The State of PH Treatments: Where We Are Now and Where We're Headed

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Objectives

Help you understand…

- How treatments can impact daily living with PH.
- Available pulmonary hypertension therapies.
- How treatment approaches continue to evolve.
- Treatment options on the horizon for the PH community.

Navigating Pulmonary Hypertension

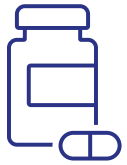
Key Steps After Diagnosis

Your Care Team

PH centers and experts for your overall care include respiratory therapists, rheumatologists, specialty pharmacy, and other PH specialists.

Diagnostic Testing

Tests to confirm diagnosis and make the right treatment decisions throughout your journey.



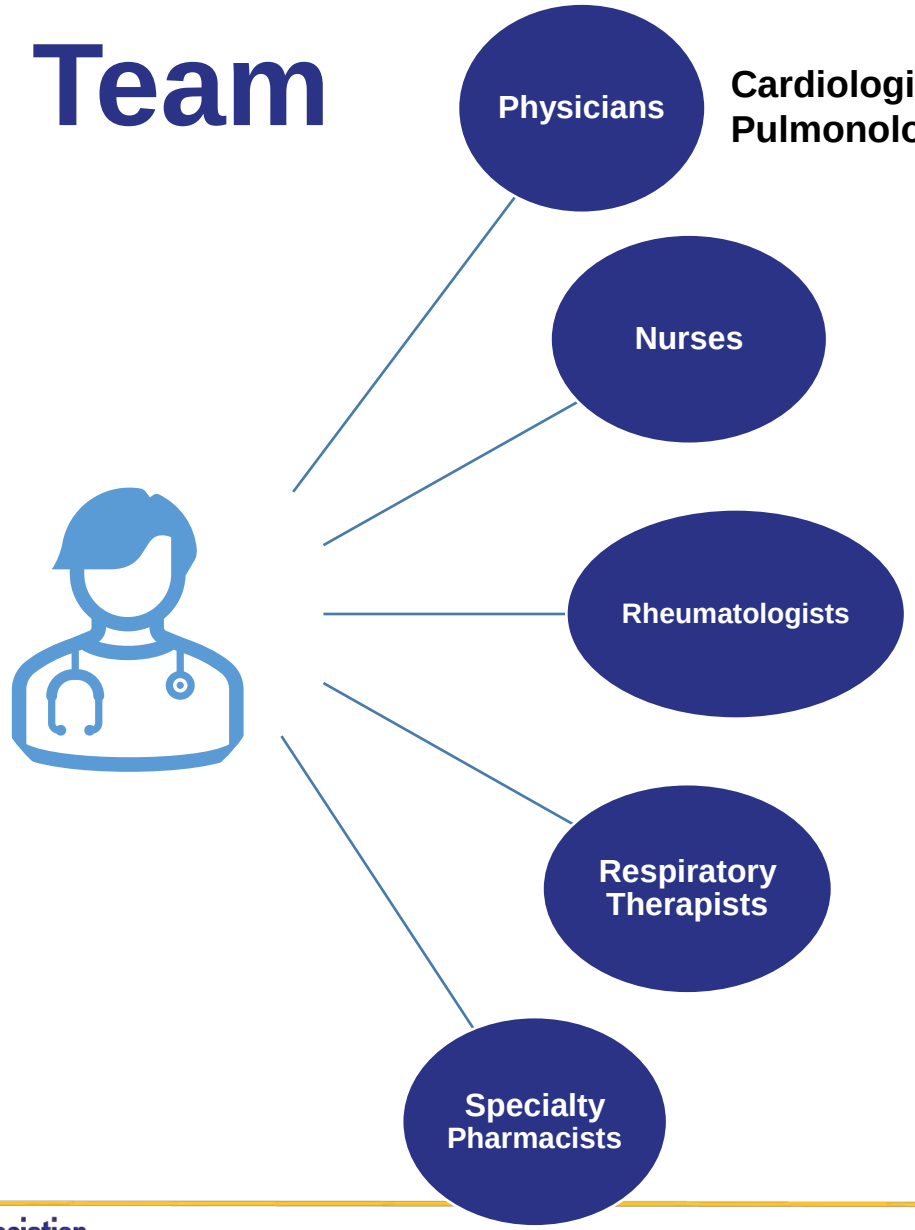
Treatment Plan

Work with your care team to decide on the best treatment plan for you.

