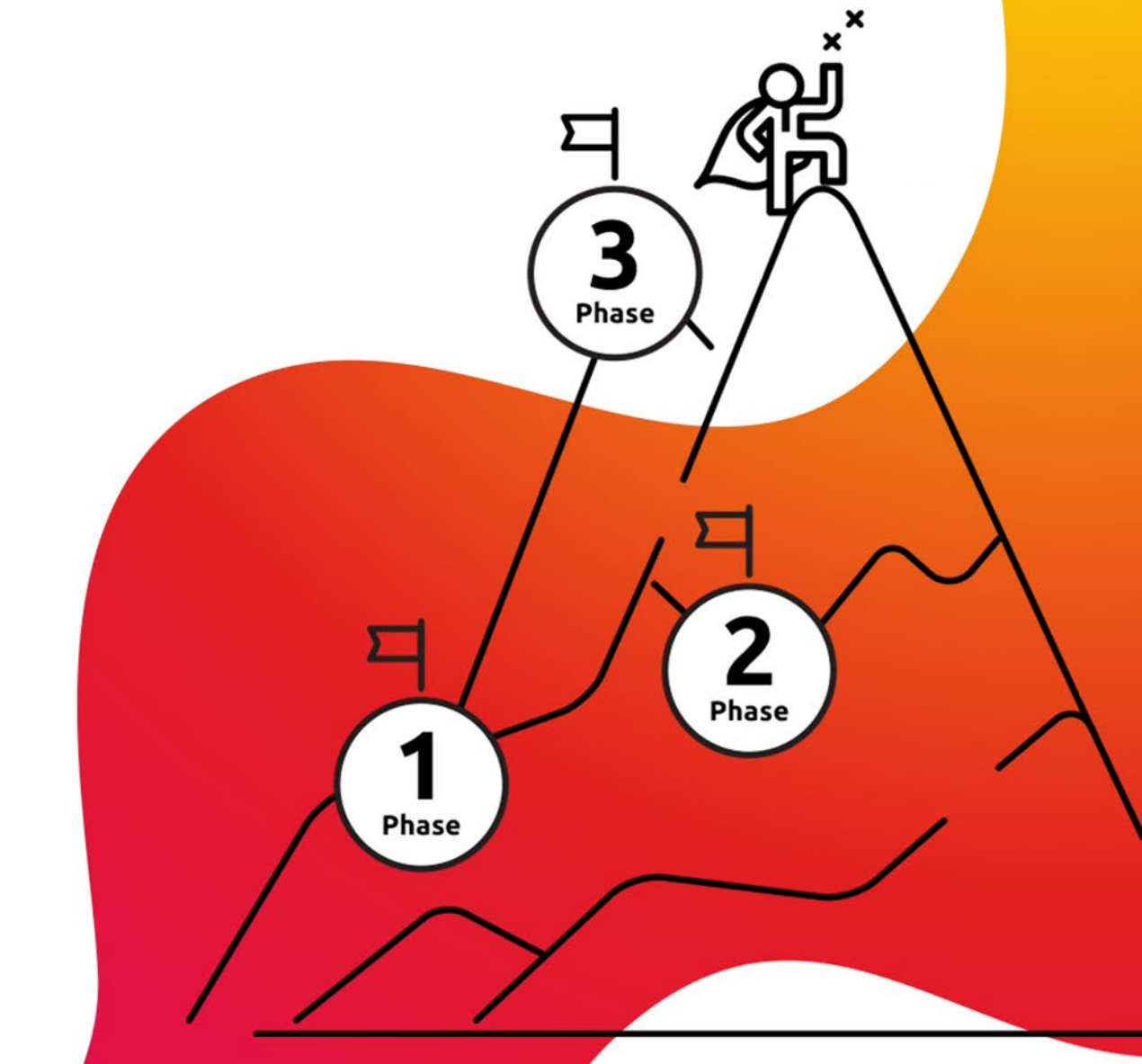
TRYVIO™ (aprocitentan) FDA approval



Investor webcast – March 20, 2024

The following information contains certain “forward-looking statements”, relating to the company’s business, which can be identified by the use of forward-looking terminology such as “estimates”, “believes”, “expects”, “may”, “are expected to”, “will”, “will continue”, “should”, “would be”, “seeks”, “pending” or “anticipates” or similar expressions, or by discussions of strategy, plans or intentions. Such statements include descriptions of the company’s investment and research and development programs and anticipated expenditures in connection therewith, descriptions of new products expected to be introduced by the company and anticipated customer demand for such products and products in the company’s existing portfolio. Such statements reflect the current views of the company with respect to future events and are subject to certain risks, uncertainties and assumptions. Many factors could cause the actual results, performance or achievements of the company to be materially different from any future results, performances or achievements that may be expressed or implied by such forward-looking statements. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those described herein as anticipated, believed, estimated or expected.

"Today, there are millions of Americans whose blood pressure is not well-controlled despite existing therapy. This is a major public health issue leading to a high incidence of cardiovascular events."

Jean-Paul Clozel
Chief Executive Officer

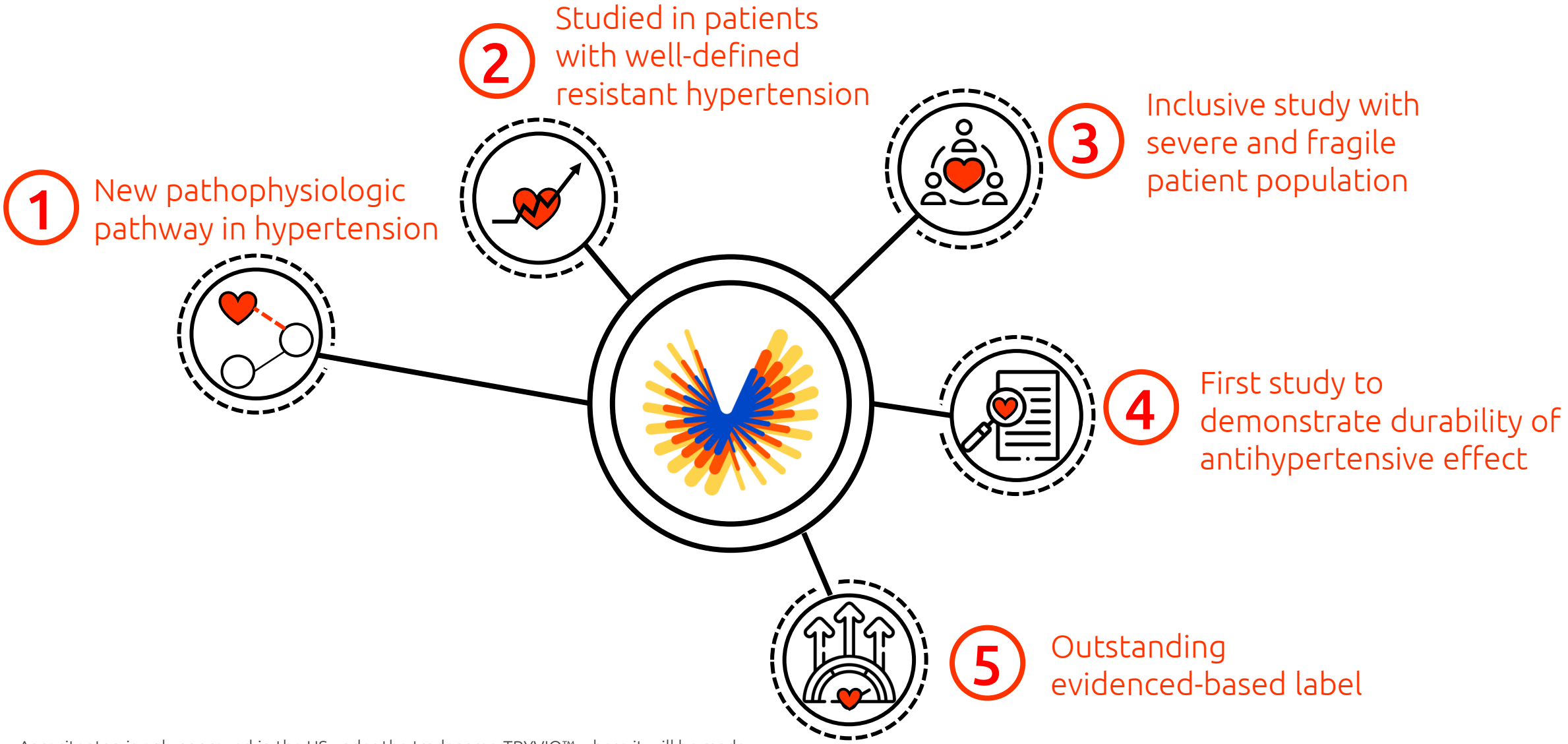
TRYVIO (aprocitentan) 12.5 mg approved by the US FDA

TRYVIO™

(aprocitentan) **12.5mg tablets**

Aprocitentan is only approved in the US under the tradename TRYVIO™ where it will be made available later in 2024. Market authorization is under review in other countries.

