PhaseBio

Corporate Overview

August 2022

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Company Overview

Therapeutic Focus		Clinical-stage biopharma company focused on the development and commercialization of novel therapies to treat cardiovascular diseases
Product Candidates	**Bentracimab (PB2452)**	Novel agent in Phase 3 development for immediate and sustained reversal of ticagrelor, the preferred antiplatelet therapy of the American College of Cardiology, the American Heart Association and the European Society of Cardiology
	PB6440	Oral aldosterone synthase inhibitor in development for treatment-resistant hypertension and potentially other cardio-renal-metabolic indications, currently in Investigational New Drug application (IND) enabling studies
Platform Technology	**ELP Technology[1]**	• Extends circulating half-life of proteins and peptides, enhances solubility, stability and bioavailability while providing a sustained-release mechanism • Enables product candidates that are straightforward to manufacture and administer

Recent Achievements & Upcoming Milestone Targets[2]

✓ Bentracimab	**Mid 2021**	First 100 patients in REVERSE-IT Phase 3 trial	**Bentracimab**	**Q4 2022**	Planned BLA Submission
✓ Bentracimab	**Q4 2021**	Topline results from Phase 2b trial	**PB6440**	**1H 2023**	Planned IND submission
✓ Bentracimab	**Q4 2021**	Topline results from interim analysis of REVERSE-IT	**PB6440**	**Mid 2023**	Target initiating first-in-human clinical trial

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1. ELP technology does not apply to bentracimab or PB6440
2. Targeted timelines could be impacted by the continued scope and duration of the COVID-19 pandemic

A Clinical Stage, Cardiovascular Focused Biopharmaceutical Company

Program	Pre-Clinical	Phase 1	Phase 2	Phase 3	Commercial Rights	Upcoming Milestone Target[2]
Bentracimab Reversal of Ticagrelor Antiplatelet Activity	**REVERSE-IT[1] Phase 3 ongoing** *Interim completed, targeting to submit BLA in Q4 2022[2]*				PhaseBio	**Q4 2022** Planned BLA submission
PB6440 Resistant Hypertension	**Pre-Clinical**				PhaseBio	**1H 2023** Submit Investigational New Drug application (IND)
Partnering Opportunities						
Pemziviptadil Pulmonary Arterial Hypertension (PAH)	**Phase 2b[3]**				PhaseBio	
GLP2-ELP Short Bowel Syndrome	**Late research**				PhaseBio	
CNP-ELP Achondroplasia	**Late research**				PhaseBio	
Early Programs	**PROPRIETARY LONG-ACTING INJECTABLE RECOMBINANT BIOPOLYMERS** (Elastin-like Polypeptides – ELPs)					

1. REVERSE-IT: Rapid and SustainEd ReVERSal of TicagrElor – Intervention Trial
2. Targeted timeline could be impacted by the continued scope and duration of the COVID-19 pandemic
3. Phase 2b trial voluntarily stopped early due to COVID-19 impacts on manufacturing, associated drug supply and the rate of enrollment in the study; PhaseBio has elected to stop further development after a strategic review in order to reprioritize resources towards pre-commercialization activities for bentracimab and the advancement of other pipeline programs, including PB6440 for resistant hypertension

PhaseBio

Corporate

Experienced Management Team

JONATHAN MOW
Chief Executive Officer

SUSAN ARNOLD, PhD
SVP Technical Operations

JONATHAN BIRCHALL
Chief Commercial Officer

GLEN BURKHARDT
SVP Human Resources

KRIS HANSON
SVP & General Counsel

JOHN LEE, MD, PhD, FACC
Chief Medical Officer

LAUREN RICHARDSON
VP Regulatory & Quality

JOHN SHARP
Chief Financial Officer

Dedicated to transforming patients' lives through science and excellence

Despite the ongoing challenges posed by the ongoing COVID-19 pandemic, 2021 and 2022, to date, have been years of significant progress for PhaseBio. In addition to refining our mission, advancing our pipeline programs and kicking off the REVERSE-IT Phase 3 clinical trial for our lead program, bentracimab, we have evolved our corporate logo and the overall look and feel of our website, drawing inspiration for the PhaseBio brand from our prospective patients, healthcare providers and our people. The new PhaseBio logo is defined by a patient-friendly representation of the heart composed of the letters 'P' and 'B' from the PhaseBio name.

This shows that cardiovascular disease is not just what PhaseBio does – it is who we are.

Q2 2022 Financial Highlights

- Sub-license revenue: $0.2M
- Operating expense: $25.5M
  - R&D: $20.9M
  - SG&A: $4.6M
- Loss from operations: ($25.3M)
- Net Loss of ($16.7M) or ($0.34) per share, basic and diluted
  - 49.2M shares used for computing Q2 2022 net loss per share
- Cash and cash equivalents as of 06/30/2022: $7.8M
- Available SFJ funding as of 06/30/2022: $21.0M

Bentracimab *(PB2452)*

Reversal Agent for Ticagrelor

$P2Y_{12}$ Inhibitors: Unmet Need and the Dilemma in Managing Surgical Patients

Significant unmet need for antiplatelet agent reversal

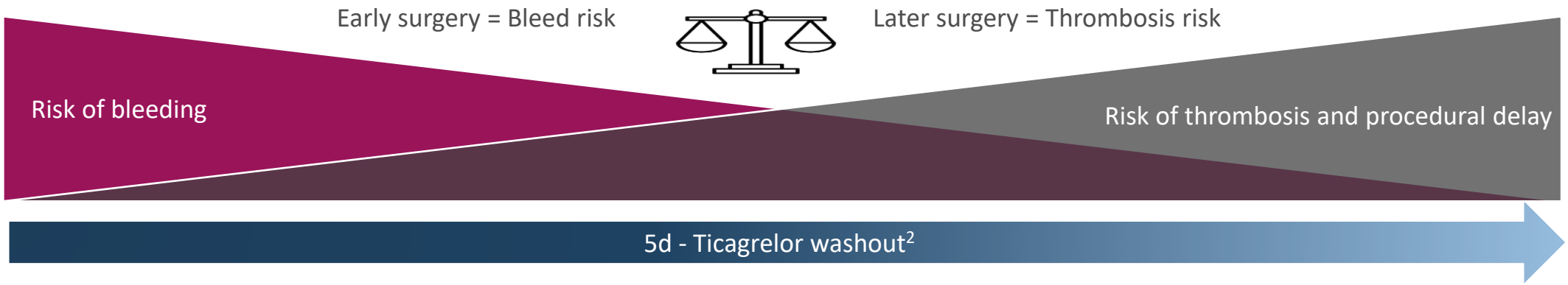
MAJOR BLEEDING

- Intracranial Haemorrhage (ICH), GI, Trauma
- All oral antiplatelet agents have the potential to cause major bleeding, which can be severe or even fatal
- Bentracimab designed to immediately and sustainably reverse the antiplatelet effects of ticagrelor

URGENT SURGERY OR INTERVENTION

- Currently oral $P2Y_{12}$ agents, including ticagrelor, require a 5-day washout prior to surgery[1,2]
  - Urgent surgery often cannot wait 5 days
  - Higher thrombotic risk during washout
- In Phase 1 and Phase 2a studies, bentracimab observed to immediately and sustainably reverse ticagrelor inhibition of platelet activation
  - Enables immediate surgery