Nutrition & Exercise

Maintaining a proper diet and exercise routine tailored for you is important.

Your Care Team



Cardiologists
Pulmonologists

Care Team is focused on…

- Setting goals
- Managing treatment
- Establishing nutrition and exercise plans
- Supporting mental health and wellness

Diagnostic Tests to Determine Treatment Plan

Test	Purpose
6-minute walk test	Measures the distance you can walk in 6 minutes
BNP/NT-proBNP (natriuretic peptides)	Blood tests that indicate amount of strain on the heart
Functional Class	Helps determine the effect of symptoms on your ability to do daily activities
Echocardiogram	Measure the pressure in the pulmonary artery
Cardiac magnetic resonance	
Right heart catheterization	

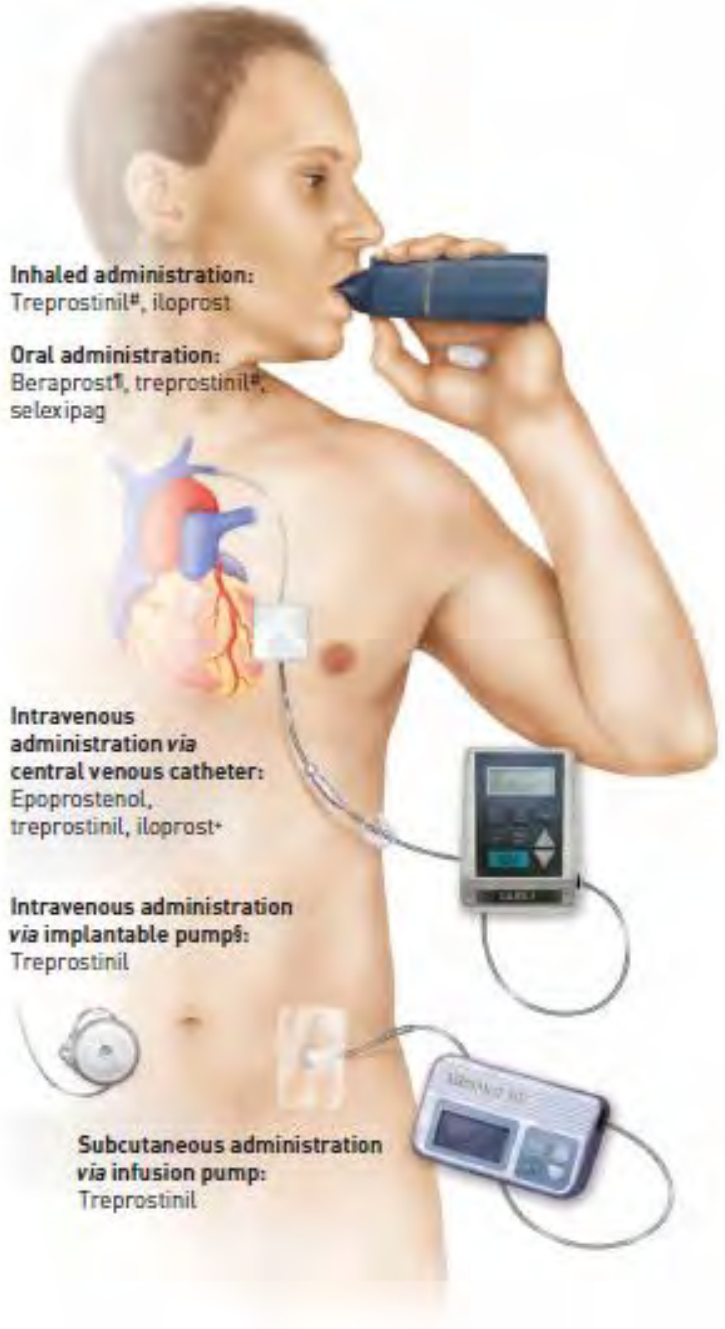
Treatments and Therapies
Pulmonary Hypertension

Setting Key Treatment Goals to Manage PH

- Help patients meet their goals with disease management
- Increase patient's ability to function and perform daily activities
- Improve breathing and quality of life
- Prevent and/or reverse disease progression
- Allow patients to live with and conquer pulmonary hypertension