A unique compound with unique data



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"Since the endothelin pathway was not yet tackled, we selected aprocitentan, an endothelin receptor antagonist with the ideal properties for use with patients whose hypertension is not adequately controlled with other antihypertensives."

Martine Clozel
Chief Scientific Officer

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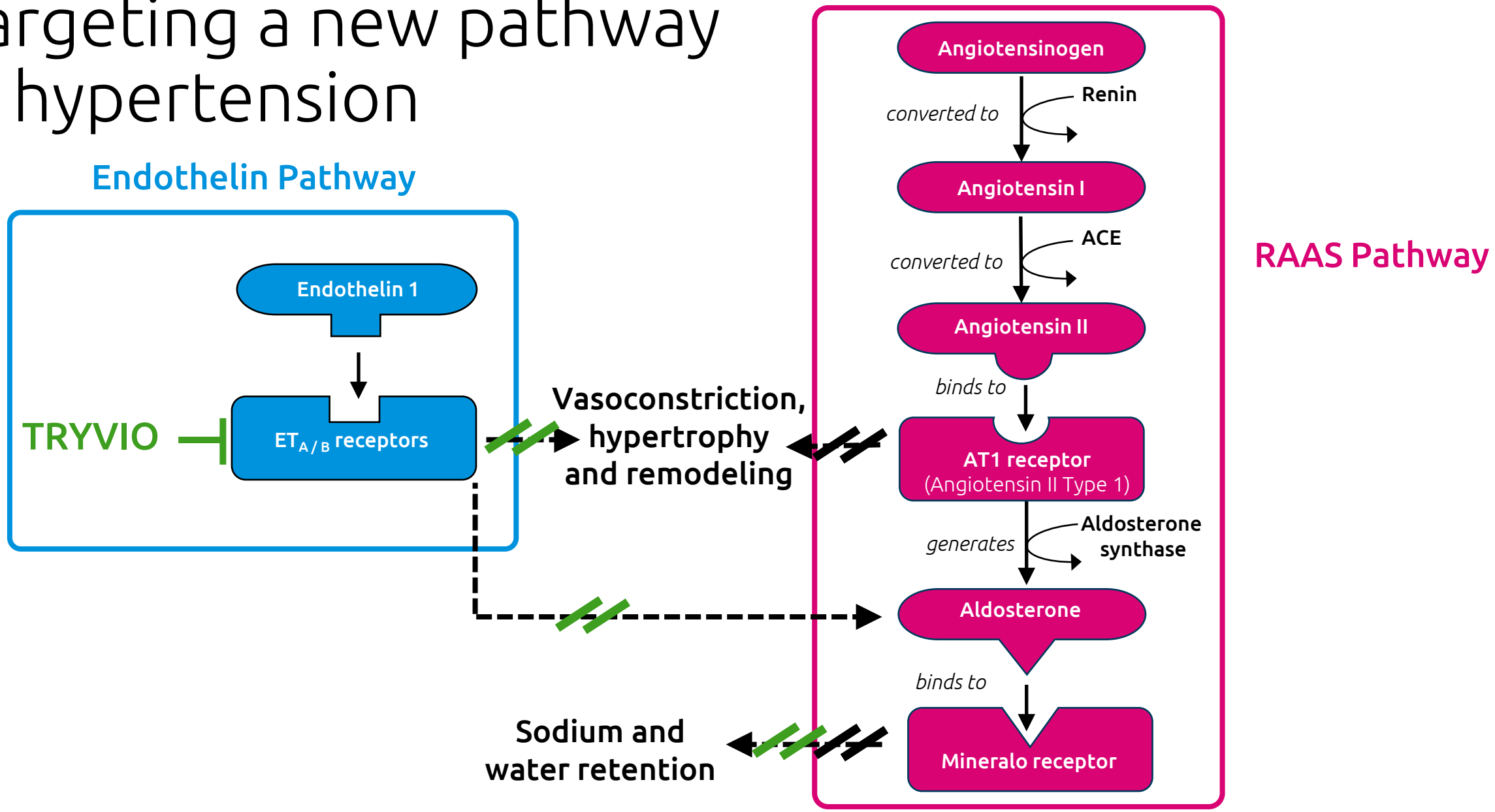
Targeting a new pathway in hypertension



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>30 years of researching the endothelin system

1988
Endothelin-1 identified

1990
ET_A and ET_B receptors identified

1993
First proof of the role of ERA published in *Nature*

1998
First evidence of dual ERA effect in hypertension published in *New England Journal of Medicine*

2007
Failed attempt by competition in resistant hypertension with selective ERA

2022
Aprocitentan – positive Phase 3 in resistant hypertension

2024
TRYVIO™ (aprocitentan) approved by US FDA

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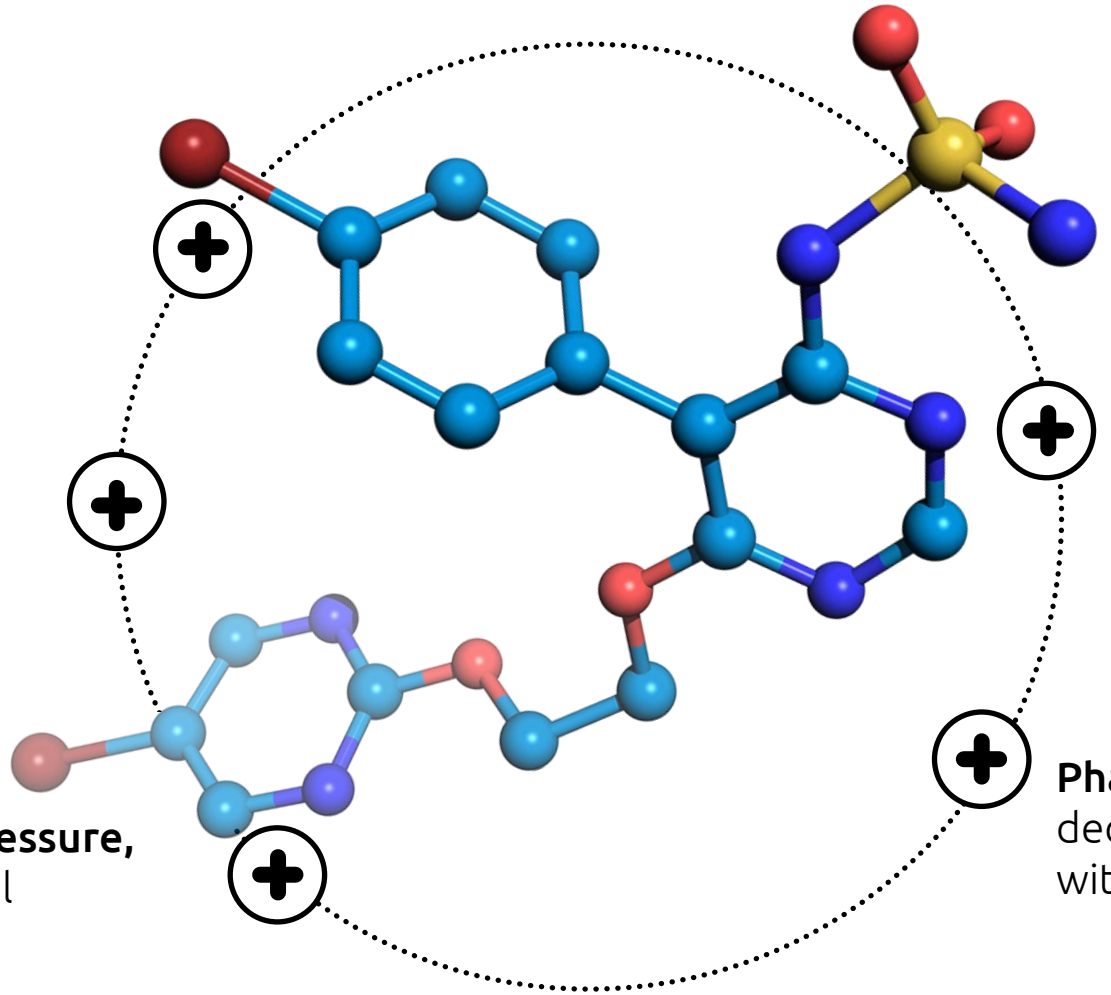
Aprocitentan selected for its ideal properties

Orally-active, potent dual ET_A and ET_B receptor antagonist

Synergistic effect with other antihypertensive drugs (RAAS blockers) in animal models

Demonstrated efficacy on blood pressure, renal and cardiac protection in animal models