Surgical Dilemma



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1. Plavix/clopidogrel Prescribing Information: https://packageinserts.bms.com/pi/pi_plavix.pdf, https://www.ema.europa.eu/en/documents/product-information/plavix-epar-product-information_en.pdf
2. Brilinta/Brilique/ticagrelor Prescribing Information: https://www.azpicentral.com/brilinta/brilinta.pdf#page=1, https://www.ema.europa.eu/en/documents/product-information/brilique-epar-product-information_en.pdf

Bentracimab: Novel Reversal Agent for Brilinta (Ticagrelor)

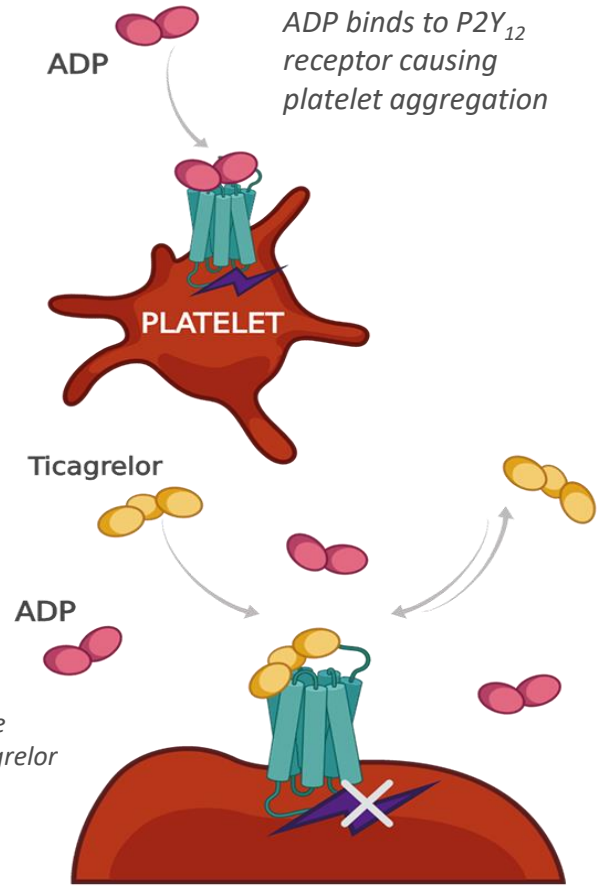
- Ticagrelor has proven superior efficacy vs. clopidogrel and a unique reversible binding profile within the oral $P2Y_{12}$ class
  - Clopidogrel and prasugrel both permanently bind to the receptor and cannot be reversed
- Bentracimab is the only specific reversal agent in development for ticagrelor for both surgical and active bleed indications
  - Bentracimab clinical data to date have demonstrated both immediate (<5 min) and sustained (~24 hours) reversal of ticagrelor antiplatelet effects
- Believe approval would differentiate ticagrelor on safety vs. other oral antiplatelet agents
  - Differentiation would drive increased ticagrelor utilization

Bentracimab has the potential to eliminate the dilemma of choosing between an increased risk of bleeding and an increased risk of thrombosis or procedural delay in patients requiring surgery

Bentracimab: Well-Characterized Mechanism of Reversal of Ticagrelor

Bentracimab

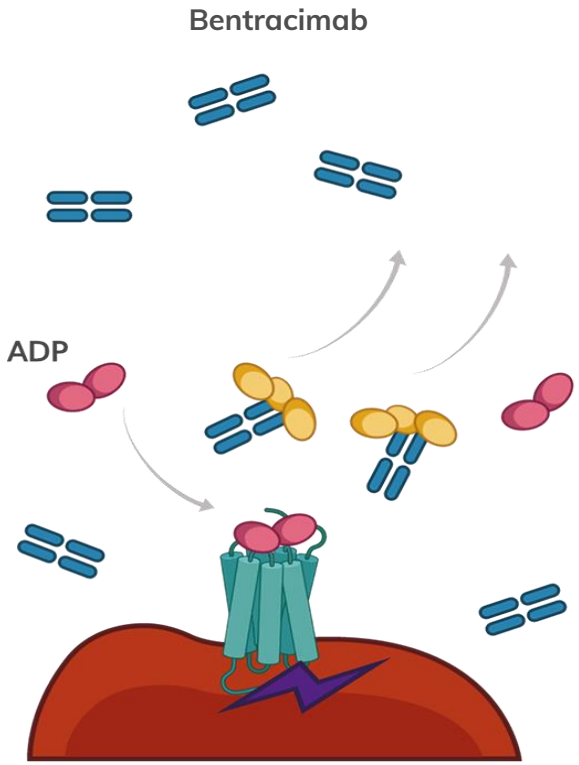
1. *ADP binds to $P2Y_{12}$ receptor causing platelet aggregation*



This is a reversible process with ticagrelor cycling on/off the P2Y12 receptors

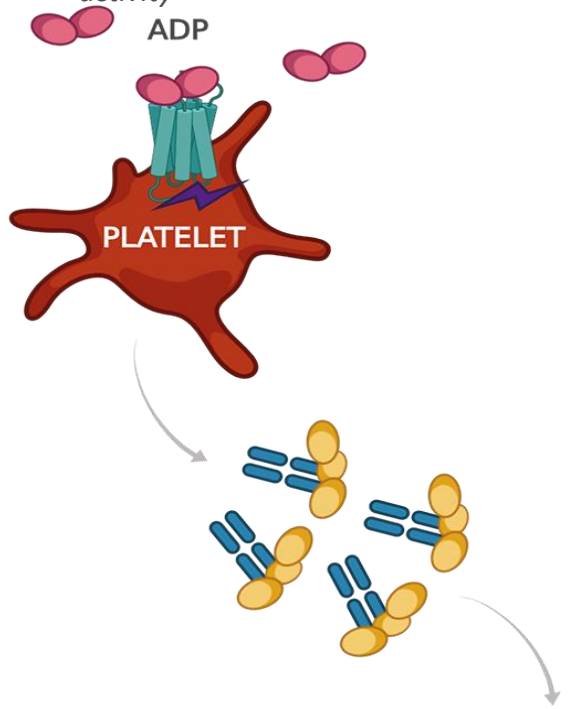
2. *Ticagrelor binds to $P2Y_{12}$, inhibiting ADP-induced platelet aggregation*

3. Bentracimab *binds to free ticagrelor with very high affinity*



Bentracimab-ticagrelor binding is preferential to ticagrelor-$P2Y_{12}$ binding due to 100x higher affinity (K_i 20 pM vs 2nM)

4. *As free ticagrelor is eliminated, ADP can again activate the $P2Y_{12}$ receptor, restoring platelet activity*



5. *Bentracimab-ticagrelor is cleared from the bloodstream*

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Clinical

Immediate and Sustained Ticagrelor Reversal with Bentracimab in Healthy Subjects in Phase 1, 2A, 2B Trials

Bentracimab

Phase 1[1]

Healthy volunteers 18–50 y

- Received ticagrelor + bolus + continuous infusion of bentracimab 18 g
- Significant reversal observed 5 minutes after initiation of bentracimab infusion
- Duration of reversal was infusion-time dependent, lasting 20–24 hours with a 16-hour infusion
- Published in the New England Journal of Medicine

Phase 2a[2]

Healthy volunteers 50–80 y

- Received ticagrelor + low-dose aspirin and bentracimab 18 g
- Ticagrelor reversal consistent with Ph 1
- Well tolerated with minor adverse events
- Bentracimab 36 g cohort for supratherapeutic ticagrelor blood levels
  - Statistically significant reversal achieved within 5 minutes of initiating bentracimab infusion, sustained for 24 hours
  - Platelet function normalized by 30 minutes following initiation of infusion and remained normal for 24 hours

