

Nasdaq: CORI



**Corplex Donepezil<sup>®</sup>**

Pilot Bioequivalence Study Preliminary Results

May 11, 2017

# Forward-looking Statements



This presentation and the accompanying oral presentation contain “forward-looking” statements that are based on our management’s beliefs and assumptions and on information currently available to management. Forward-looking statements include all statements other than statements of historical fact contained in this presentation, including information concerning our business strategy, future financial and operating performance, business plans and objectives, potential growth and market opportunities, financing plans, competitive position, industry environment, product pipeline, clinical trial timing and plans, cash and resource requirements, clinical and regulatory pathways for our development programs, the achievement of clinical and commercial milestones, the advancement of our technologies and our proprietary, co-developed and partnered products and product candidates.

Forward-looking statements are subject to known and unknown risks, uncertainties, assumptions and other factors including, but not limited to, those related to our future financial performance, market acceptance of our proprietary technology platforms for transdermal drug delivery, our ability to develop and maintain partnerships, our ability to identify, develop and market new products in a timely manner, our ability to maintain, protect and enhance our brand and intellectual property, and our ability to continue to stay in compliance with applicable laws and regulations. Moreover, we operate in a very competitive and rapidly changing environment, and new risks may emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. These factors, together with those that may be described in greater detail in our filings with the Securities and Exchange Commission (“SEC”), may cause our actual results, performance or achievements to differ materially and adversely from those anticipated or implied by our forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. Although our management believes that the expectations reflected in our forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances described in the forward-looking statements will be achieved or occur. Moreover, neither we, nor any other person, assume responsibility for the accuracy and completeness of the forward-looking statements. These forward-looking statements speak only as of the date of this presentation, and we undertake no obligation to publicly update any forward-looking statements for any reason after the date of this presentation to conform these statements to actual results or to changes in our expectations, except as required by law.

# Study Objectives and Preliminary Results

Determine optimal patch size for Pivotal Bioequivalence (BE) Trial



Establish intra-subject variability of AUC and  $C_{\max}$



Determine optimal number of subjects required in Pivotal BE Trial



Demonstrate acceptable skin and gastrointestinal tolerability



Demonstrate acceptable adhesion over one week



Determine required frequency of blood sampling for Pivotal BE Trial



Measure elimination half-life for both oral and patch (washout)



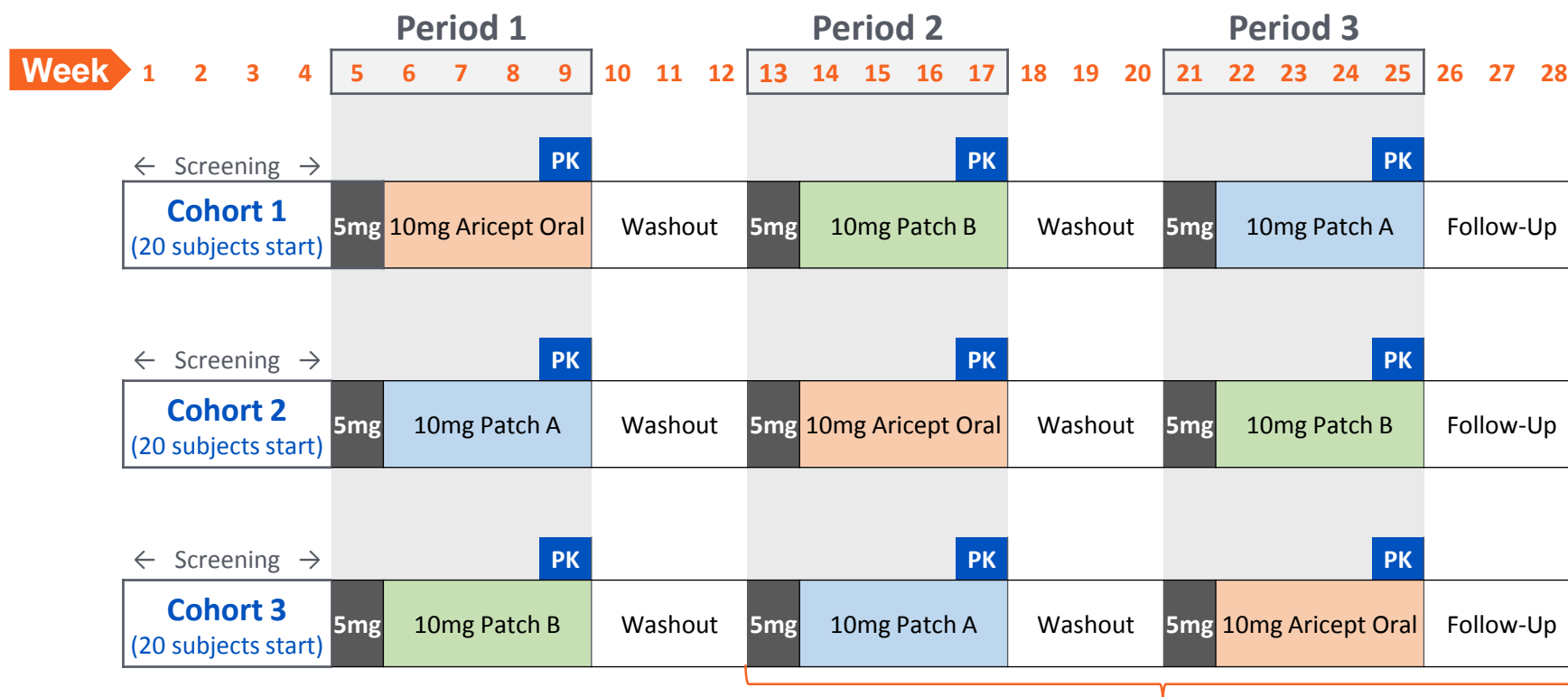
# Preliminary Conclusion



Although not an objective of this study,  
***statistical bioequivalence was achieved***