Low potential for drug-drug interaction

Phase 2 study shows blood pressure decrease as monotherapy in patients with hypertension

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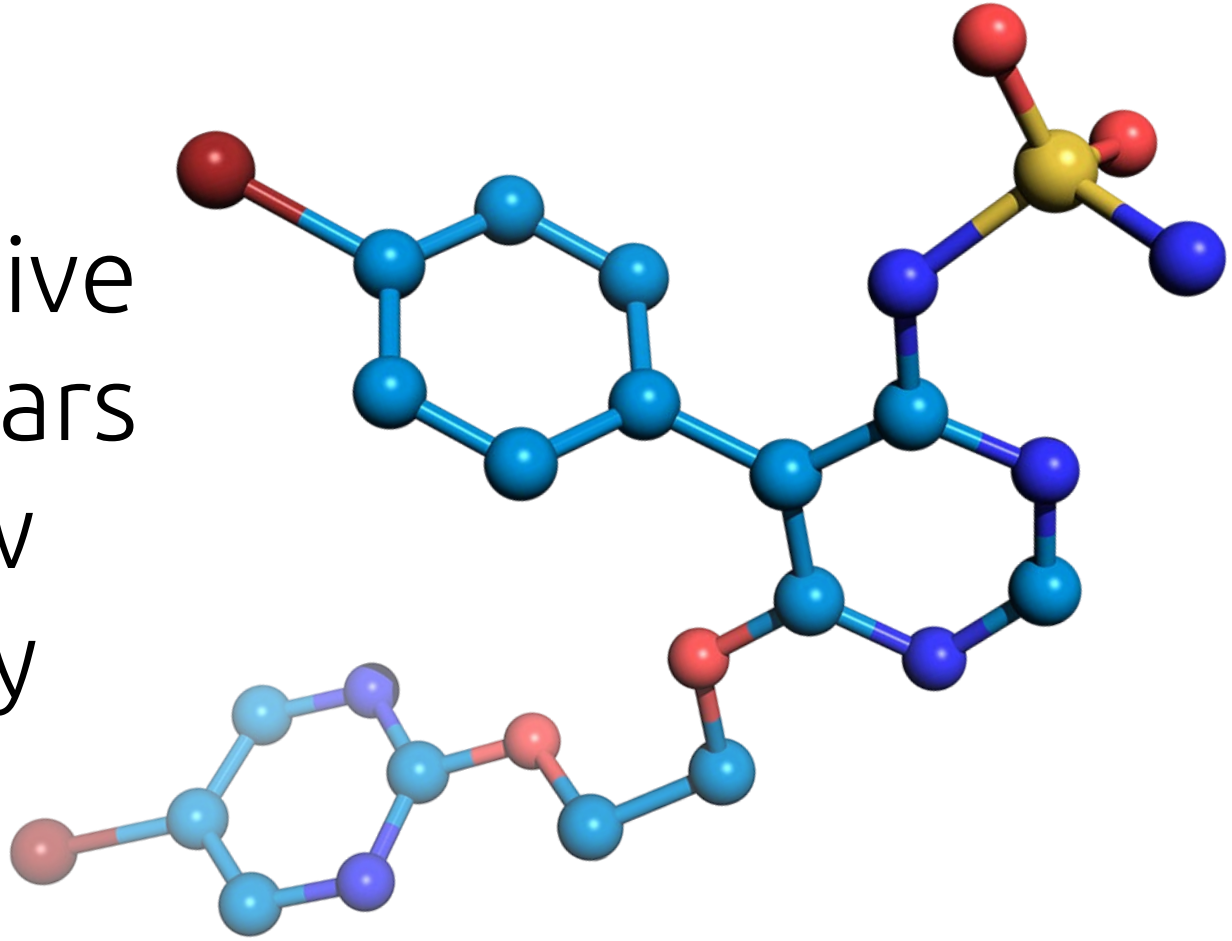
TRYVIO™
(aprocitentan) 12.5mg tablets

The first anti-hypertensive therapy in almost 40 years which works on a new physiological pathway



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"TRYVIO demonstrated a clear and consistent effect across all endpoints of blood pressure measurement and in key sub-populations."

Alberto Gimona
Head of Global Clinical Development

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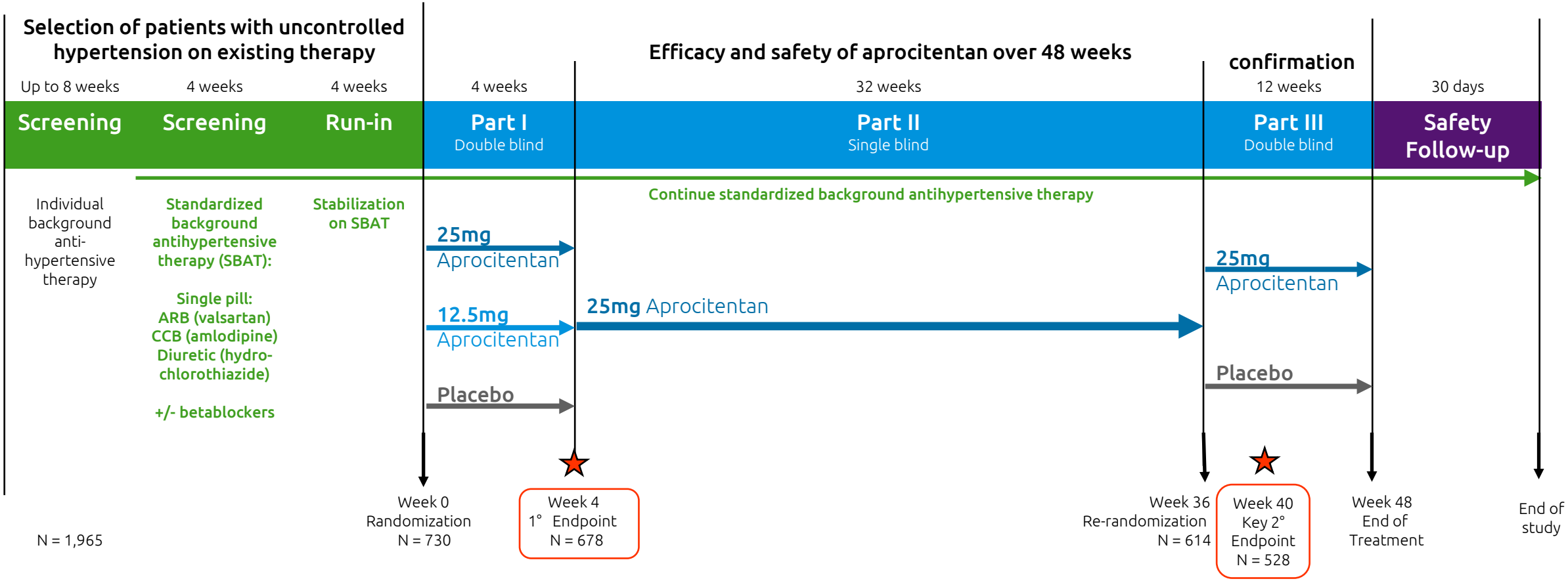
PRECISION investigated durability of BP reduction



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Frail population with multiple co-morbidities

Total: N = 730 [n (%)]

Age (years)		
Mean (SD)	61.7	(10.6)
18 to <65	409	(56.0)
65 - <75	**249**	**(34.1)**
≥75	**72**	**(9.9)**
Race		
White	605	(82.9)
Black or African American	**82**	**(11.2)**
Asian	38	(5.2)
Other	5	(0.7)
BMI# (kg/m^2)		
Mean (SD)	**33.7**	**(6.2)**
SiSBP / SiDBP (mmHg)*		
Mean (SD)	153.3 (8.9) / 87.6 (9.7)	

Antihypertensive therapies#		
3	269	(36.8)
4	337	(46.2)
≥ 5	123	(16.8)
UACR [mg/g]*		
< 30	453	(63.2)
30–300	**174**	**(24.3)**
> 300	**90**	**(12.6)**
missing	13	
eGFR [mL/min]*		
< 30	**21**	**(2.9)**
30 – < 45	**48**	**(6.6)**
45 – < 60	**93**	**(12.7)**
≥ 60	568	(77.8)

Medical history		
Diabetes mellitus	**395**	**(54.1)**
Congestive heart failure	**143**	**(19.6)**
Sleep apnea syndrome	103	(14.1)
Stroke	57	(7.8)
Myocardial infarction	51	(7.0)

BMI: *body mass index*
eGFR: *estimated glomerular filtration rate*
RHT: *resistant hypertension*
SD: *standard deviation*
SiDBP: *sitting diastolic blood pressure*
SiSBP: *sitting systolic blood pressure*
UACR: *urine albumin-to-creatinine ratio*

