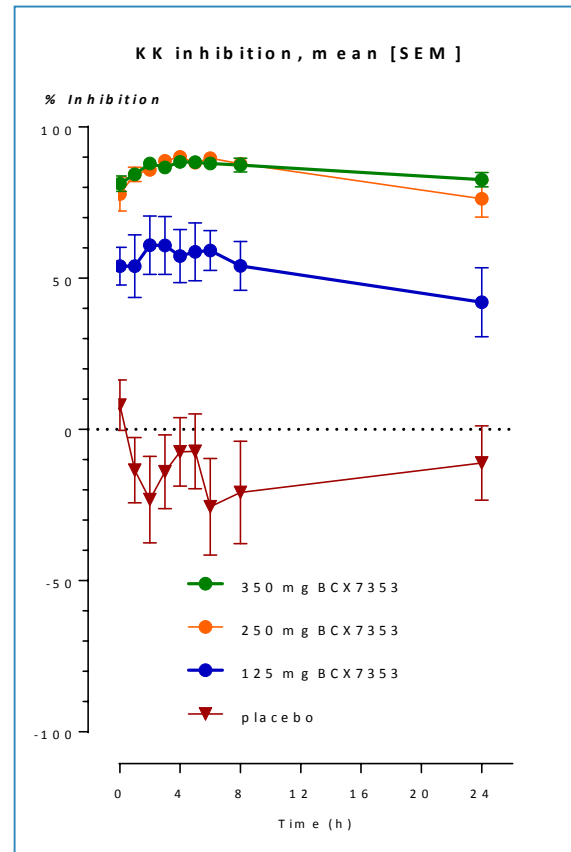
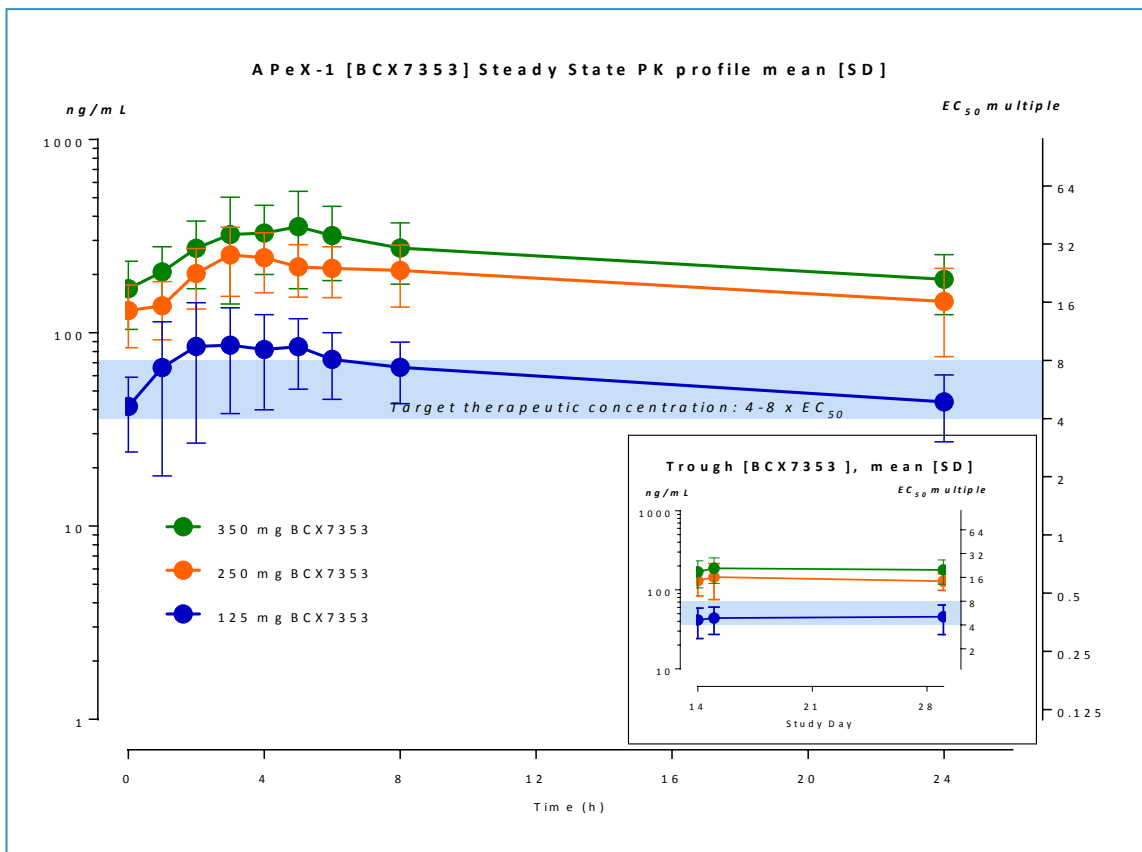
Attack rate per week, PP analysis weeks 2-4