# Donepezil Pilot Study: Overall Design and Timing

## Three period, three-treatment, randomized crossover study



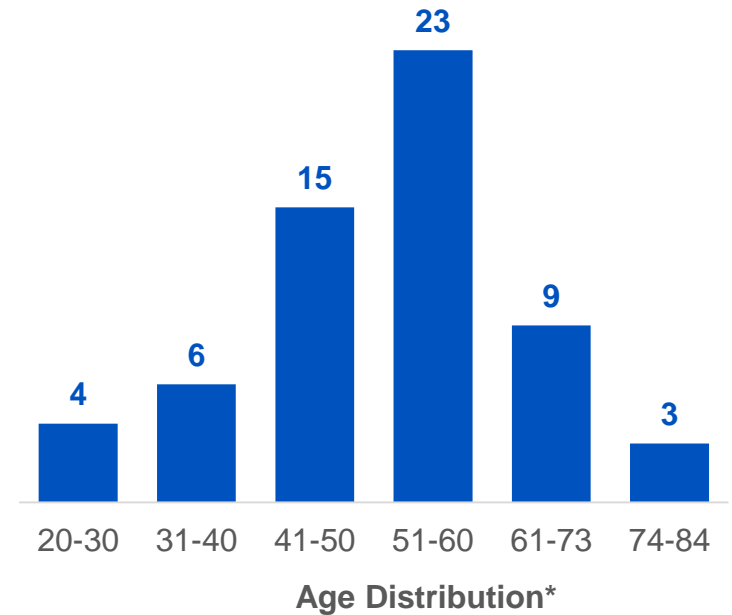
Actual sequence of final two treatments was randomized

Patch A and Patch B were two different patch sizes of the same formulation  
 Drug-containing surface area of Patch B was ~20% larger than Patch A  
 Steady-state PK assessments were made during 5<sup>th</sup> week of each period

# Subject Demographics

- 60 healthy volunteers enrolled at beginning of study
- Very low attrition: 50 completed the study
- >80% were more than 40 years old

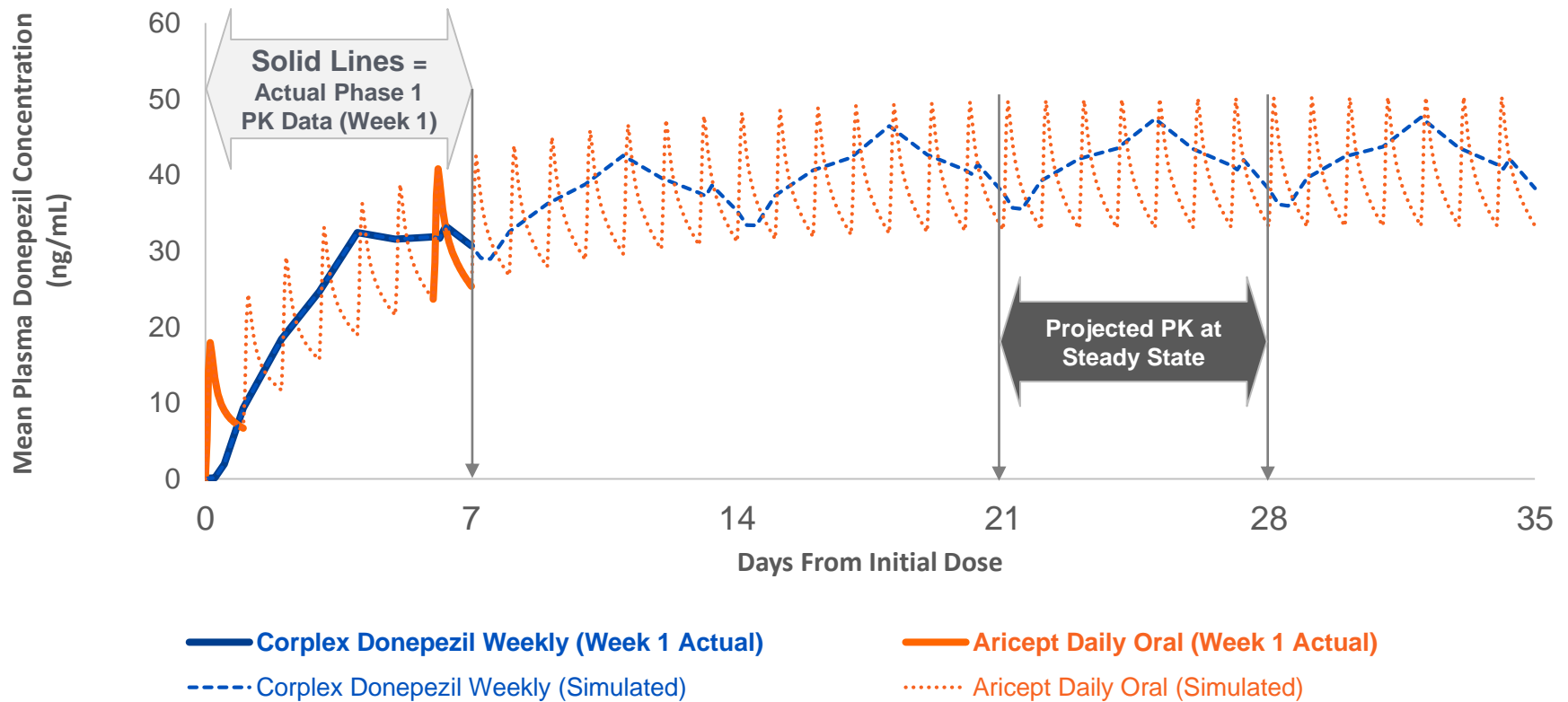
Demographic	Distribution
Age	20-78 years
Male/Female	57% / 43%
Non-Hispanic Caucasian/ Hispanic	75% / 25%