**** at baseline***
 # at screening

Danaietash P et al., *J Clin Hypertens* 2022 Jul; 24(7):804-813

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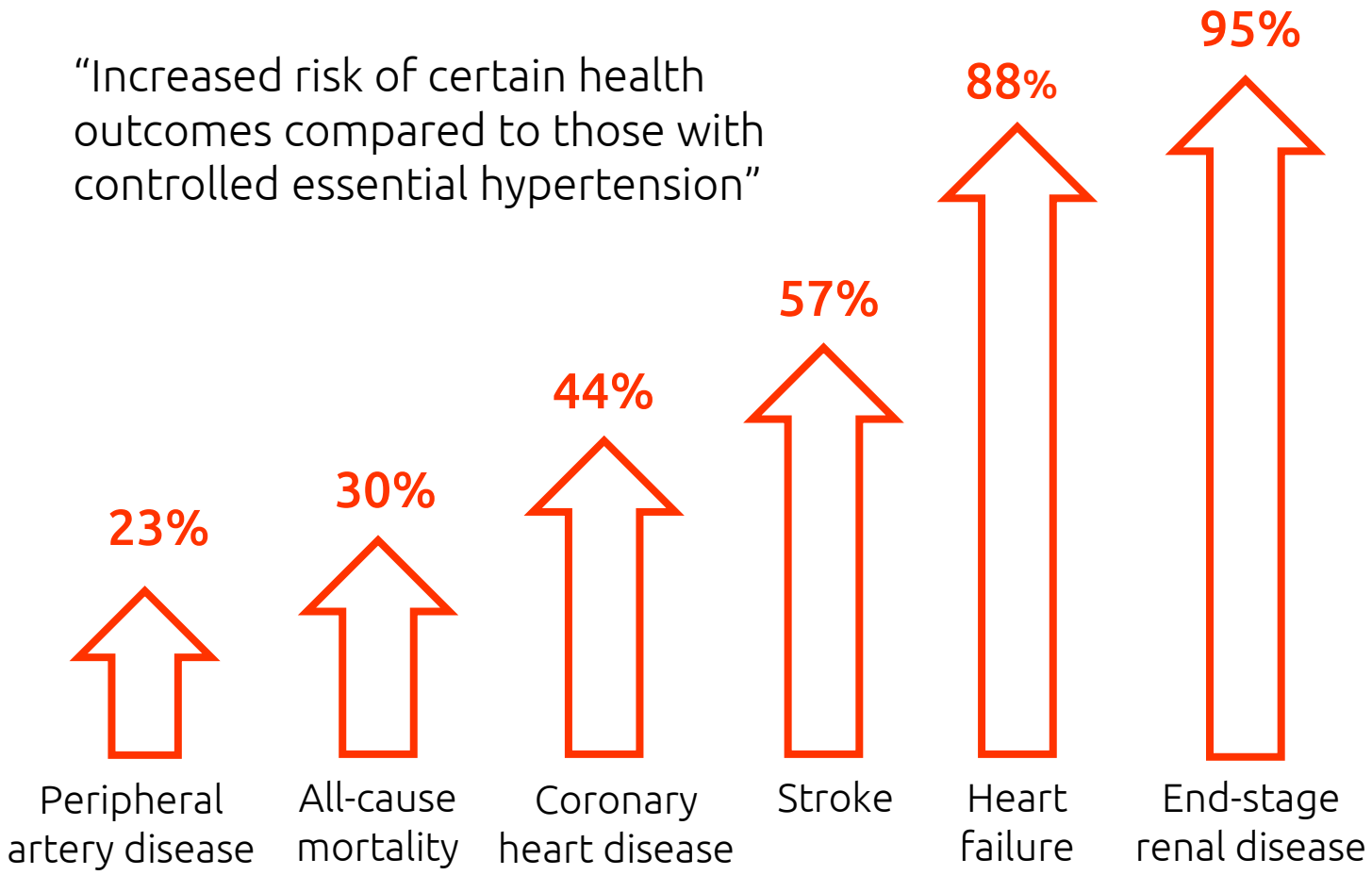
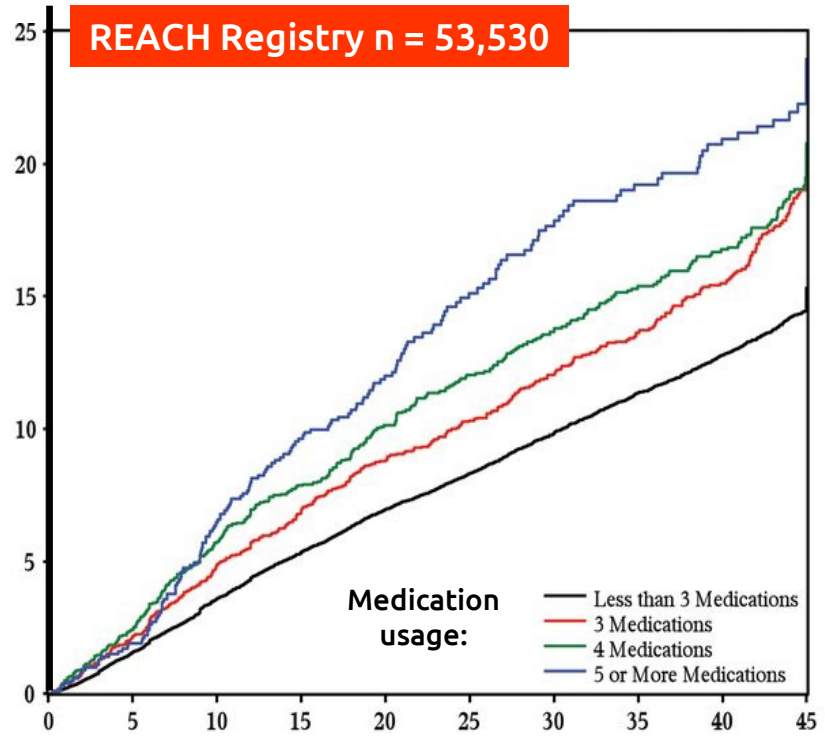
Disease burden when hypertension is uncontrolled

"Increased risk of certain health outcomes compared to those with controlled essential hypertension"



Muntner et al., 2014

Higher incidence of major cardiovascular events



European Heart Journal, 2013

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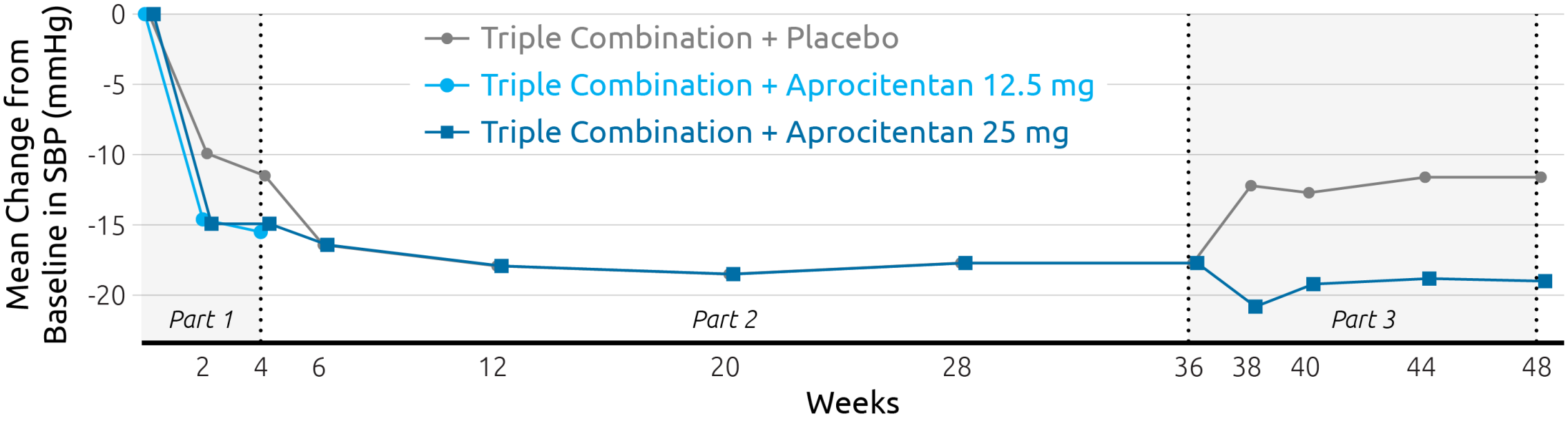
Significant and sustained BP reduction

Absolute BP reduction of 15 mmHg

TRYVIO™ (aprocitentan) 12.5mg tablets



Primary endpoint
12.5 mg vs placebo: -3.8 mmHg, P=0.0042
25 mg vs placebo: - 3.7 mmHg, P=0.0046

Key secondary endpoint
25 mg vs placebo: - 5.8 mmHg P<0.0001

Triple combination: single pill ARB (valsartan), CCB (amlodipine) , diuretic (hydrochlorothiazide) +/- beta blockers

Schlaich MP, et al. The Lancet, 2022; Dec 3;400(10367):1927-1937.