# Percent of subjects attack-free, PP analysis



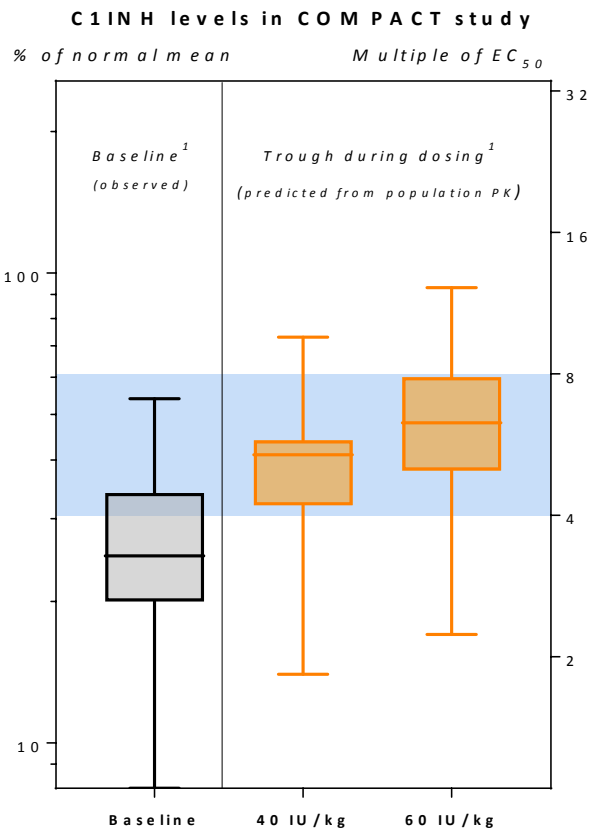
# PK and KK inhibition profiles at steady state for BCX7353 dose levels 125 mg, 250 mg and 350 mg QD in HAE subjects in APeX-1



Steady state drug levels greatly exceeded the target therapeutic range for both 250 mg and 350 mg QD and trough levels for the 125 mg dose, were generally within the target range