Phase 2b[3]

Healthy volunteers 50–80 y

- Received ticagrelor + low-dose aspirin and bentracimab 18 g
- Achieved primary endpoint of ticagrelor reversal measured by VerifyNow $P2Y_{12}$ assay
  - Statistically significant reduction in % inhibition of PRU within 4 hours; similar extent of reversal to Phase 1 and 2A
- Safety profile consistent with Phase 1 and 2A studies
  - No treatment emergent AEs or SAEs considered related to bentracimab
  - No thrombotic events observed
- Phase 2B results presented during a Late Breaking Featured Clinical Research session at the American College of Cardiology Annual Scientific Session & Expo being held in Washington, D.C., April 2-4, 2022

PhaseBio

1. Bhatt DL, Pollack CV, Weitz JI, et al. *N Engl J Med*. 2019;380:1825-33; NCT03492385; 2. NCT03928353; 3. NCT04122170.

REVERSE-IT: Bentracimab Pivotal Phase 3 Trial Overview

REVERSE-IT
Rapid and SustainEd ReVERSal of TicagrElor – Intervention Trial
bentracimab

- REVERSE-IT: Rapid and SustainEd ReVERSal of TicagrElor – Intervention Trial
- Open-label, single-arm study in patients with uncontrolled major or life-threatening bleeding or who require urgent surgery or invasive procedure
- Total of 200 patients targeted for total enrollment
  - First 176 patients to form the basis of accelerated BLA filing in US and MAA in EU
  - Accelerated BLA endpoint is restoration of platelet function based on VerifyNow® PRUTest® platelet function assay
- Additional endpoints related to hemostasis captured as part of the primary outcome analysis
- US FDA Breakthrough Therapy designation, EMA PRIME designation and Breakthrough designation in China

REVERSE-IT
Rapid and SustainEd ReVERSal of TicagrElor – Intervention Trial

REVERSE-IT Interim Results Published in December 2021

NEJM Evidence

Digital journal from the *New England Journal of Medicine* Group.
First issue, January 2022.
Article is posted at https://evidence.nejm.org/

Bentracimab for Ticagrelor Reversal in Patients Undergoing Urgent Surgery

- Deepak L. Bhatt, MD, MPH, Charles V. Pollack, Jr., MD, C. David Mazer, MD,
- Dominick J. Angiolillo, MD, PhD, Ph. Gabriel Steg, MD, Stefan K. James, MD, PhD,
- Jeffrey I. Weitz, MD, Rohit Ramnath, PhD, Susan E. Arnold, PhD, Michael C. Mays, BS,
- Bret R. Umstead, MS, Barbara White, MD, Lisa L. Hickey, MS, Lisa K. Jennings, PhD,
- Benjamin J. Curry, PhD, John S. Lee MD, PhD, Subodh Verma, MD, PhD,
- on Behalf of the REVERSE-IT Investigators

REVERSE-IT: Baseline Characteristics

REVERSE-IT
Rapid and SustainEd ReVERSal of TicagrElor – Intervention Trial
bentracimab

Characteristic	Surgical (N=142)	Bleeding (N=8)	Total (N=150)
Age (years), Mean (SD)	64.8 (10.46)	67.0 (13.40)	65.0 (10.59)
Sex, n (%)			
Male	112 (78.9)	4 (50.0)	116 (77.3)
Female	30 (21.1)	4 (50.0)	34 (22.8)
Weight (kg), Mean (SD)	85.2 (19.33)	76.9 (29.72)	84.8 (19.87)
Height (cm), Mean (SD)	170 (8.62)	169 (11.69)	171 (8.75)
BMI (kg/m^2), Mean (SD)	29.1 (6.21)	27.8 (11.46)	29.1 (6.49)
Ethnicity, n (%)			
Hispanic or Latino	1 (0.7)	2 (25.0)	3 (2.0)
Not Hispanic or Latino	141 (99.3)	6 (75.0)	147 (98.0)
Race, n (%)			
White	118 (83.1)	7 (87.5)	125 (83.3)
Black or African American	5 (3.5)	1 (12.5)	6 (4.0)
Asian	16 (11.3)	0 (0)	16 (10.7)
American Indian or Alaskan	1 (0.7)	0 (0)	1 (0.7)
Other	2 (1.4)	0 (0)	2 (1.3)
Hypertension	114 (80.3)	6 (75.0)	120 (80.0)
Diabetes	57 (40.1)	2 (25.0)	59 (39.3)
Myocardial infarction	118 (83.1)	4 (50.0)	122 (81.3)
Baseline eGFR (MDRD)			
eGFR < 60, n (%)	32 (22.5)	0 (0)	32 (21.3)
Time from last ticagrelor, n (%)			
0-1 days	100 (70.4)	7 (87.5)	107 (71.3)
2 days	29 (20.4)	1 (12.5)	30 (20.0)
3 days	13 (9.2)	0 (0)	13 (8.7)