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USPI Highlights: Indication and Usage

TRYVIO™ (aprocitentan) 12.5mg tablets

----------INDICATIONS AND USAGE----------

TRYVIO is an endothelin receptor antagonist indicated for the treatment of hypertension in combination with other antihypertensive drugs, to lower blood pressure in adult patients who are not adequately controlled on other drugs. Lowering blood pressure reduces the risk of fatal and non-fatal cardiovascular events, primarily strokes and myocardial infarctions. (1)

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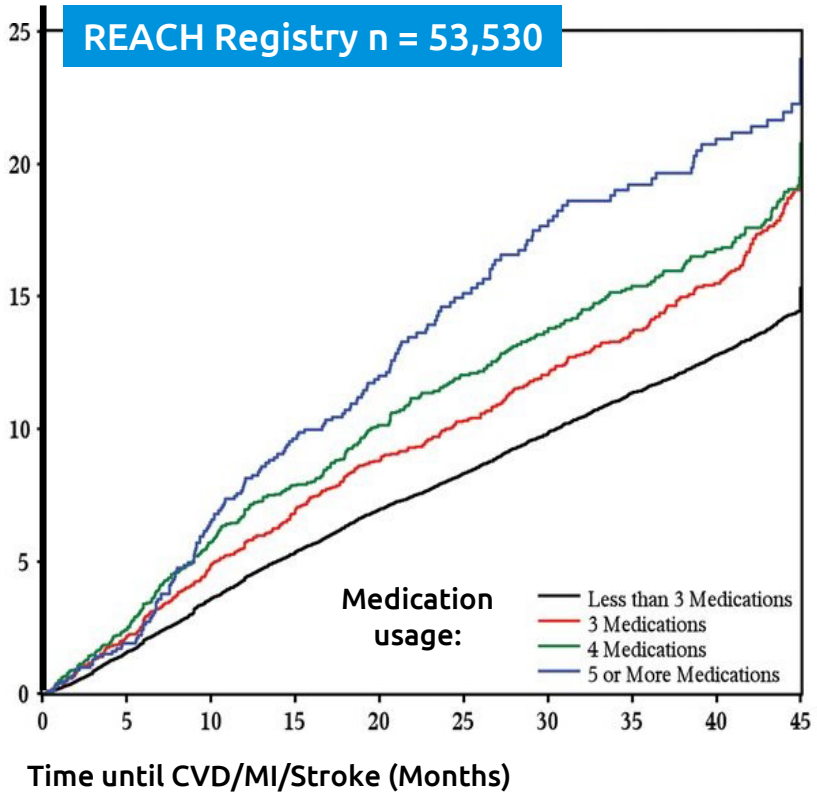
Disease burden when hypertension is uncontrolled

Higher incidence of major cardiovascular events



European Heart Journal, 2013

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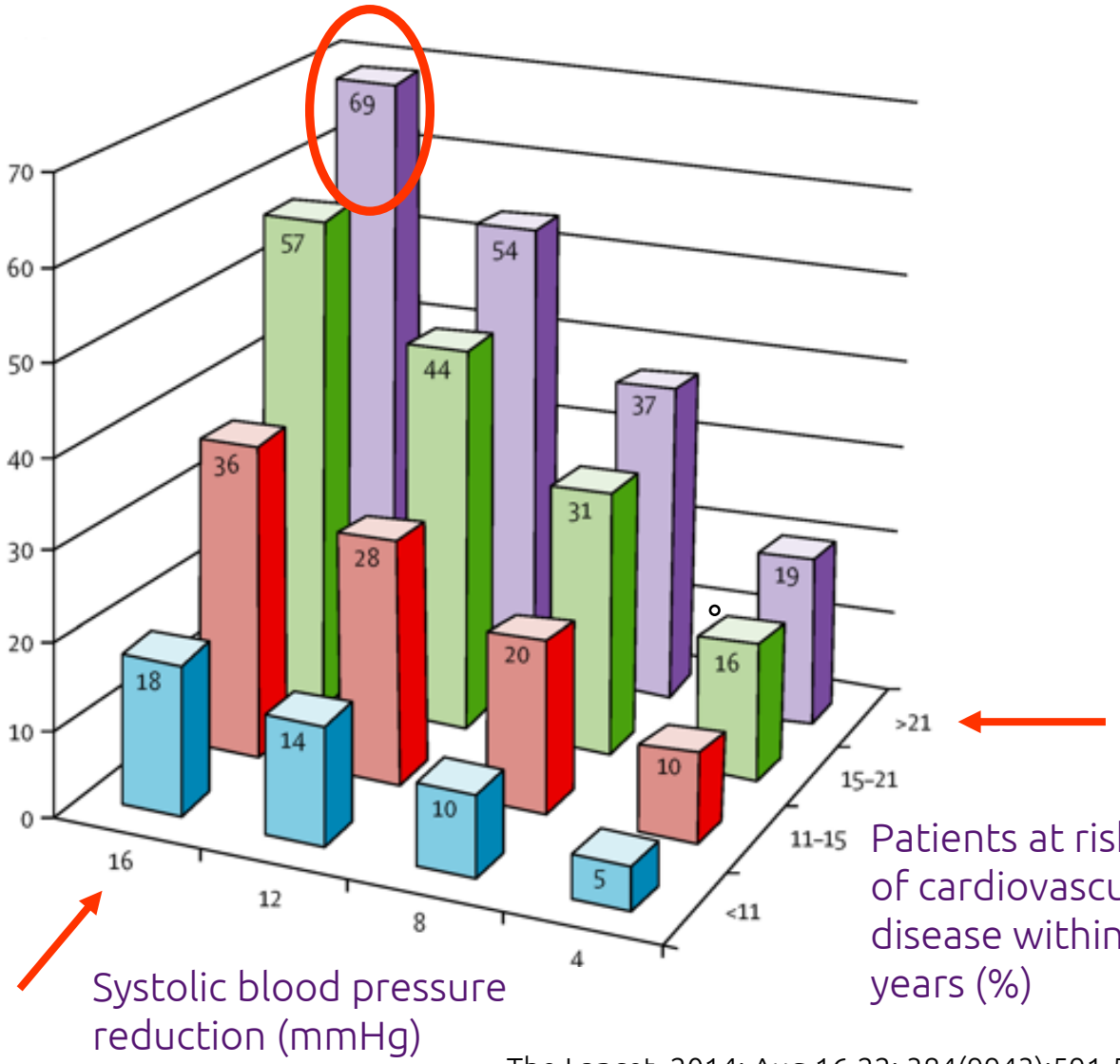
Reduction in BP will prevent CV events

16-mmHg (uAOBPM) reduction in SBP vs baseline would avoid approximately 70 CV events per 1000 patients over the following 5 years



The Lancet, 2014; Aug 16-22; 384(9943):591-598.

NB: There are no controlled trials demonstrating reduction of risk of these events with TRYVIO

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USPI Highlights: Dosage and Administration

TRYVIO™ (aprocitentan) 12.5mg tablets

----------DOSAGE AND ADMINISTRATION----------

- The recommended dosage of TRYVIO is 12.5 mg orally once daily, with or without food. (2.1)

USPI Section 14: Clinical Studies

TRYVIO **long-term sustained effect**

The persistence of the BP-lowering effect of TRYVIO was demonstrated in part 3 of the trial, in which patients on aprocitentan were re-randomized to placebo or 25 mg aprocitentan following a period during which all patients were treated with 25 mg. In patients re-randomized to placebo, the mean SiSBP increased, whereas in patients re-randomized to 25 mg aprocitentan the mean effect on SiSBP was maintained and was statistically superior to placebo at Week 40. The treatment effect was consistent for SiDBP.

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USPI Section 14: Clinical Studies

TRYVIO (aprocitentan) 12.5mg tablets

TRYVIO consistent **effect in subgroups** and across **measures**

Most of the BP-lowering effect occurred within the first two weeks of treatment with TRYVIO.

TRYVIO's BP-lowering effect appeared consistent among subgroups defined by age, sex, race, BMI, baseline eGFR, baseline UACR, medical history of diabetes, and between BP measurement methodologies (uAOBP and ambulatory BP measurements).