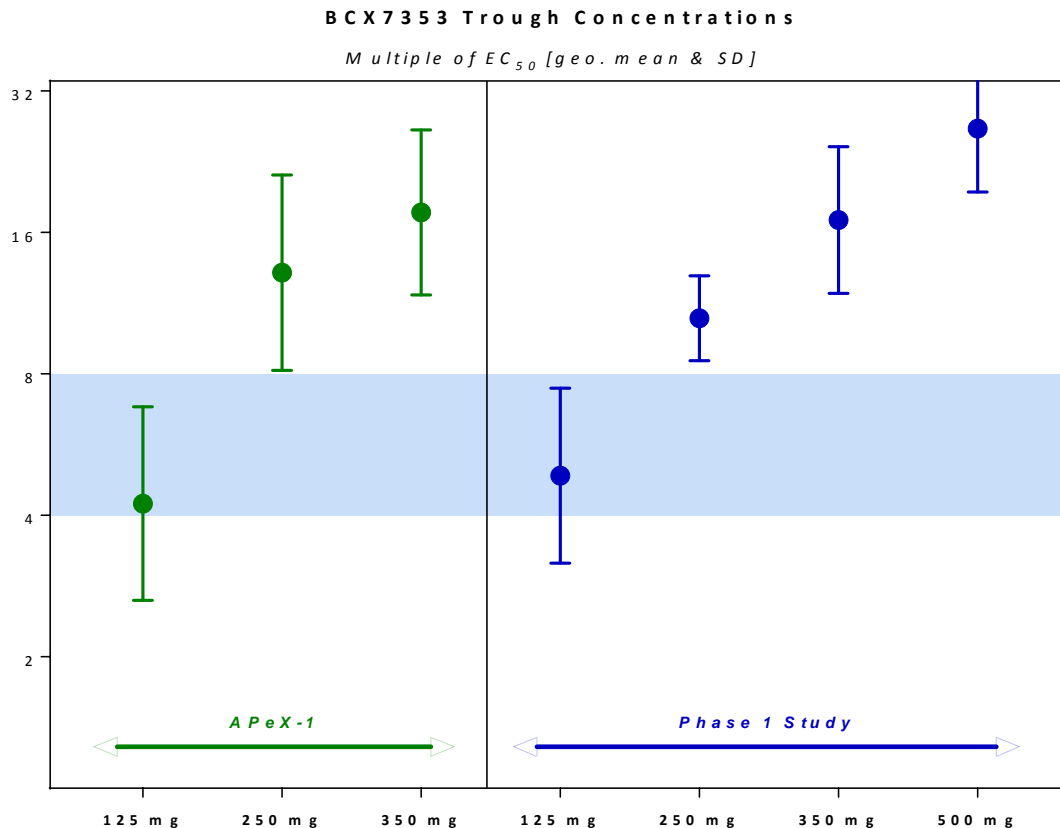
# Exposure in APeX-1 and Phase 1 BCX7353 trials, and SC C1INH

## CSL-830 Phase 3 study



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

## BCX7353 APeX-1 & Phase 1



BCX7353 plasma concentrations at 24 hours post-dose

<sup>1</sup> Longhurst, H. et al. N Engl J Med 376, 1131-1140 (2017). 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 Second interim analysis safety summary

Category	BCX7353			
	125 mg n=7	250 mg n=6	350 mg n=18	Placebo n=20
Subjects with any Serious AE, n (%)	0	0	0	0
Subjects with Drug-Related Grade 3/4 AE, n (%)	0	0	1	0
Subjects with AE Leading to D/C from Study Drug, n (%)	0	0	3	0
Non- drug-related, n (%)	0	0	1 <sup>1</sup>	0
Drug-related, n (%)	0	0	2 <sup>2</sup>	0

<sup>1</sup> -Pre-existing liver disorder (improved from baseline, but persisting). Previously reported in 1<sup>st</sup> interim analysis

<sup>2</sup> -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). Previously reported in 1<sup>st</sup> interim analysis

- Vomiting/ abdominal cramps concurrent with menses

# APeX-1 Second interim analysis safety summary

Category	BCX7353			
	125 mg n=7	250 mg n=6	350 mg n=18	Placebo n=20
Treatment-Emergent Adverse Events occurring in ≥2 subjects overall, n (%)				
Nasopharyngitis	0	0	5 (28%)	6 (30%)
Diarrhoea	0	1 (17%)	4 (22%)	2 (10%)
Abdominal pain	0	0	3 (17%)	0
Nausea	0	2 (33%)	3 (17%)	0
Fatigue	0	0	2 (11%)	1 (5%)
Flatulence	0	0	2 (11%)	0
Vomiting	0	0	2 (11%)	0
Constipation	0	0	1 (6%)	1 (5%)
Headache	2 (29%)	0	1 (6%)	3 (15%)
Constipation	0	0	1 (6%)	1 (5%)
Migraine	1 (14%)	0	1 (6%)	0
Pharyngitis	0	1 (17%)	1 (6%)	0
Clin. significant changes in clin. chem., hematology or urinalysis, n (%)	0	1 <sup>1</sup>	1 <sup>2</sup>	0

<sup>1</sup> Treatment-emergent ALT elevation to >3X ULN (ALT 4.1 x ULN, AST 1.9 x ULN). 20 years androgen use, Baseline increase in liver enzymes