\*At study initiation

# Donepezil Projected Steady State PK Profile

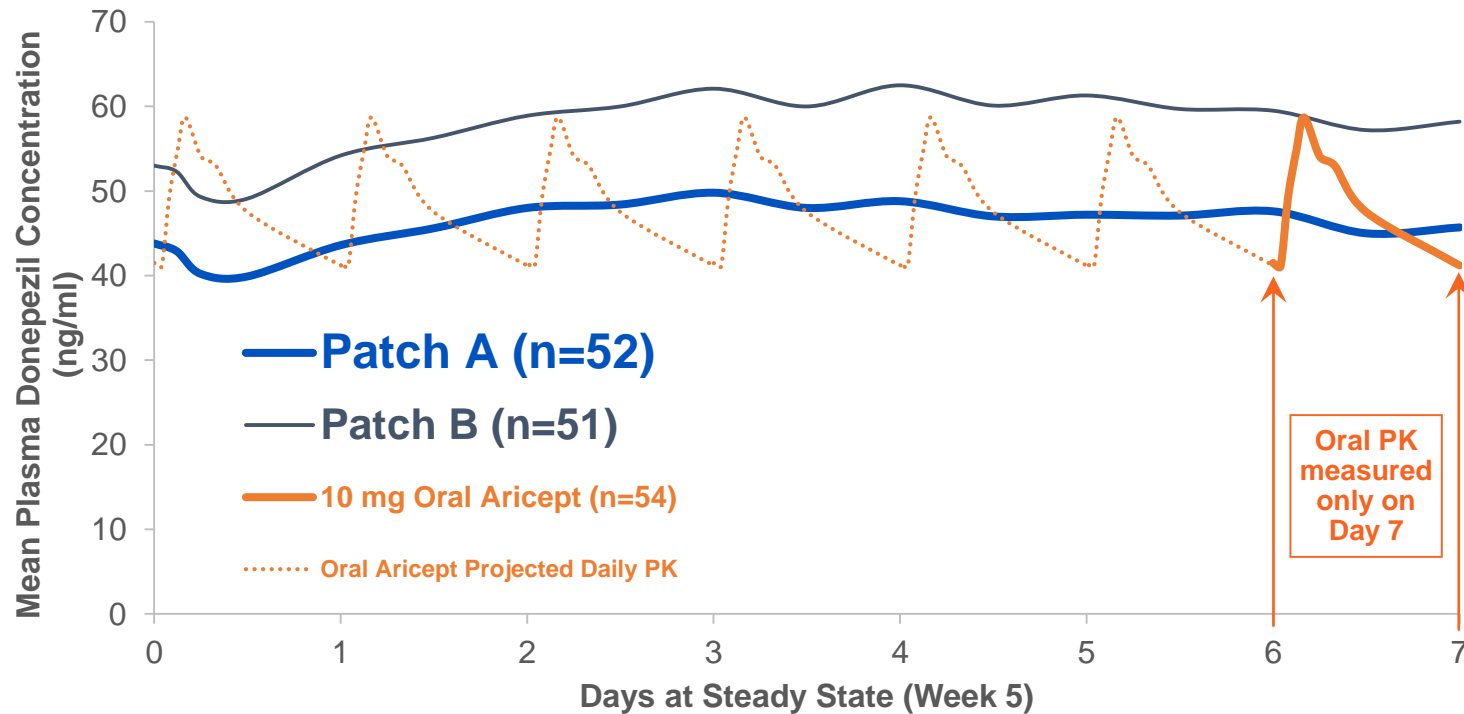
Mean Projected\* Plasma Concentrations  
Simulated to Steady State



\* Projections based on one-week PK study (September 2016, n=6) of Complex Donepezil and one week PK study (June 2016, n=6) of oral Aricept

# Observed PK Profiles at Steady State

## Transdermal Delivery Exhibits Similar PK Profile to Oral Aricept Patch A and B exhibit dose proportionality



Plasma sampling for patch treatments taken throughout Week 5  
Plasma sampling for Aricept taken only on last day (day 7) of Week 5