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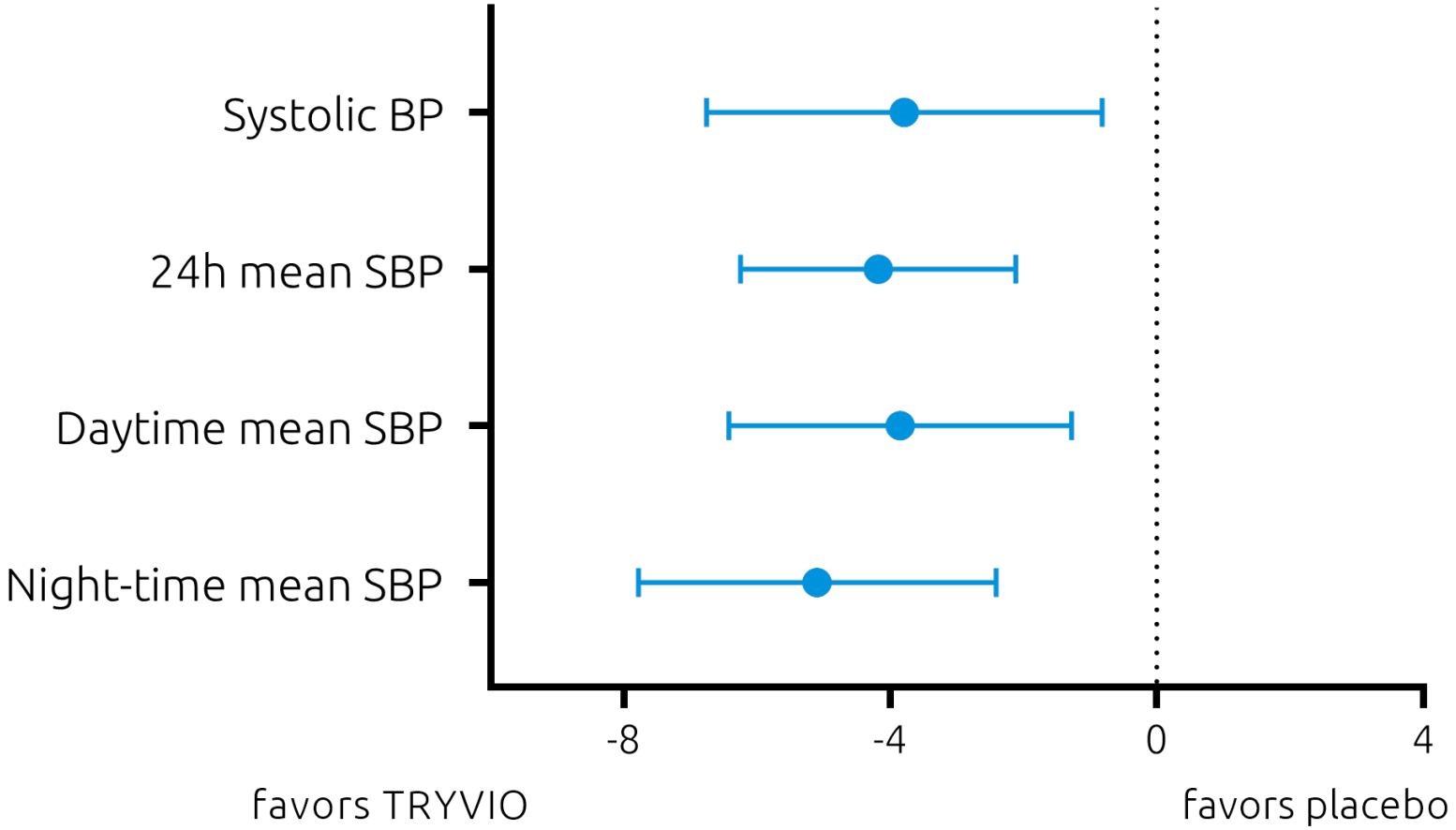
Consistent effect between BP measurement methodologies

TRYVIO™ (aprocitentan) 12.5mg tablets



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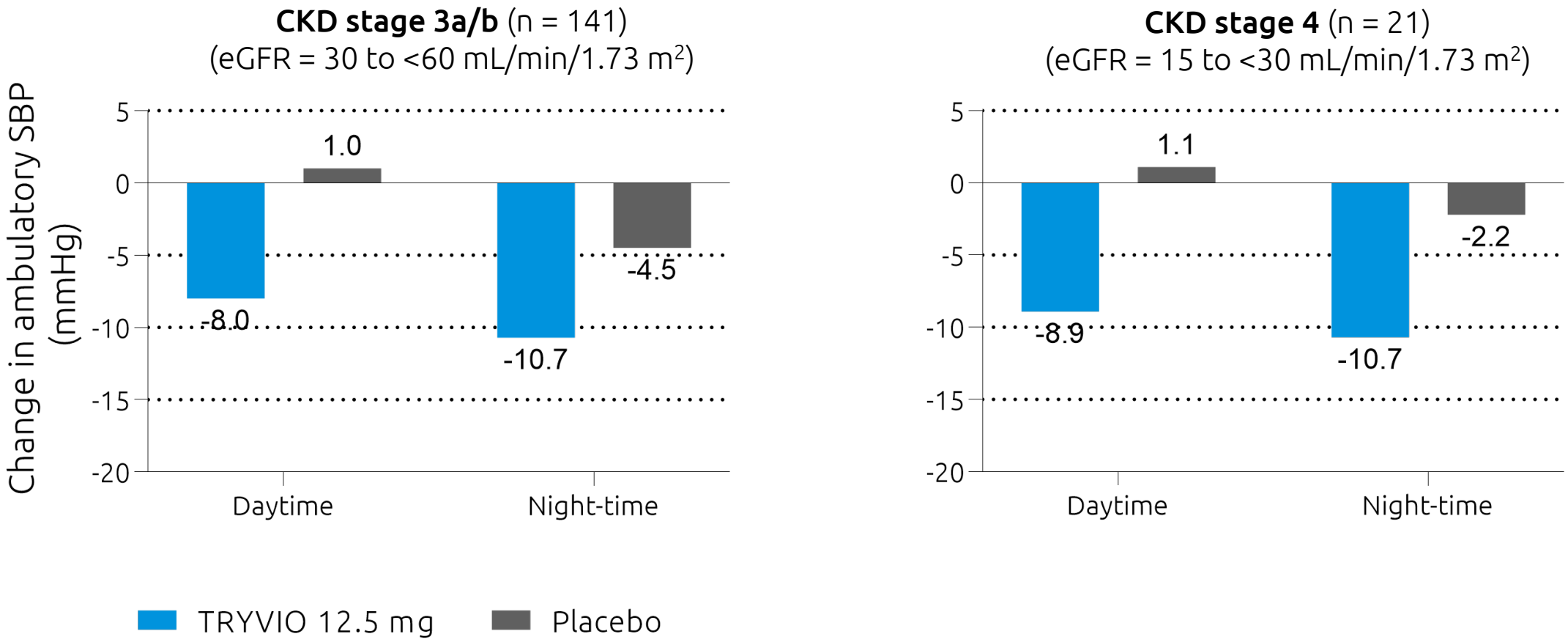
Consistent effect among subgroups: E.g., Patients with chronic kidney disease

TRYVIO™ (aprocitentan) 12.5mg tablets



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USPI Section 6: Adverse Reactions

TRYVIO™ (aprocitentan) 12.5mg tablets

Table 1 Adverse reactions reported with a frequency of ≥2% in TRYVIO-treated patients and greater (≥1%) than in placebo-treated patients during the initial 4-week double-blind placebo-controlled treatment (part 1)

Adverse Reaction	12.5 mg N = 243 %	Placebo N = 242 %
Edema/fluid retention	9.1	2.1
Anemia	3.7	0