<sup>2</sup> 1 event previously reported: ALT elevation > 3X ULN (ALT 3.9 x ULN, AST 1.8 xULN, GGT10.7 X ULN) Pre-existing colitis, hepatic steatosis (fatty liver), > 20 years androgen use, Baseline increase in liver enzymes



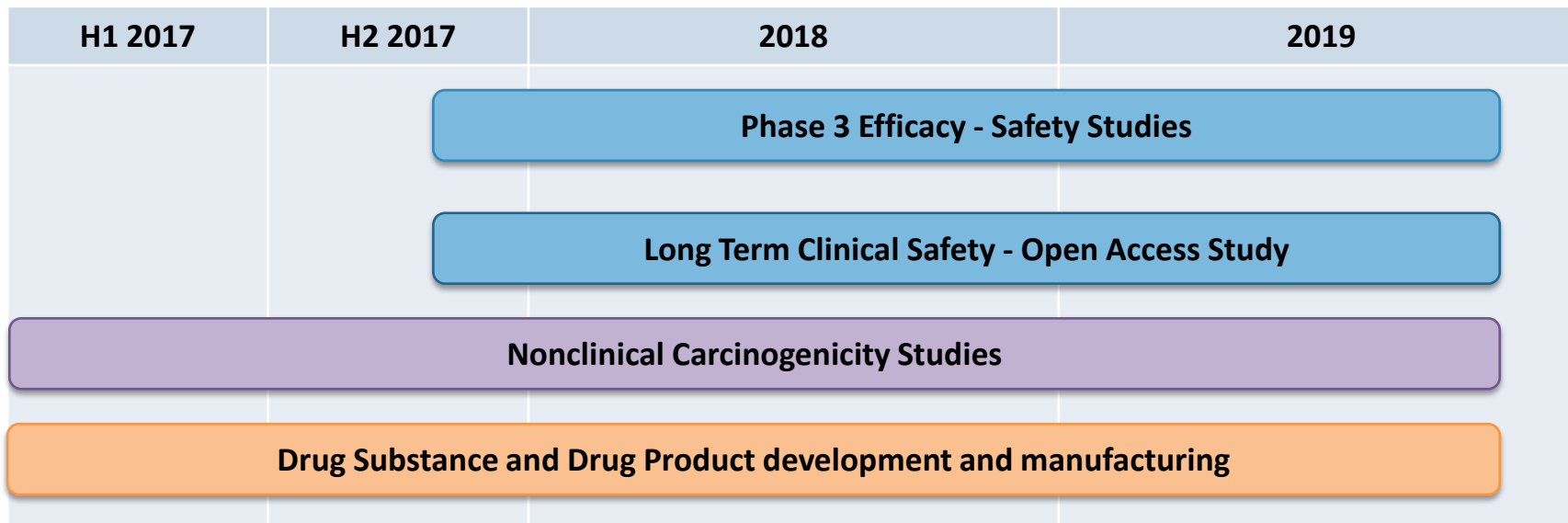
# Conclusions

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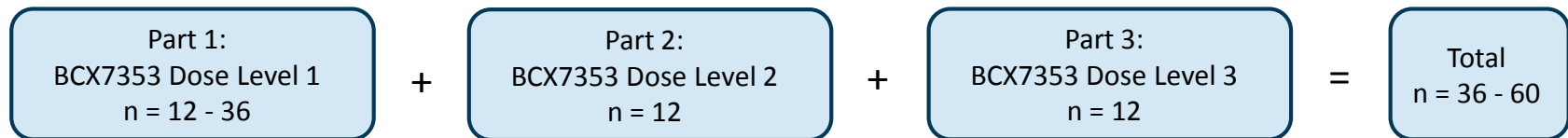
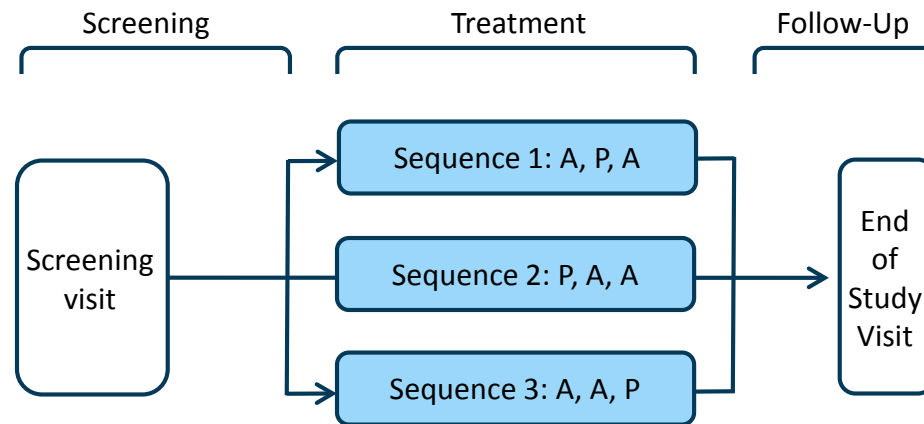
- BCX7353 once daily for 4 weeks showed clinically meaningful and statistically significant reductions in the rate of angioedema attacks
  - 125 mg dose showed a reduction of 73% in overall attack rate ( $p=0.002$ )
- Oral BCX7353 once daily over 4 weeks was generally safe and well tolerated
- A dose related improvement in GI tolerability was observed in the 250 mg and 125 mg dose groups
- No significant treatment emergent abnormalities in laboratory safety parameters were observed in the 250 mg and 125 mg dose groups
- Steady state trough drug levels (24 hours after dosing) greatly exceeded the target therapeutic range at the 250 mg and 350 mg dose levels. Trough levels for the 125 mg dose were generally within the target range
- PK profile and kallikrein inhibition levels were similar to those seen at the same dose levels in Phase 1 healthy subjects
- Completion of Part 3 will help to round out the dose response data necessary to select doses for Phase 3