PHA

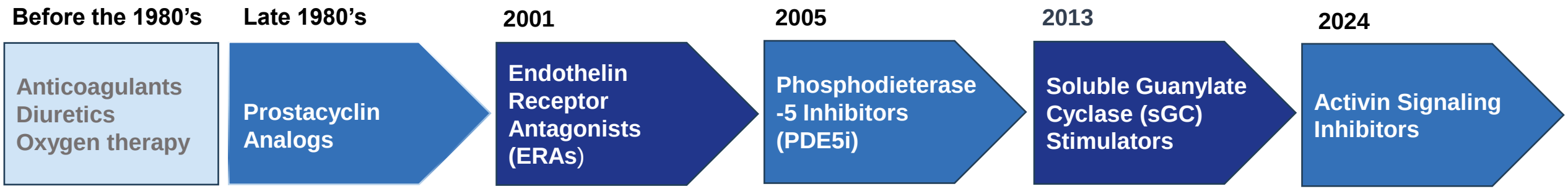
Adapted from Galiè N, et al. Eur Heart J. 2016;37(1):67-119.
Galie N et al. Eur Respir J 2019; 53: 1802148



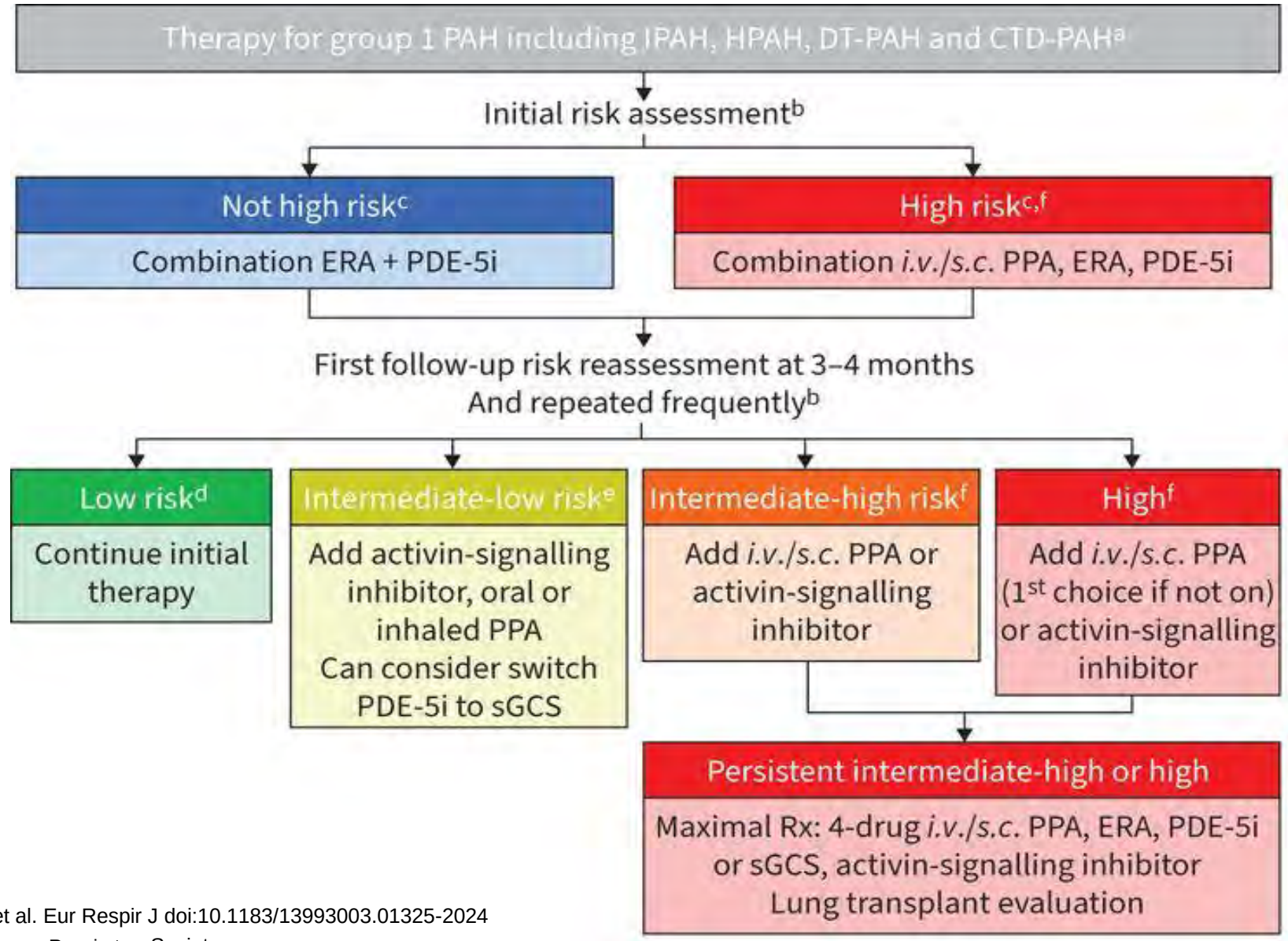
Farber HW et al. Eur Respir Rev. 2016;25(142):418-430