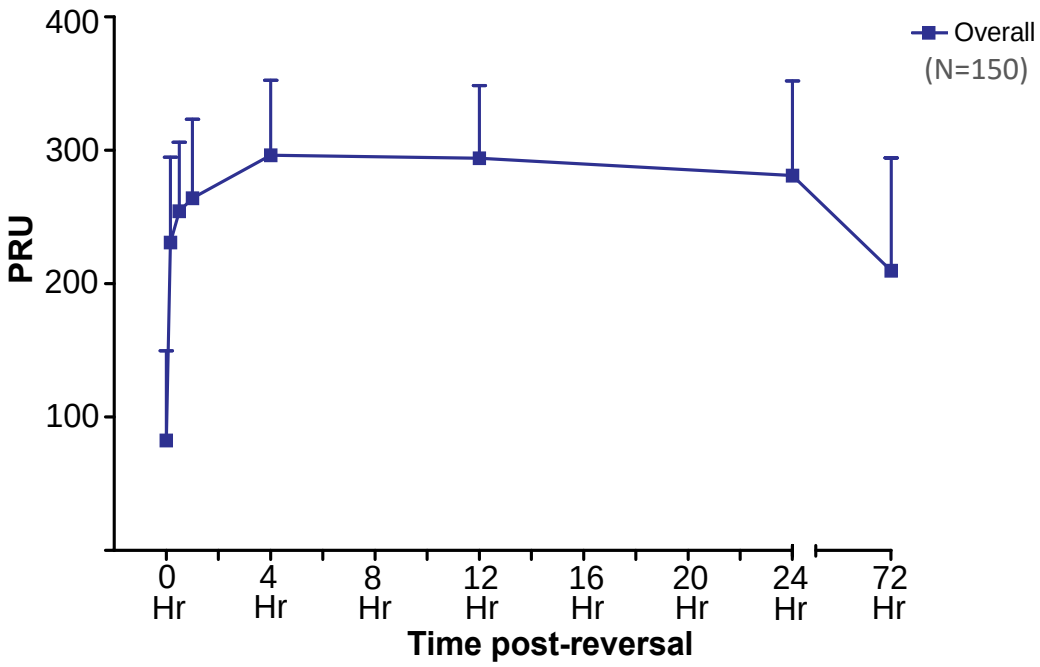
PhaseBio

https://evidence.nejm.org/doi/pdf/10.1056/EVIDoa2100047

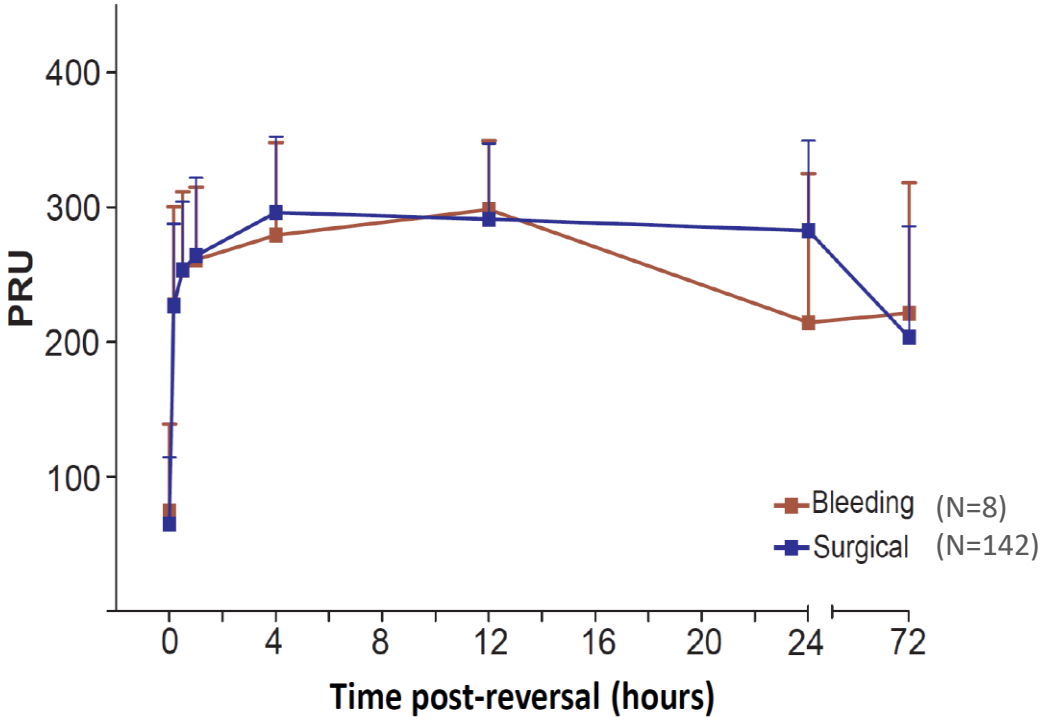
REVERSE-IT: Platelet Reversal

REVERSE-IT
Rapid and SustainEd ReVERSal of TicagrElor – Intervention Trial
bentracimab

PRU analysis in all patients



PRU analysis in surgical vs bleeding patients



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https://evidence.nejm.org/doi/pdf/10.1056/EVIDoa2100047

REVERSE-IT: Adjudicated Surgical and Bleeding Hemostasis

REVERSE-IT
Rapid and SustainEd ReVERSal of TicagrElor – Intervention Trial
bentracimab

Adjudicated and Investigator-Reported Surgical Outcomes

Hemostasis in Surgical Patients	n (%)
Adjudicated achieved hemostasis (N=113)	113 (100.0)
GUSTO Mild	75 (66.4)
GUSTO Moderate	38 (33.6)
GUSTO Severe	0 (0)
Investigator-reported achieved hemostasis (N=142)	135 (95.1)
Normal or mildly abnormal bleeding	110 (77.5)
Moderately abnormal	25 (17.6)
Severely abnormal or unknown	7 (4.93)
Blood Product Transfusions	**n (%)**
Total blood transfusions (pRBCs or whole blood)	56 (39.04)
Blood transfusions for bleeding event	10 (7.04)
Total platelets transfusions	19 (13.4)
Platelet transfusions for bleeding event	6 (4.22)
Other Surgical Outcomes	
Restarted $P2Y_{12}$ inhibition, n (%)	111 (74%)
Time to restart (median), days (min, max)	2 (0, 22)
Total mortality, n (%)	4 (2.8)

pRBC, packed red blood cells. Investigators were required to specify in case report forms whether allogeneic blood and platelet products were transfused for bleeding events or other routine perioperative use. Total transfusions and transfusions for bleeding events are shown above.

Adjudicated and Investigator-Reported Bleeding Outcomes

Hemostasis in Bleeding Patients	n (%)
Adjudicated achieved hemostasis (N=9)	7 (77.8)
Excellent hemostasis	6 (66.7)
Good hemostasis	1 (11.1)
Poor hemostasis	1 (11.1)
Unable to determine	1 (11.1)
Investigator-reported achieved hemostasis (N=8)	7 (87.5)
Median time to hemostasis, hrs (min, max)	23 (112, 7)
Blood Product Transfusions	**n (%)**
Total blood transfusions (pRBCs or whole blood)	5 (62.5)
Blood transfusions for bleeding event	5 (62.5)
Total platelet transfusions	2 (25.0)
Platelet transfusions for bleeding event	1 (12.5)
Other Outcomes in Bleeding Patients	
Restarted $P2Y_{12}$ inhibition, n (%)	5 (62.5)
Time to restart (median), days (min, max)	5 (0, 8)
Total mortality, n (%)	0 (0.0)

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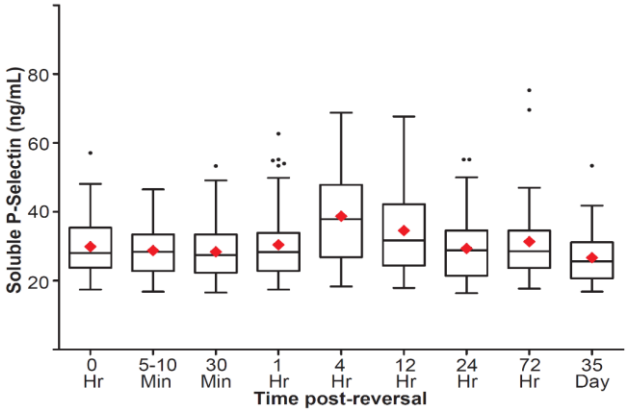
https://evidence.nejm.org/doi/pdf/10.1056/EVIDoa2100047

REVERSE-IT: No Platelet Rebound Activity and No Thrombotic Events Related to Bentracimab

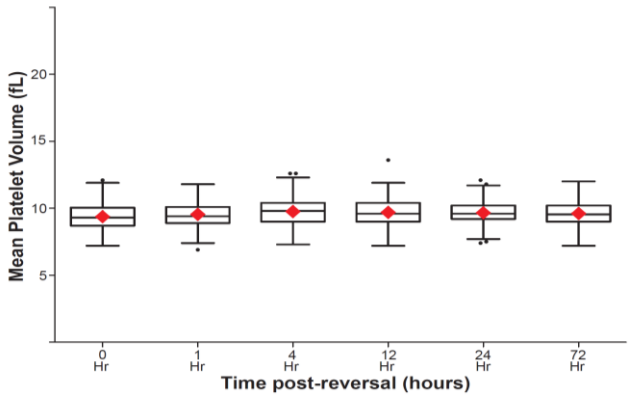
REVERSE-IT
Rapid and SustainEd ReVERSal of TicagrElor – Intervention Trial
bentracimab

Effect of Bentracimab Treatment on P-Selectin and Mean Platelet Volume (MPV). Soluble P-selectin and MPV were measured pre-dose and at multiple timepoints post-initiation of bentracimab treatment to assess for a potentially prothrombotic rebound increase in platelet reactivity post-reversal. Shown are the soluble P-selectin levels in surgical and bleeding patients treated with bentracimab (left). MPV was measured in surgical and bleeding patients treated with bentracimab (right).