# BCX7353 Remaining activities after APeX-1

Estimated timing of key activities to support NDA/MAA filing




# ZENITH-1 trial design



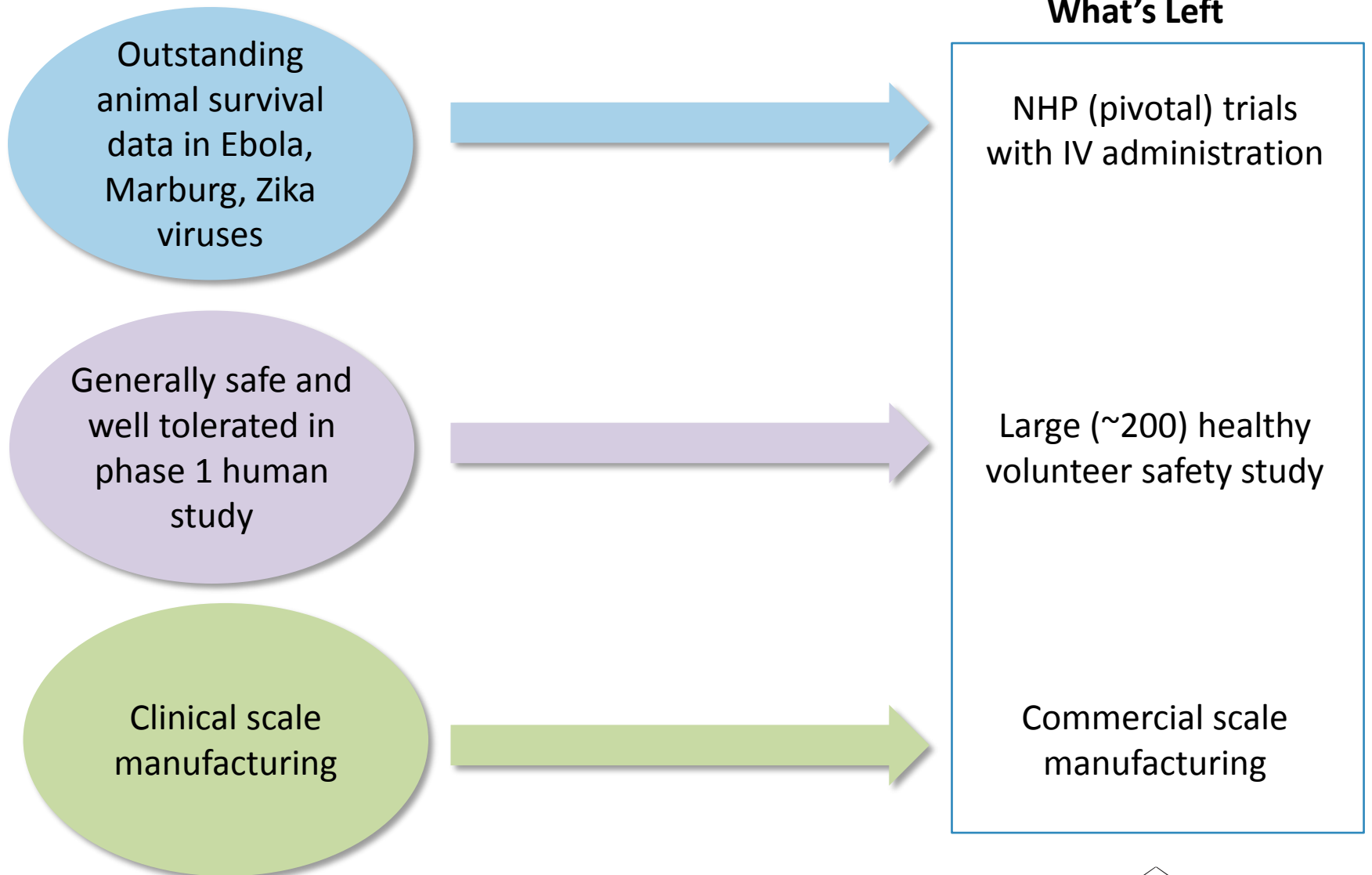
- The ZENITH-1 trial will evaluate the potential for an oral liquid formulation of BCX7353 to treat acute angioedema attacks
- Each subject is intended to have 3 attacks treated with blinded study drug
  - 2 with BCX7353 (A) and 1 with Placebo (P)
- Primary efficacy endpoint: proportion of subjects with improved or stable composite visual analog scale (VAS) score at 4 hours post-dose

# 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
	<p>First and only one-dose IV treatment for influenza</p>	<p>Over \$200M US Government funding to support development and approval</p>	<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>
<p><b>Galidesivir (BCX4430)</b></p>	<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>	<p>Approximately \$80M US Government contract development funding</p>	<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



# Stockpiling and Voucher Comparables

## Precedent highly pathogenic countermeasures

Product	Pathogen	Company	Doses	Cost
BioThrax vaccine	Anthrax	Emergent BioSolutions	29M	\$691M
Raxibacumab antitoxin (CY '13)	Anthrax	GSK	60K	\$193M
AbThrax antibody	Anthrax	HGS (now GSK)	65K	\$326M
Botulinum antitoxin	Botulism	Cangene	200K	\$427M
MVA vaccine	Smallpox	Bavarian Nordic	20M	\$505M
ACAM2000 vaccine (CY '08)	Smallpox	Acambis	>72M	\$425M-\$660M
ST-246 antiviral	Smallpox	Siga	1.7M	\$433M