# Bioequivalence Assessment of Patch A

## Patch A is Bioequivalent to Aricept

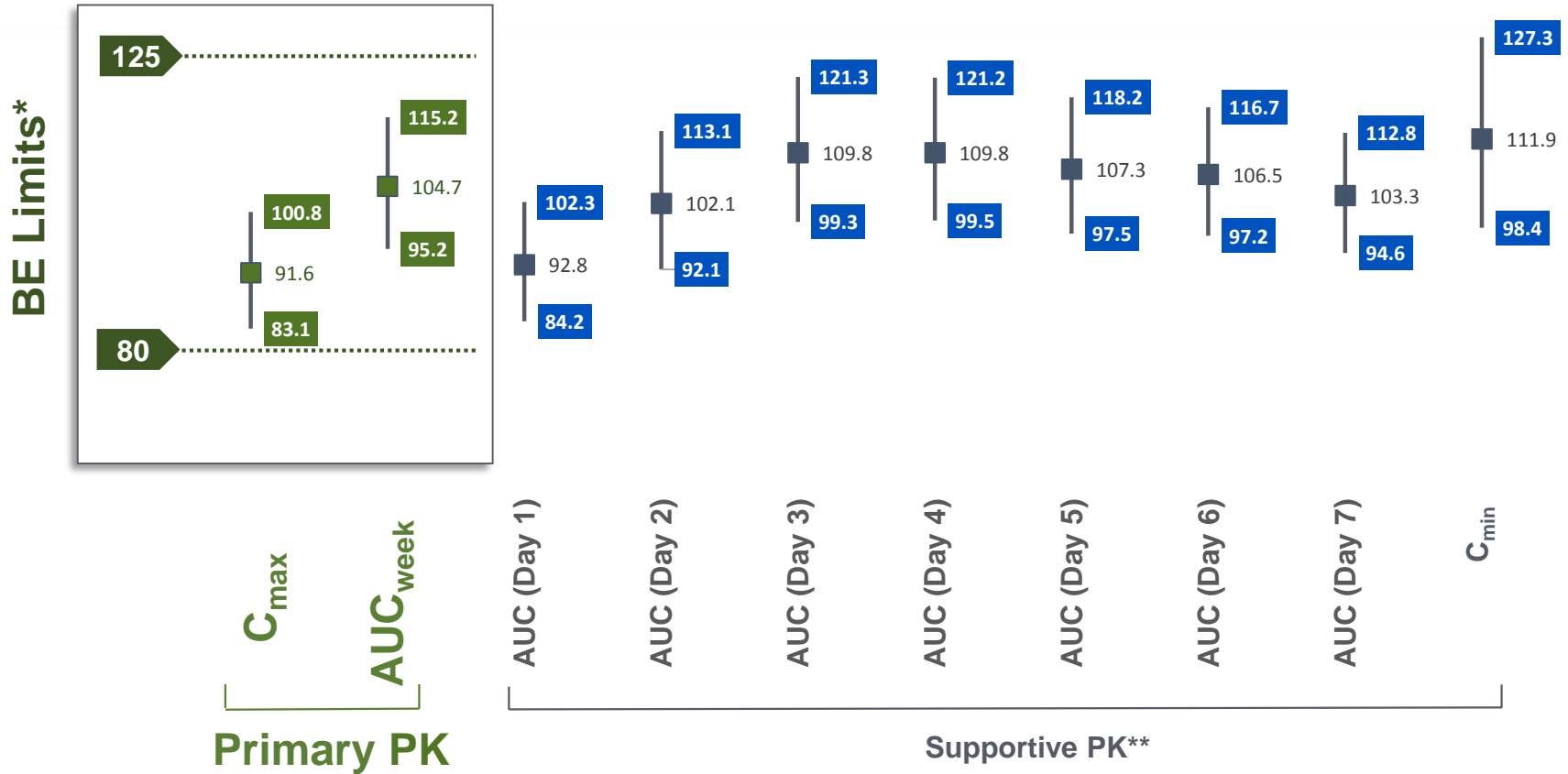
BE requires the 90% confidence intervals for the geometric mean ratios of  $AUC_{ss}^{**}$  and  $Cmax_{ss}^*$  for Patch A vs. Aricept to each be within 80-125%

Primary PK Parameters	Geometric Mean Ratio (%) (Patch A vs. Oral Aricept)	BE Limits (Target 80-125%)
$AUC_{ss}$ (ng-hr/ml)	104.7	95.2 - 115.2
$Cmax_{ss}$ (ng/ml)	91.6	83.1 - 100.8

\* $AUC_{ss}$  - area under the curve at steady state (for patch, observed area under the curve throughout week 5; for Aricept, observed AUC day 7 of week 5 multiplied by 7)

\*\* $Cmax_{ss}$  - maximum concentration at steady state (for patch, maximum observed conc. during week 5; for Aricept, maximum observed conc. during day 7 of week 5)