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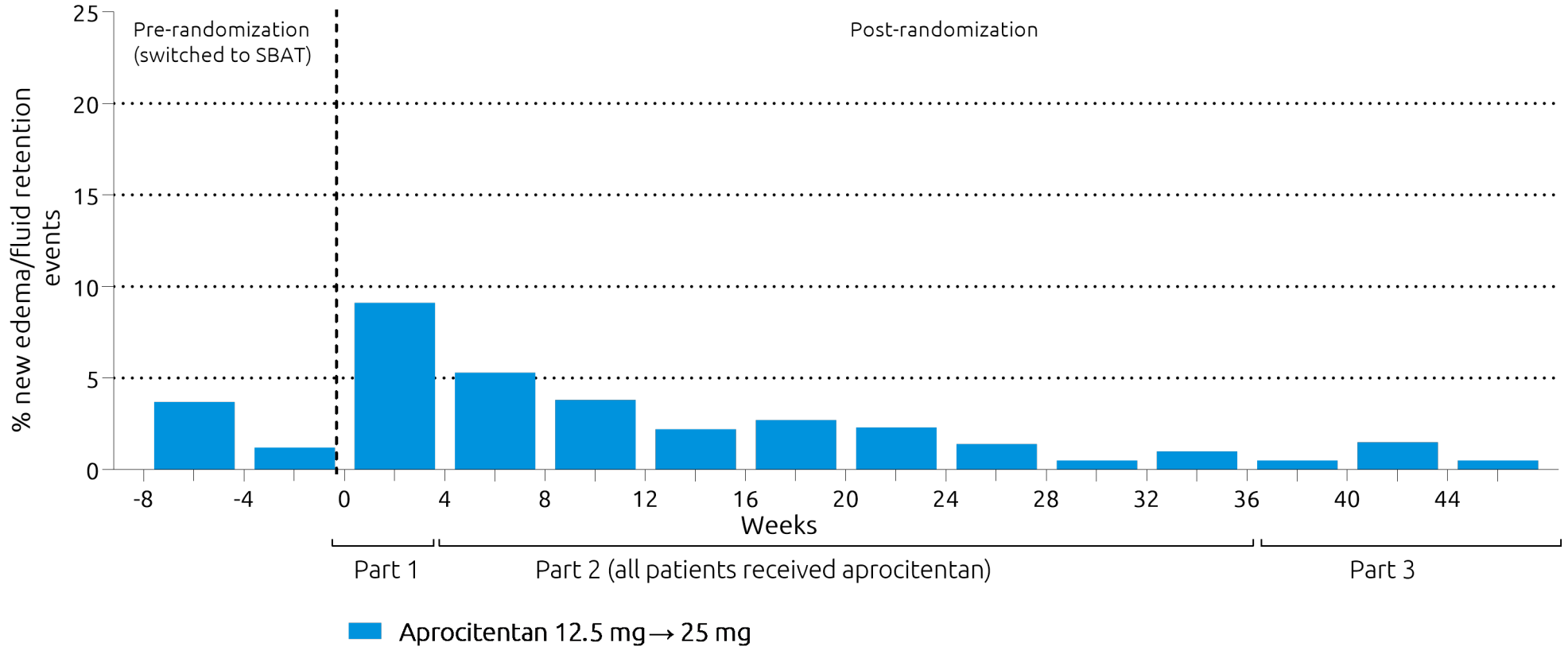
Incidence of edema

TRYVIO™ (aprocitentan) 12.5mg tablets

Returns to levels observed before randomization 8 weeks after treatment



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USPI Section 5.2: TRYVIO REMS

5.2 TRYVIO REMS

TRYVIO is available only through a restricted program under a REMS called the TRYVIO REMS because of the risk of embryo-fetal toxicity *[see Contraindications (4.1), Warnings and Precautions (5.1), Use in Specific Populations (8.1, 8.3)]*.

Important requirements of the TRYVIO REMS include the following:

- Prescribers must be certified with the TRYVIO REMS by enrolling and completing training.
- Pharmacies that dispense TRYVIO must be certified with the TRYVIO REMS.

Further information is available at www.TRYVIOREMS.com or 1-866-429-8964.

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“We are eager to provide physicians and patients with a novel medicine working in a new pathway in uncontrolled hypertension that can provide additional blood pressure control”

Tausif ‘Tosh’ Butt
President Idorsia US

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Hypertension is the leading modifiable risk factor for early death and disability

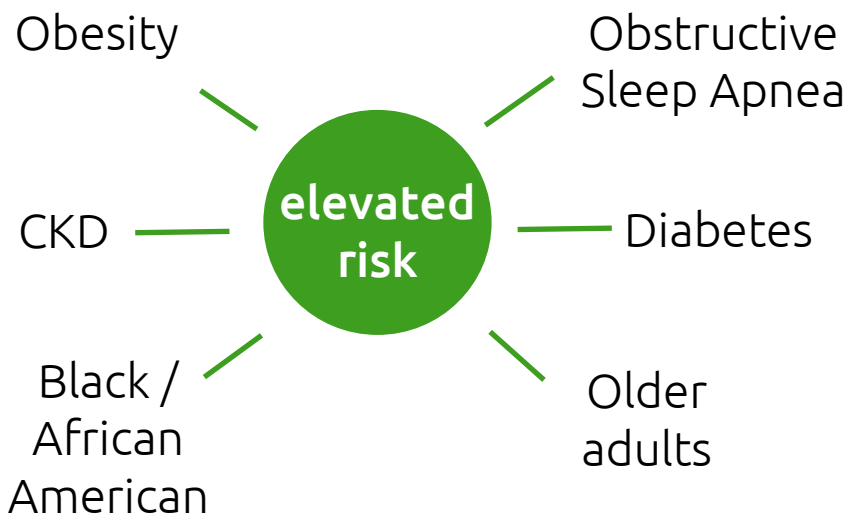
The importance of treating hypertension is well established

The risk of developing **uncontrolled hypertension is elevated in certain subgroups** of patients

2-6x
Greater Risk

especially for uncontrolled patients at high risk of cardio- and neurovascular events

5 mmHg reduction in SBP
= ~10% reduction in the risk of major cardiovascular events



Uncontrolled hypertension patients have a **greater risk** for CV events and end-stage renal disease

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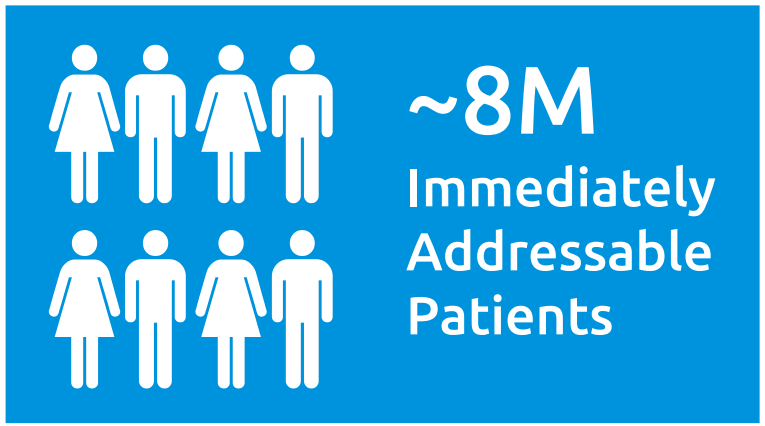
~8M patients immediately addressable at launch* – most with multiple comorbidities

TRYVIO™ (aprocitentan) 12.5mg tablets

3.5M Patients
on **3 meds for hypertension are not controlled**

4.6M Patients
on 4+ meds for hypertension



90% of these patients have comorbidities and are taking branded meds

* in line with Phase 3 criteria

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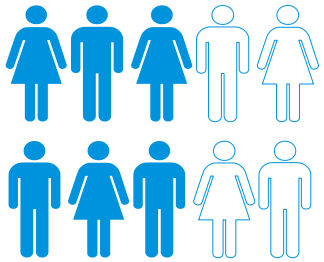
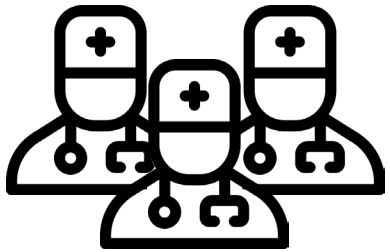
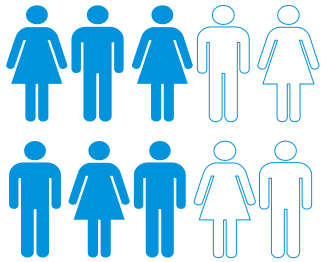
Prescribers span several specialties – often more than one HCP involved

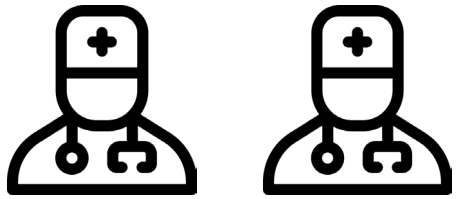


60% of Patients
on 3+ Meds were treated by 2 or more HCPs

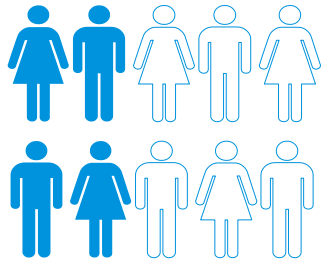




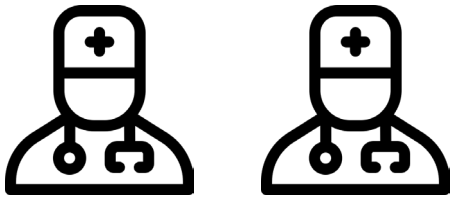
50-60% of patients
on 3+ Meds were treated by cardiologists and nephrologists



cardiologists nephrologist



30-40% of patients
on 3+ Meds were treated by primary care physicians (PCPs)/other



PCPs other

Source: Komodo claims; 3-Year Dx: Sep'20 - Aug'23; 1-Year Rx: Sep'22 - Aug'23

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Early dialogues with Payers suggest an overall favorable reaction to TRYVIO clinical profile