P-selectin in surgical and bleeding patients



Mean platelet volume in surgical and bleeding patients



Adjudicated Thrombotic Events Occurring Post-Reversal

Patient Type	Type of Event	Days from Bentracimab and Surgery	P2Y12 restarted before event	Related to bentracimab
51 yr old man, s/p CABG	Myocardial infarction	7	Yes	No
78 yr old woman, s/p CABG	Transient ischemic attack	2	Yes	No
70 yr old man, s/p CABG	Lacunar stroke	1	No	No
58 yr old man, s/p CABG	Anterior, inferior STEMI with total graft occlusion	1	No	No
69 yr old man, s/p CABG, intraortic balloon pump, and thrombectomy	RLE arterial thromboembolism	1	No	No
73 yr of woman, s/p CABG	Acute ischemic stroke	5	No	No
44 yr old male, s/p CABG	Acute coronary syndrome with graft failure	29	Yes	No
47 yr old man, s/p CABG +aortic dissection repair	Acute ischemic right leg immediately post-op	1	No	No

Post-Reversal Thrombotic Events within 30 Days in Reversal Trials

Thrombotic Events	REVERSE-IT [1] (N=150)	REVERSE-AD [2] (N=503)	ANNEXA-4 [3] (N=325)
Total Thrombotic Events, n (%)	8 (5.3)	24 (4.8)	34 (10.5)
Myocardial Infarction	3 (2.0)	6 (1.2)	7 (2.2)
TIA or Stroke	3 (2.0)	7 (1.4)	15 (4.6)
Venous (e.g., PE or DVT)	0 (0)	10 (2.0)	5 (1.5)
Other (e.g., arterial)	2 (1.3)	2 (0.4)	0

1. https://evidence.nejm.org/doi/pdf/10.1056/EVIDoa2100047
2. Pollack CV Jr, Reilly PA, van Ryn J, Eikelboom JW, Glund S, Bernstein RA, et al. Idarucizumab for dabigatran reversal: Full cohort analysis. *N Engl J Med* 2017; **377**: 431–441. https://www.nejm.org/doi/full/10.1056/nejmoa1707278
3. Connolly SJ, Crowther M, Eikelboom JW. et al; ANNEXA-4 Investigators. Full study report of andexanet alfa for bleeding associated with factor Xa inhibitors. N Engl J Med 2019; 380 (14) 1326-1335 https://www.nejm.org/doi/full/10.1056/NEJMoa1814051#article_citing_articles

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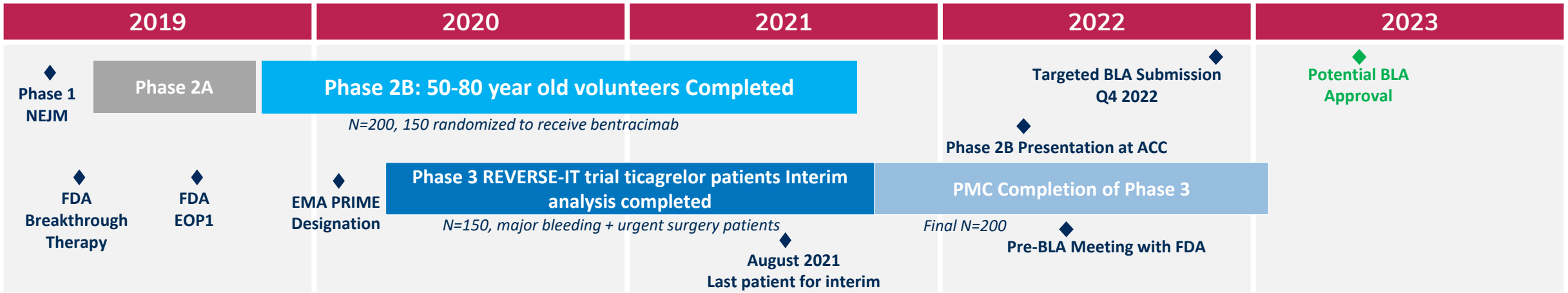
https://evidence.nejm.org/doi/pdf/10.1056/EVIDoa2100047

Regulatory

Pre-BLA Meeting Summary

- Type B pre biologics license application (pre-BLA) meeting held in April 2022
- PhaseBio proposed plans to submit a BLA with data from a total of 25-30 patients with uncontrolled bleeding, together with data from the fully-completed surgical cohort, to support a label with both bleeding and surgical indications
- FDA agreed that the plan appeared reasonable, but the final label would be a review issue based on the data submitted
- To date, and pending final adjudication, the REVERSE-IT trial has enrolled more than 35 patients taking ticagrelor who experienced uncontrolled bleeding events
- FDA noted they would consider separating the indications for possible Accelerated Approval of either uncontrolled bleeding or surgery, if the application was deemed adequate to support approval for only one of the two
- For post-marketing requirements, the FDA confirmed prior recommendations:
  - Complete enrollment in the Phase 3 REVERSE-IT trial and submit data from a total of at least 200 patients from this trial
  - Establish a post-approval registry study that will be active ahead of a product launch following a potential Accelerated Approval

Bentracimab Development Program



Targeted timelines could be impacted by the continued scope and duration of the COVID-19 pandemic
NEJM= New England Journal of Medicine, EOP1=End-of-Phase 1 Meeting, BLA=Biologics License Application

- Phase 1 study published in NEJM (Bhatt DL, Pollack CV, Weitz JI, et al. *N Engl J Med*. 2019; 380:1825-1833)
- Phase 2B study enrollment completed, results presented at ACC April 2022
- Interim analysis of REVERSE-IT Phase 3 trial completed in November 2021, published *NEJM Evidence* January 2022
- US BLA on track for submission in Q4 2022 following outcome of pre-BLA meeting
  - Breakthrough status in US, PRIME designation in EU and Breakthrough in China (NMPA)

Opportunity for Accelerated/Conditional Approval

Bentracimab

Planned Approval Packages Based on Phase 3 - Interim Analysis

- Initial BLA/MAA filing package based on a minimum safety requirement of at least 100 Phase 3 patients
  - US: Accelerated (Based on biomarker)
  - EU: Conditional (Based on interim analysis)
    - FDA and EMA agreed the PRU biomarker endpoint at interim likely predictive of clinical benefit in all patients
- ***Pre-BLA Meeting provided opportunity to add uncontrolled bleeding subjects to current data set – US and Europe filing***

Clinical confirmation of interim biomarker endpoint at Phase 3 Completion – Full Approval

- US and EU: Phase 3 completion and registry cohorts
- China: Initial submission will include completed Phase 3 study