# Bioequivalence Assessment (Patch A)



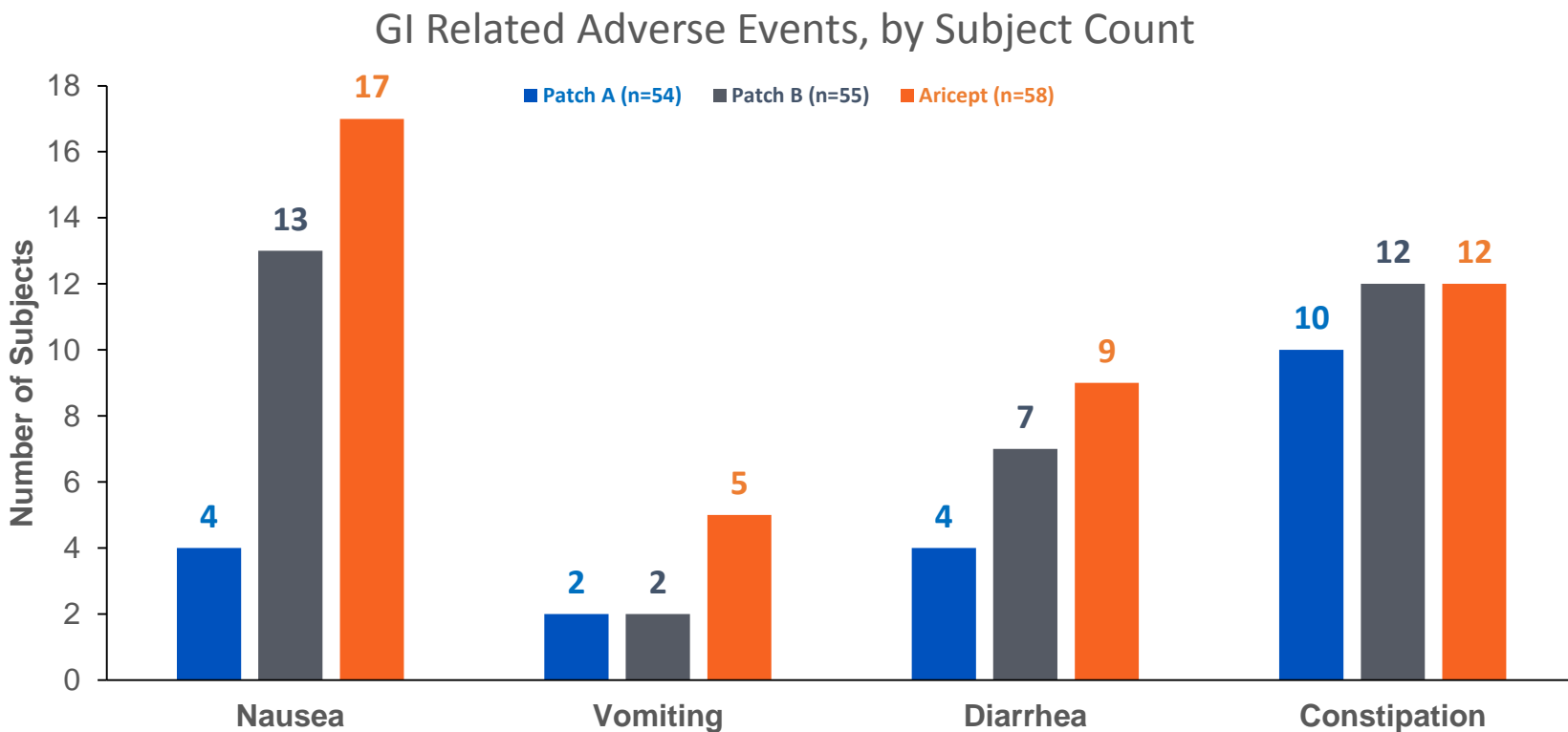
\* At 90% confidence intervals

The 80 – 125% criteria do not apply to supportive PK parameters; FDA has indicated that these will be tested for “no significant difference” compared to oral Aricept

\*\* % Fluctuation data not shown; as expected, the patch achieved less fluctuation between  $C_{max}$  and  $C_{min}$  due to controlled delivery

# Most Common GI\* Side Effects

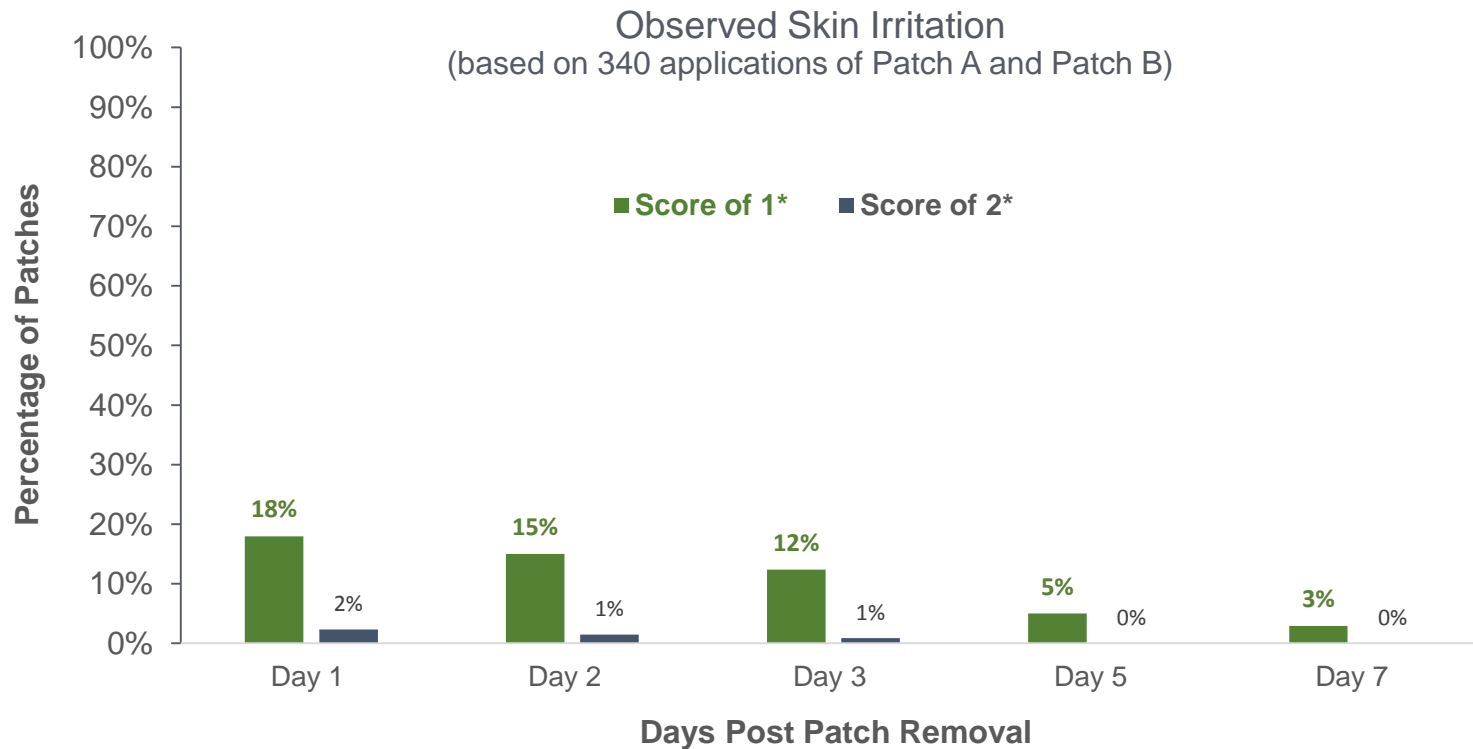
***Patch A incidence of nausea was more than 4x less than Aricept***