- Recognize the unmet patient need of uncontrolled hypertension
- Favorable reaction to Phase 3 trial design
- Perceive efficacy as favorable, highlighting BP differences vs placebo clinically meaningful
- Product available through med exception process until the NTM / NDC Blocks removed

NTM: New To Market; NDC: National Drug Code

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Important aspects of TRYVIO for US market

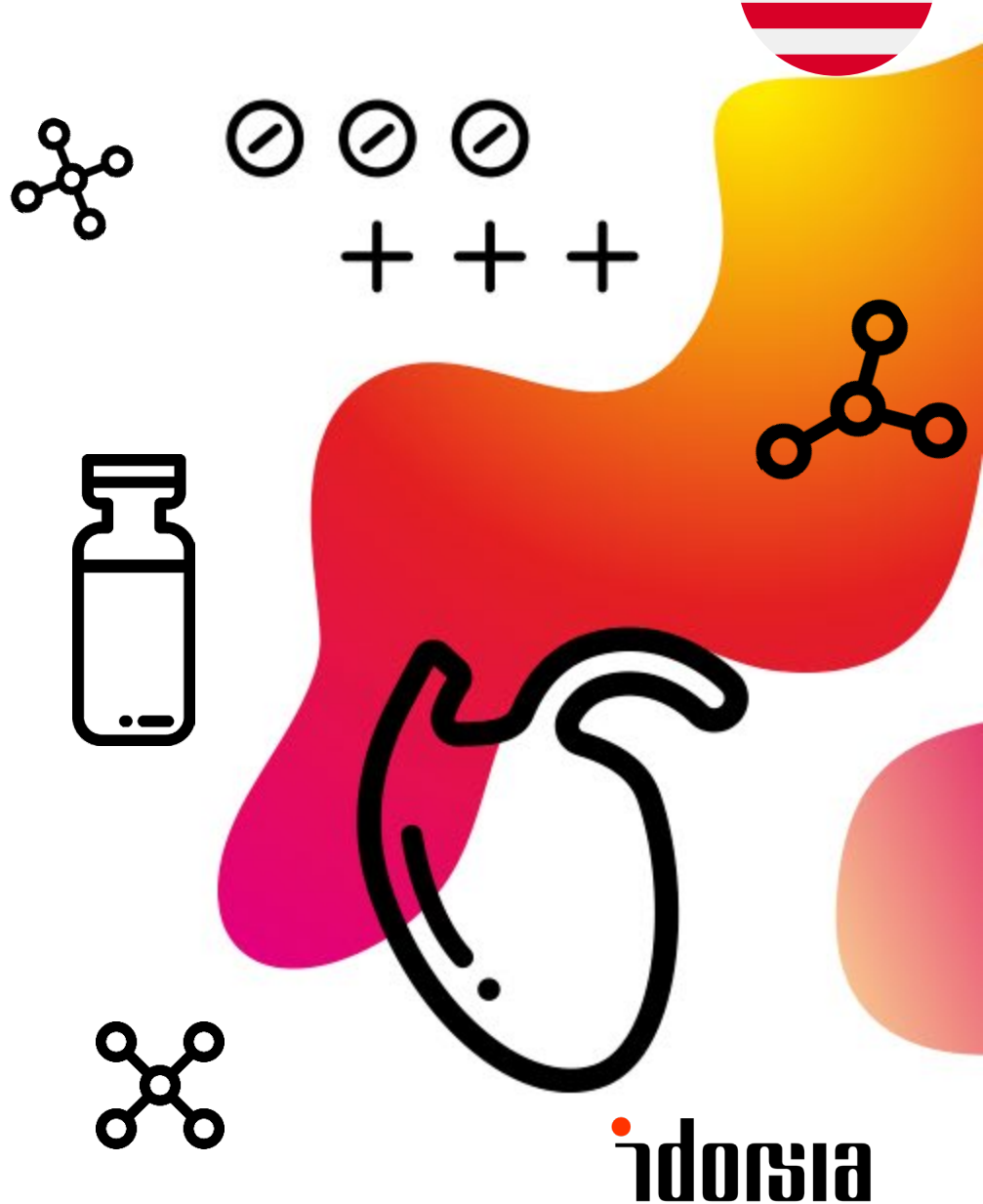
TRYVIO™
(aprocitentan) 12.5mg tablets

Easy to prescribe

- **One dose** for all patients
- No clinically relevant drug-drug interactions
- Manageable side-effect profile
- One-time REMS certification for HCP and Pharmacy only

Easy to use

- **Oral** once-daily tablet, with or without food
- **Long half-life** (approx. 41 hours)



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“The approval of TRYVIO heralds a new era of endothelin research beyond hypertension, where we intend to investigate the utility of aprocitentan for first-in-class applications in new indications.”

Martine Clozel
Chief Scientific Officer

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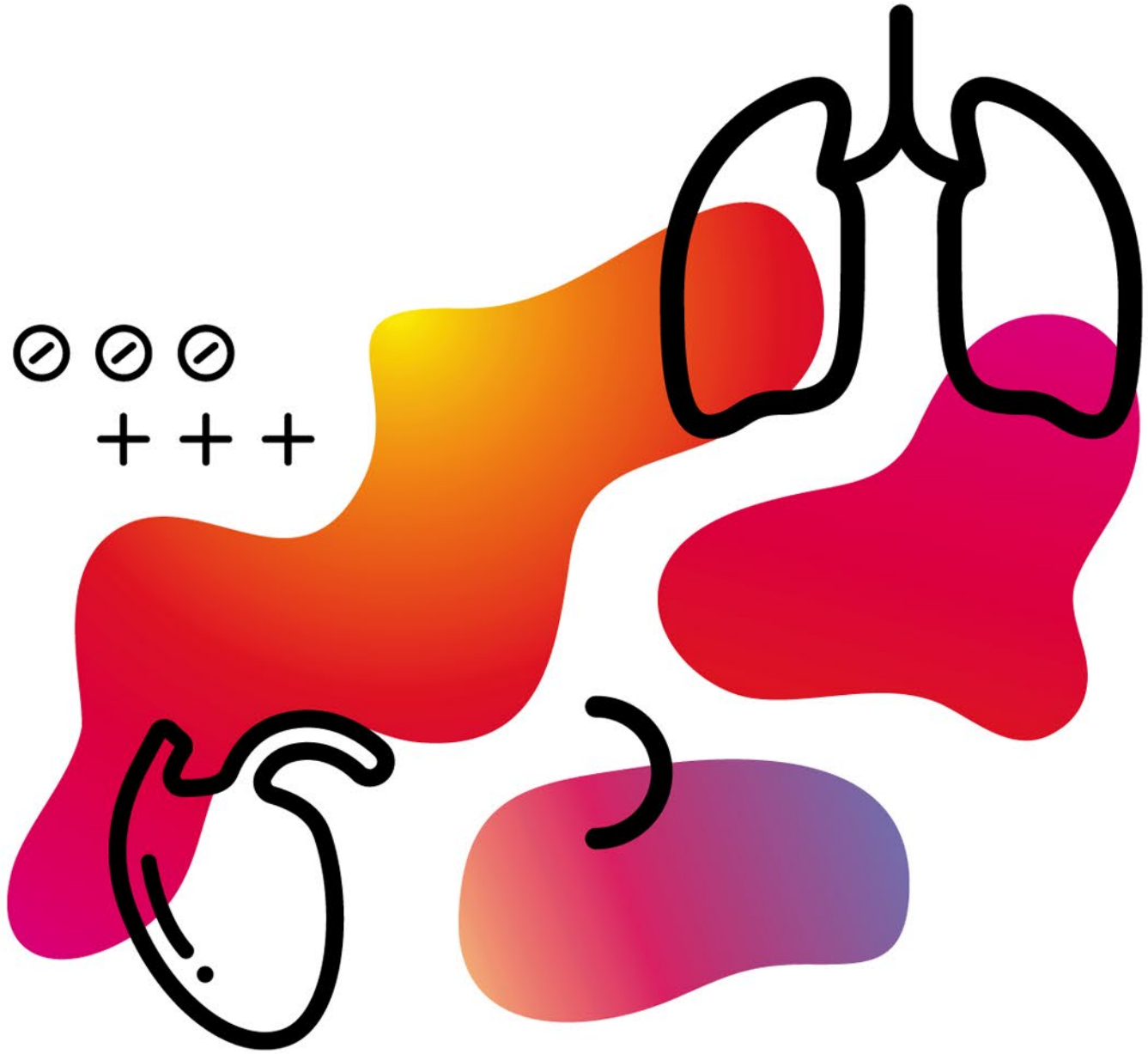
Questions?



TRYVIO™
(aprocitentan) 12.5mg tablets

Once-daily TRYVIO is the first & only dual ERA to lower blood pressure in combination with other medications for patients with hypertension who are not adequately controlled

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