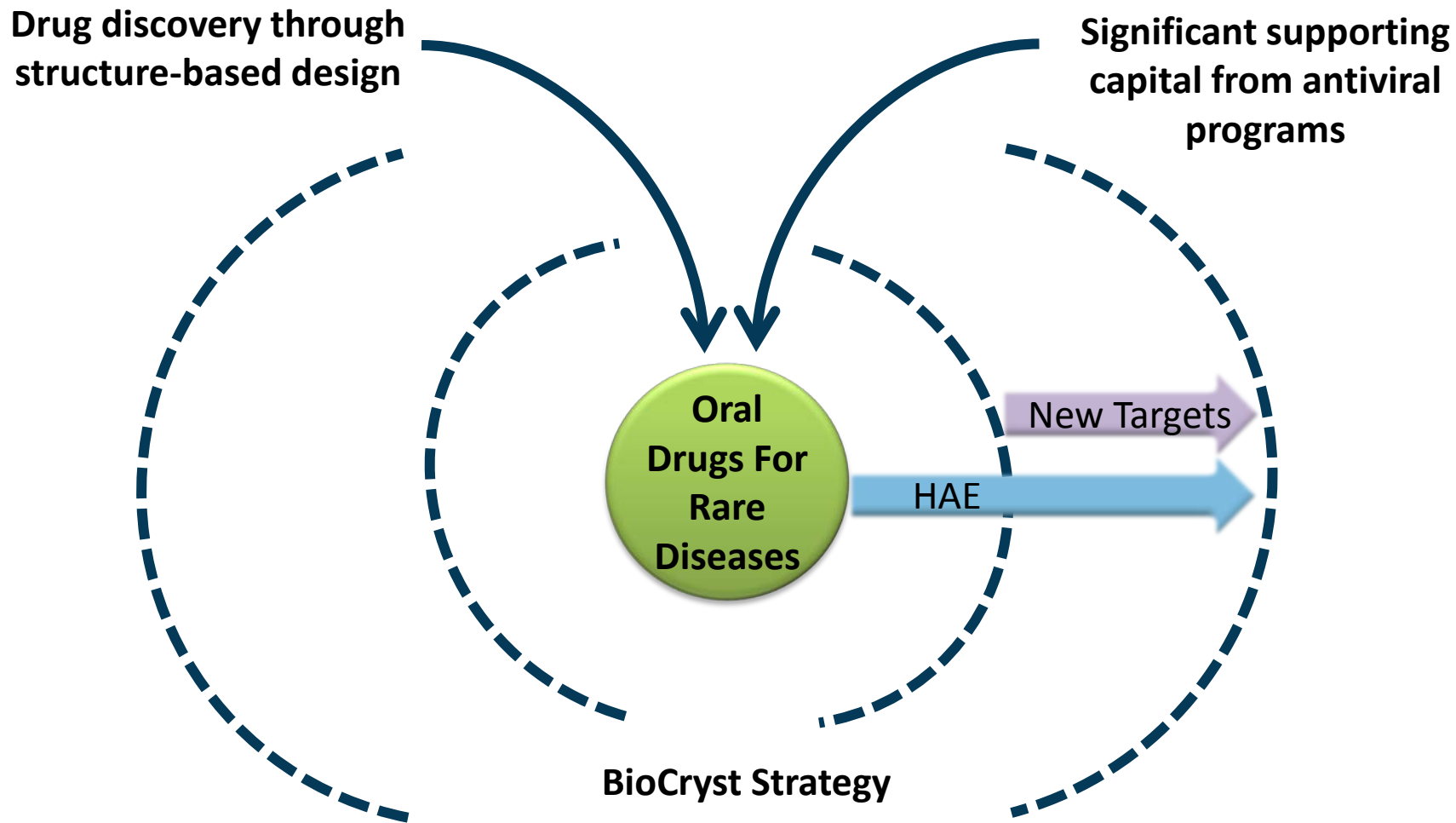
## Precedent voucher purchases

Disease	Drug	Seller (Buyer)	Price
Morquio A syndrome	Vimizim (elosulfase alfa)	BioMarin (Sanofi)	\$67.5M
Leishmaniasis	Impavido (miltefosine)	Knight (Gilead)	\$125M
High-risk neuroblastoma	Unituxin (dinutuximab)	United Therapeutics (Abbvie)	\$350M
Rare bile acid synthesis disorders	Cholbam	Retrophin (Sanofi)	\$245M

Stockpiling data from FY2014 Budget for Public Health and Social Services Emergency Fund, pg 116  
<http://www.hhs.gov/budget/fy2014/fy2014-phssef.pdf>

Voucher data sourced from public reports

# Building a company to generate expanding and sustainable value



## Cash position & 2017 guidance (in millions)

Cash & investments at December 31, 2016	\$65
<b>Cash &amp; investments at March 31, 2017</b>	<b>\$105</b>
Senior Credit Facility	\$23

### Guidance for 2017:

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

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