\* GI = Gastrointestinal

# Favorable Skin Tolerability

**80% of patches had an irritation score of “0”**



\* Score on a rating scale of 0 (none) to 7 (strong reaction beyond patch application site) per FDA draft guidance on dermal response  
Percentage of patches exhibiting no irritation (score of 0) are not displayed in chart above

# Favorable Skin Adhesion

**Observed Mean Adhesion Score\* = 95.6%**

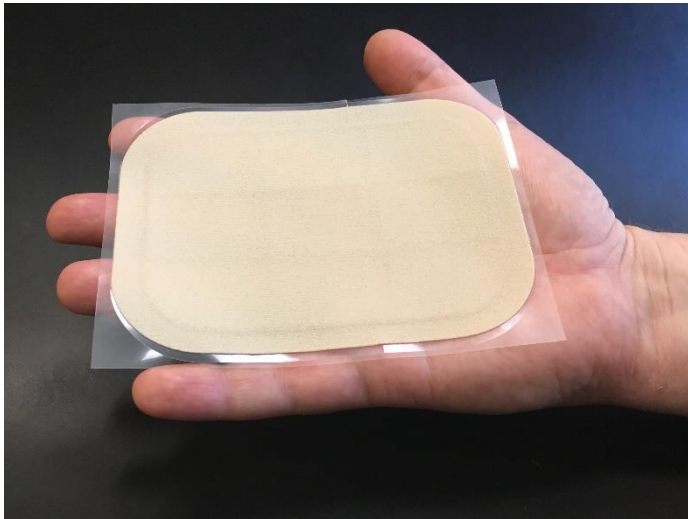
**Target Objective:  $\geq 90\%$**

<b>Adhesion Score</b>	<b>Adhered Portion(%)</b>	<b>Observed Frequency(%)</b>
0	100	65.9
1	$\geq 90$	27.8
2	$\geq 80$	4.4
3	$\geq 70$	1.4
4	$\geq 60$	0.2
5	$\geq 50$	None
6	$< 50$	0.3

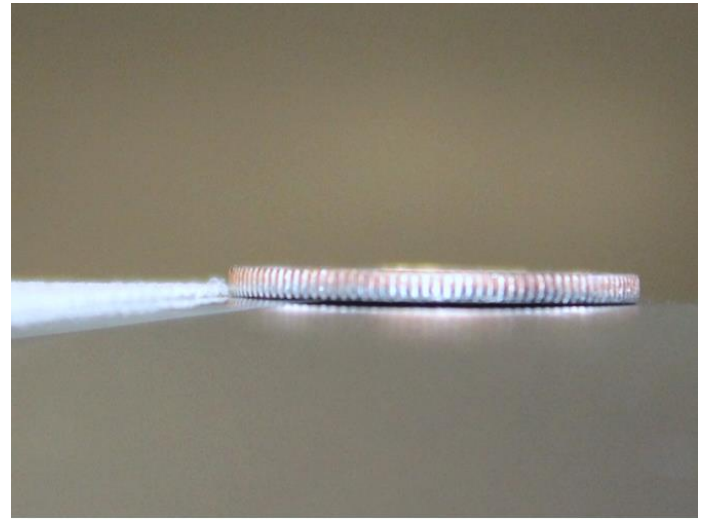
\* Mean adhesion score derived from individual adhesion scores taken every 12 hours over the course of each one week treatment with Patch A and Patch B