Commercial

Expect Continued Long-Term Rx Growth of Ticagrelor

Bentracimab approval has the potential to drive continued positive momentum

Bentracimab

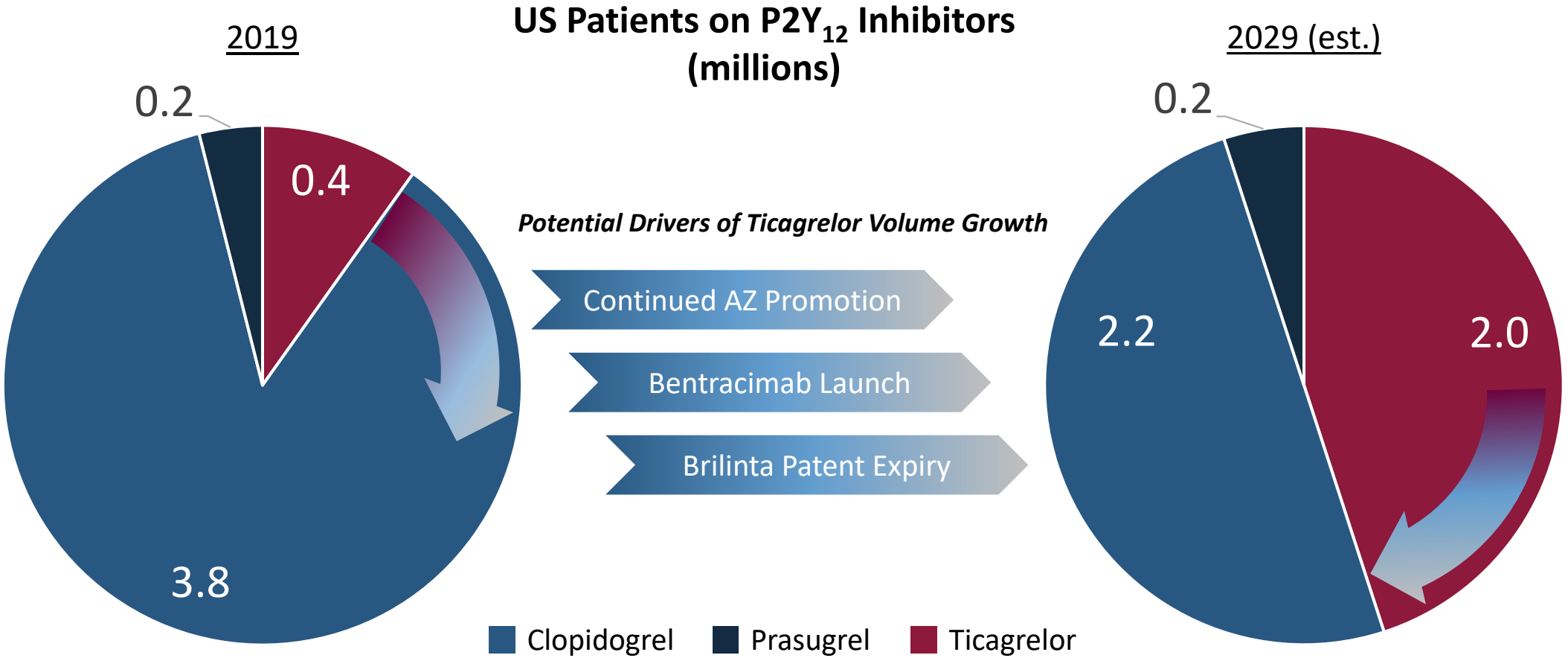
- Brilinta/Brilique sales in 2021 were approximately $1.5B
  - Pandemic impact dampened 2020 and 2021 growth
- In February 2019, Brilinta Phase 3 THEMIS[1] trial met primary endpoint in patients with established coronary artery disease and type-2 diabetes; in May 2020, FDA approved a label update[2] for BRILINTA in the US to include the reduction of the risk of a first heart attack or stroke in high-risk patients with coronary artery disease
- In January 2020, Brilinta Phase III THALES[3] trial met primary endpoint in patients with acute ischemic stroke or patients with high-risk transient ischemic attack; in November 2020[4], FDA approved a label update for Brilinta in the US to include the reduction of the risk of stroke in patients with acute ischemic stroke or high-risk transient ischemic attack

Ticagrelor Differentiation *vs. clopidogrel*	**Now**	**Post Bentracimab Launch**	**Post LOE of ticagrelor**
Efficacy	✓	✓	✓
Safety	≈ *(no reversal agent)*	✓	✓
Price	✗ *(branded vs. generic)*	✗ *(branded vs. generic)*	✓

PhaseBio

1. https://www.astrazeneca.com/media-centre/press-releases/2019/brilintas-phase-iii-themis-trial-met-primary-endpoint-in-patients-with-established-coronary-artery-disease-and-type-2-diabetes-25022019.html
2. https://www.astrazeneca.com/content/astraz/media-centre/press-releases/2020/brilinta-approved-in-the-us-to-reduce-the-risk-of-a-first-heart-attack-or-stroke-in-high-risk-patients-with-coronary-artery-disease.html
3. https://www.astrazeneca.com/media-centre/press-releases/2020/brilinta-met-primary-endpoint-in-phase-iii-thales-trial-in-stroke-27012020.html
4. https://www.astrazeneca.com/media-centre/press-releases/2020/brilinta-approved-in-the-us-in-stroke.html#:~:text=AstraZeneca's%20Brilinta%20(ticagrelor)%20has%20been,transient%20ischaemic%20attack%20(TIA).

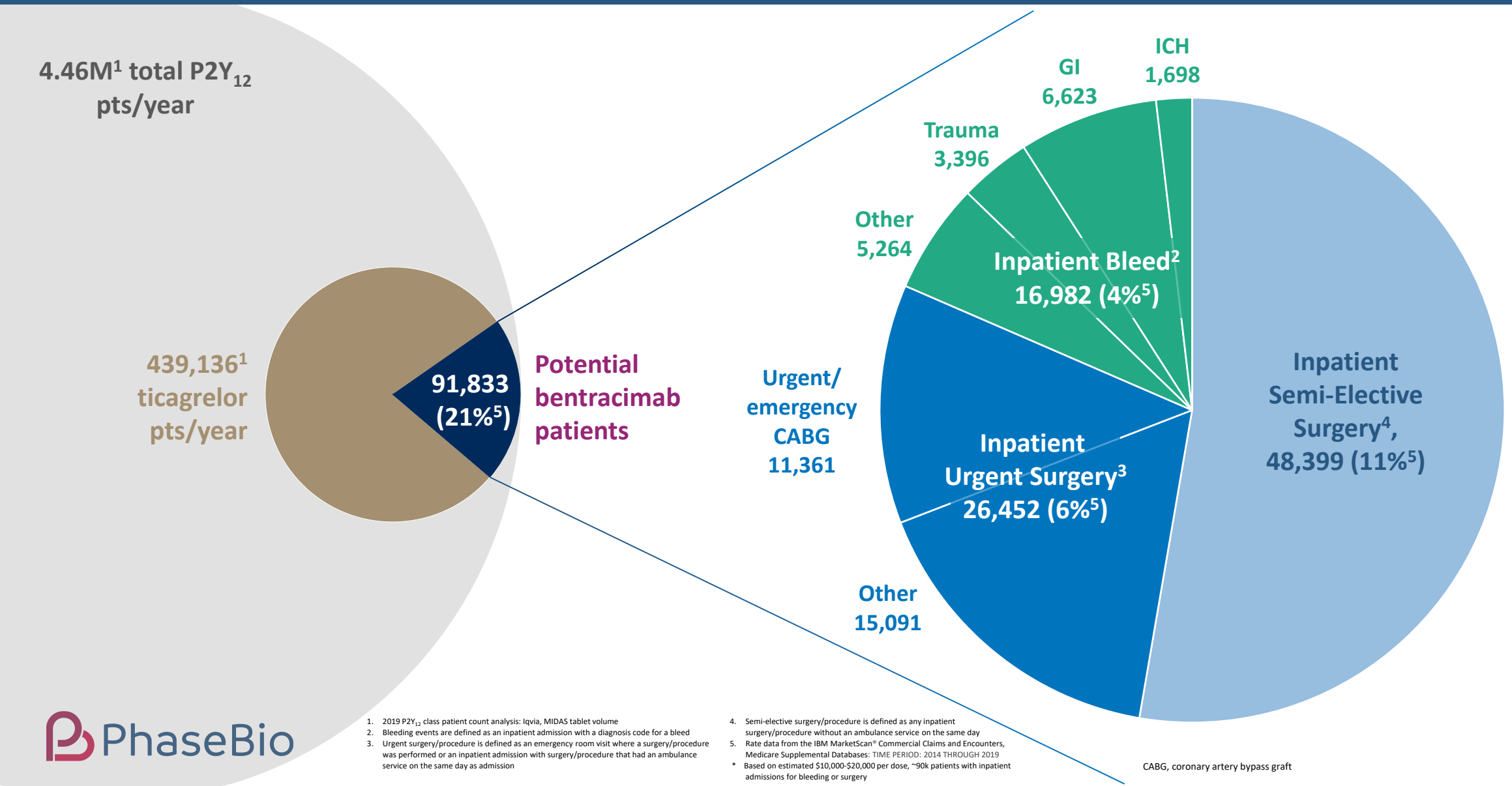
US Patients on $P2Y_{12}$ Inhibitors: Potential for Significant Long-Term Ticagrelor Patient Growth