# Patch A Wearability: Thin and Flexible

~150cm<sup>2</sup> Delivers 7 Days of Drug

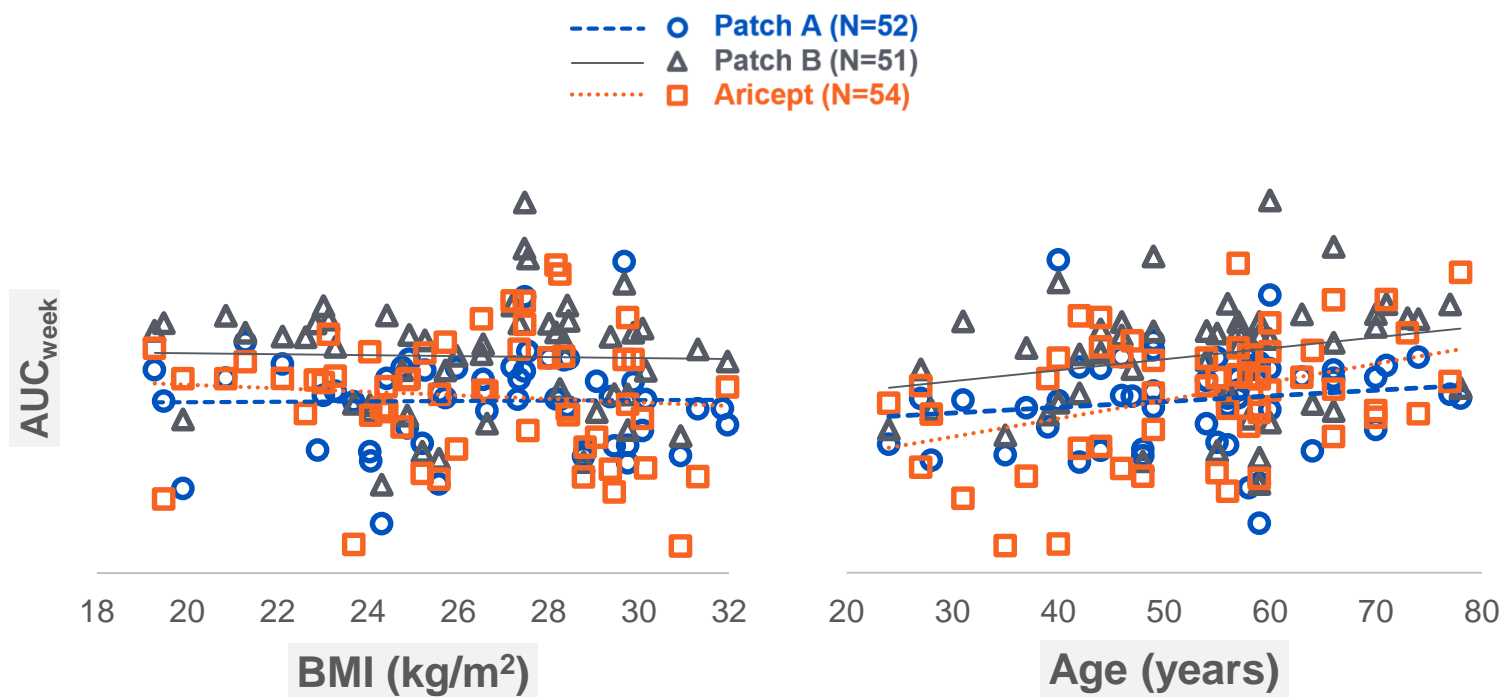


Thinner Than a Dime



# No Apparent BMI\* or Age Effects

## No Apparent Effect of BMI or Age on $AUC_{week}$



\*BMI = Body Mass Index

# Next Steps

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- Finalize patch size for use in Pivotal Study (~11cm x 14cm)
- Manufacture three lots of final patch at 10% commercial batch scale
- Put samples from all three lots on long-term stability testing
- Meet with FDA this summer to reconfirm finalized study parameters
- Commence Pivotal Study in September/October 2017
- Preliminary Results expected in February 2018
- File NDA as early as Q3 CY 2018



# Pivotal Study Design More Streamlined

## Pilot

3-way crossover, randomized

Healthy Volunteers

Enroll **60** to complete at least **30**  
*(50 actually completed)*

3 treatments  
(2 patch sizes and oral Aricept)

Each Period = 5 weeks of treatment  
(5mg Week 1 followed by 10 mg Weeks 2-5)

3-week washout

Primary Objective: Assess  $C_{max}$  and AUC

Study Duration: 6 months

## Pivotal

2-way crossover, randomized

Healthy Volunteers

Enroll **64-100** to complete **54-86**  
*(to be finalized mid-June)*

2 treatments  
(Final patch size and oral Aricept)

Each Period = 5 weeks of treatment  
(5mg Week 1 followed by 10mg Weeks 2-5)

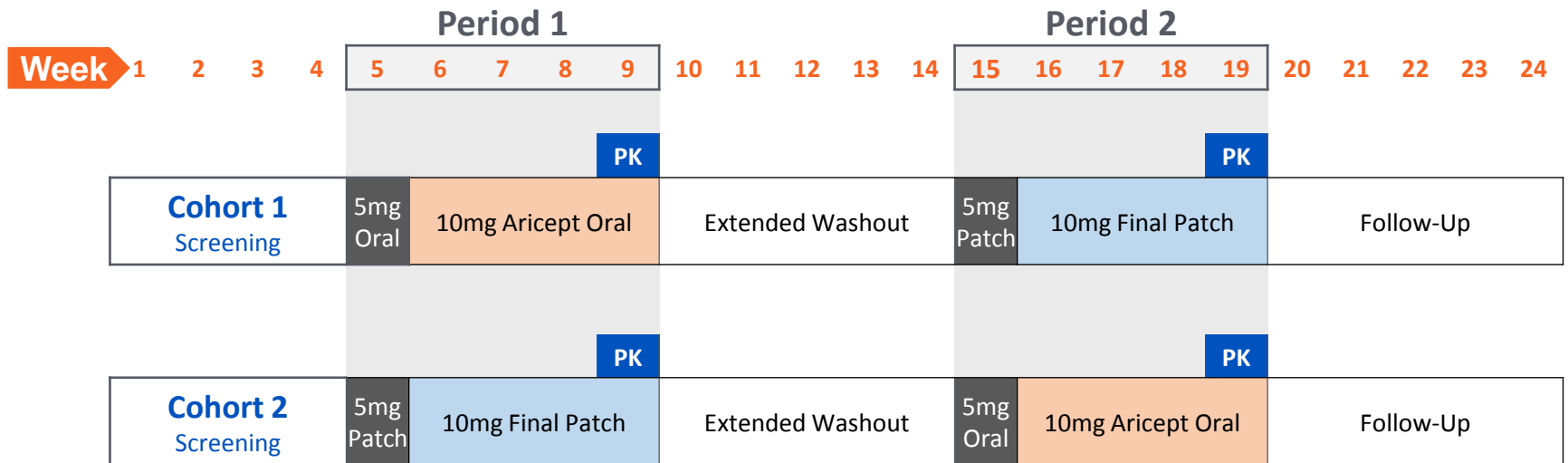
5-week washout

Primary Objective: BE for  $C_{max}$  and AUC

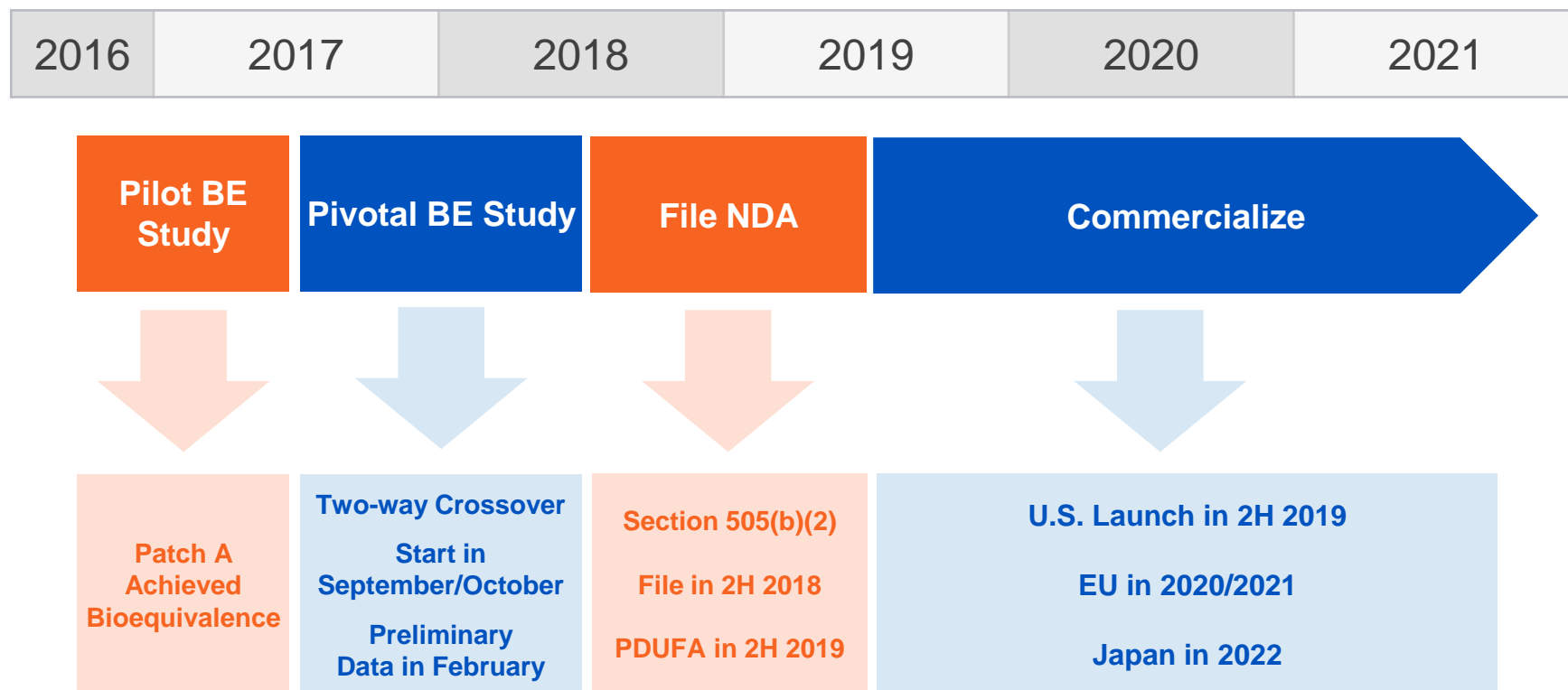
5 months

# Donepezil Pivotal Study Design

Each subject will be randomized into one of two treatment sequences



# Expected Donepezil Pathway to Commercialization



All years are calendar years

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Thank You

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