PhaseBio

Iqvia® Analysis of MIDAS Data

Bentracimab Patient Opportunity (2019) Implies $1-2B* Addressable Market



1. 2019 $P2Y_{12}$ class patient count analysis: Iqvia, MIDAS tablet volume
2. Bleeding events are defined as an inpatient admission with a diagnosis code for a bleed
3. Urgent surgery/procedure is defined as an emergency room visit where a surgery/procedure was performed or an inpatient admission with surgery/procedure that had an ambulance service on the same day as admission
4. Semi-elective surgery/procedure is defined as any inpatient surgery/procedure without an ambulance service on the same day
5. Rate data from the IBM MarketScan® Commercial Claims and Encounters, Medicare Supplemental Databases: TIME PERIOD: 2014 THROUGH 2019

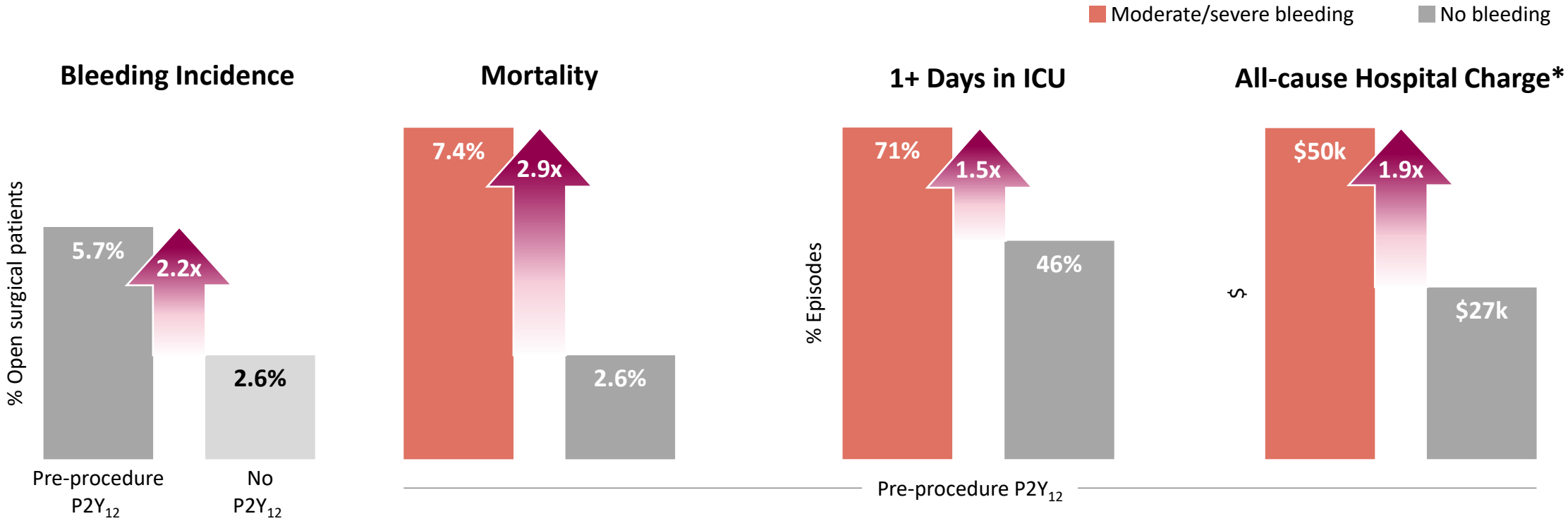
* Based on estimated $10,000-$20,000 per dose, ~90k patients with inpatient admissions for bleeding or surgery

CABG, coronary artery bypass graft

PhaseBio

Increased Mortality and Health-System Costs Associated with Bleeding from Open Surgical Procedures Highlight Opportunity for Bentracimab

Bentracimab



Each washout decision today must weigh increasing **the patients' bleeding risk against risk of thrombosis**

PhaseBio

*All charges by the hospital for the inpatient episode – includes drugs, devices, professional fees, room and board etc.
'Bleed' = Moderate to Severe Bleeding identified via bleeding Dx codes, bleed control procedure codes, or 2+ units of blood visible in the inpatient episode. Additional details available in 'Key Assumptions & Definitions' section.
Data Source: In-Patient Hospital Admissions in 2019 from Premier Chargemaster Data; Statistical significance testing has not been conducted.

PB6440

Aldosterone Synthase Inhibitor for Resistant Hypertension

PB6440 for Resistant Hypertension

- Upwards of 10 million patients in the United States have resistant hypertension and are at risk for serious, costly medical consequences (stroke, heart attack, kidney failure, etc.)[1]
- Physicians currently prescribe numerous combinations of antihypertensives to lower blood pressure and diminish risk
- Blocking aldosterone has been shown to be an effective mechanism for treating resistant hypertension
  - Currently available aldosterone blockers suffer from poor potency and pharmacokinetics (eplerenone) or poor tolerability (spironolactone) and thus are rarely used
  - Recent clinical data from other aldosterone synthase inhibitor (ASI) programs support blocking aldosterone as an effective approach to treating resistant hypertension
- Draft guidance from the FDA outlines a streamlined regulatory path for novel drugs to treat resistant hypertension without the need for large outcomes studies[2]
- Market research indicates that payors aware of high medical costs associated with resistant hypertension

Large, growing patient population, coupled with a high unmet need, creates an attractive opportunity for a novel therapy to help patients and care-providers better manage blood pressure

PhaseBio

1. Carey RM, Sakhuja S, Calhoun DA, Whelton PK, Muntner P. Prevalence of apparent treatment-resistant hypertension in the United States: comparison of the 2008 and 2018 American heart association scientific statements on resistant hypertension. Hypertension. 2019; 73: 424- 431. Available at: https://www.ahajournals.org/doi/full/10.1161/HYPERTENSIONAHA.118.12191?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dpubmed. Accessed February 2020
2. U. S. Food and Drug Administration. Center for Drug Evaluation and Research. (2018) Hypertension: Conducting Studies of Drugs to Treat Patients on a Background of Multiple Antihypertensive Drugs Guidance for Industry. Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/hypertension-conducting-studies-drugs-treat-patients-background-multiple-antihypertensive-drugs. Accessed February 2020

PB6440: A Promising CYP11B2 Inhibitor

- Potential for an oral, once-daily dosing regimen with a best-in-class profile from a safety and efficacy perspective
- Validated mechanism of action positions ASIs as a new class of therapies with the potential to address a significant unmet need
- As of Q2 2022, PhaseBio has completed development and optimization of robust manufacturing process for PB6440 to support anticipated upcoming clinical proof-of-concept trials
- Potential indications include resistant hypertension and other indications where elevated aldosterone is known to contribute to disease process, such as uncontrolled hypertension, chronic kidney disease, and heart failure
- An investigational new drug application (IND) is targeted for submission to the FDA in the first half of 2023, with first-in-human trials planned to initiate in mid-2023

Characteristics Of PB6440	
High in vitro selectivity for CYP11B2 over CYP11B1	✓
High in vitro selectivity for CYP11B2 over drug metabolizing and other steroidal CYPs	✓
High oral bioavailability	✓
Long half-life in vivo consistent with once-daily dosing	✓
Oral PK and selectivity profiles yield a large therapeutic index in vivo	✓
Suppression of plasma aldosterone levels >90% in an ACTH-challenge model; no effect on cortisol, DOC or 11-b deoxycortisol levels	✓

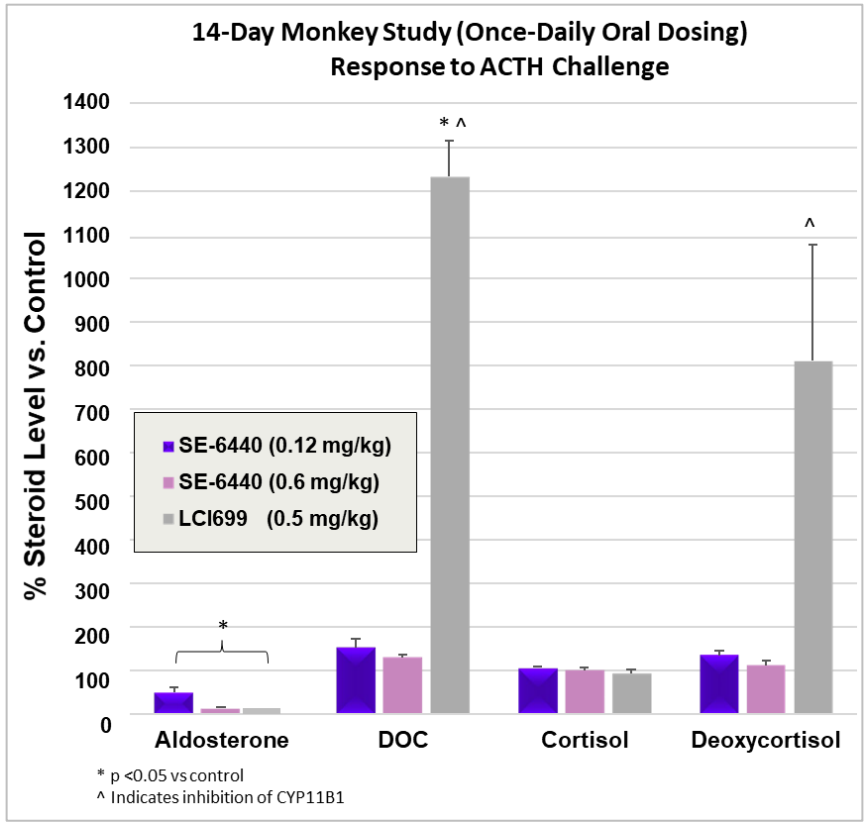
PB6440 Is Highly Selective for Aldosterone Synthase (CYP11B2)

Selectivity and Potency Demonstrated in Primate Chronic Oral Dosing Model

CYP11B Potency and Selectivity (IC_{50}, µM)

	Human			Monkey		
	CYP11B2	CYP11B1#	Selectivity	CYP11B2	CYP11B1	Selectivity
PB6440	0.024	4.859	**202**	0.016	5.802	**363**
LCI699*	0.0007	0.013	**19**	0.016	0.059	**3.7**

Steroid 11β-hydroxylase
*Discontinued Novartis compound; active in Phase 2 studies, but blocked cortisol production, likely due to inadequate selectivity



In a primate model, oral PB6440 demonstrated a sustainable reduction in aldosterone without a significant increase in steroids upstream of CYP11B1, suggesting no significant inhibition of CYP11B1 *in vivo*

Resistant Hypertension (rHTN)[1]: Hypertensive patient on three or more antihypertensive medications and still above goal

Large market opportunity[2]

- ~75M hypertensives in the US
- ~55M diagnosed and treated
- ~10-15M resistant to treatment
- Other potential indications include uncontrolled hypertension, kidney disease, heart failure and primary aldosteronism

Resistant Hypertension increases risk of serious events

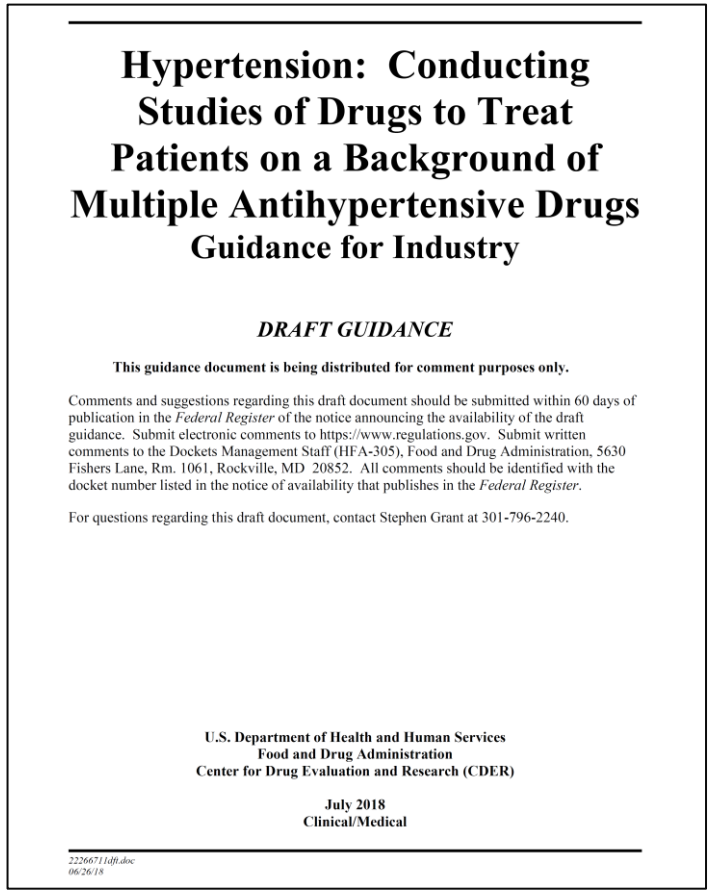
- Heart attack +42%; Stroke +67%
- Heart failure +97%; Kidney failure +225%

Unmet need driving FDA resistant hypertension guidance

- FDA identified rHTN as a key area of unmet need in July 2018 Guidance for Industry

Blocking aldosterone proven to be the best treatment for rHTN

- Aldosterone receptor blocker spironolactone (approved in 1959) demonstrated as most effective treatment for rHTN
- Spironolactone is used in <10% of patients due to side effects[3]



Hypertension: Conducting Studies of Drugs to Treat Patients on a Background of Multiple Antihypertensive Drugs

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact Stephen Grant at 301-796-2240.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

July 2018
Clinical/Medical

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1) Resistant Hypertension (rHTN): on three or more antihypertensive medications and blood pressure still above goal (American Heart Association (AHA) and American College of Cardiology (ACC)
2) U.S. Center for Disease Control and Prevention (CDC); Roberie, 2012
3) Hwang 2017