	Drug Class	Generic Name	Trade Name(s)	Route
Vasodilation – relaxes the blood vessels	**Endothelin Receptor Antagonist (ERA) Pathway** Prevents blood vessels from narrowing	Bosentan	Tracleer	Oral
		Ambrisentan	Letairis	Oral
		Macitentan	Opsumit	Oral
	Nitric Oxide (NO) Pathway Increases NO to fuel cGMP production	Sildenafil	Revatio	Oral
		Tadalafil	Adcirca	Oral
		Tadalafil	Tadliq	Oral Suspension
		Riociguat	Adempas	Oral
	Nitric Oxide (NO) + Endothelin Receptor Antagonist (ERA) Pathway	Macitentan/ Tadalafil	Opsynvi	Oral
	Prostacyclin Pathway Allows blood vessels in the lungs to relax	Epoprostenol	Flolan, Veletri	Intravenous
		Treprostinil	Remodulin, Tyvaso, Tyvaso DPI Orenitram, Yutrepia	IV, SC, Inhaled, Oral
		Selexipag	Uptravi	Oral, Intravenous
Activin Signaling Pathway Anti Proliferative-reduces the growth of the vessel		Sotatercept	Winrevair	Subcutaneous

Beginning of Targeted Therapies



Treatment Approach



Kelly M. Chin et al. Eur Respir J doi:10.1183/13993003.01325-2024

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Oral Therapies: Frequently Reported Side Effects

PDE5 Inhibitors

- Headache
- Flushing
- Acid reflux
- Gastrointestinal upset
- Muscle aches
- Changes to hearing or vision (rare but serious)

Endothelin Receptor Antagonists

- Swelling or bloating
- Sinus congestion
- Headache
- Gastrointestinal upset

Prostacyclin Analogues

- Headache
- Flushing
- Jaw pain/"1st bite pain"
- Gastrointestinal upset
- Muscle aches
- Low blood pressure
- Lower platelet counts

Soluble Guanylate Cyclase Stimulator

- Low blood pressure
- Dizziness/lightheadedness
- Acid reflux
- Gastrointestinal upset
- Headache

Calcium Channel Blockers (for vasoresponders)

- Low blood pressure
- Dizziness/lightheadedness
- Lower extremity swelling

Endothelin-1 Receptor Antagonists (ERA)

Flushing	Avoid hot and humid places if possible
Heartburn	Acid reducing medications: antacids, famotidine, lansoprazole, omeprazole, pantoprazole
Leg/feet swelling	If weight gain is present, treat with increased diuretics (fluid pills) with guidance from your care team
Harm to unborn fetus	• Talk with your care team about effective contraceptives • If pregnant, contact your PH team immediately
Nasal congestion	• Saline nasal spray • If also have seasonal allergies, use antihistamines: cetirizine, fexofenadine, loratadine, etc.

Nitric Oxide Pathway Medications

Flushing	Avoid hot and humid places if possible
Heartburn	Acid reducing medications: antacids, famotidine, lansoprazole, omeprazole, pantoprazole
Leg/feet swelling	If weight gain is present, treat with increased diuretics (fluid pills) with guidance from your care team
Harm to unborn fetus *(riociguat only)	• Talk with your care team about effective contraceptives • If pregnant, contact your PH team immediately
Headache/muscle pain	• Acetaminophen as needed, avoid NSAIDs • Caffeine (small amount) • Ice compress
Vision change (rare)	Talk to your care team for further testing

Prostacyclin Pathway Medications

Flushing	Avoid hot and humid places if possible
Nausea/vomiting	Ondansetron, prochlorperazine, promethazine, scopolamine patches (as determined by your PH provider)
Dizziness/lower blood pressure	• Use caution when getting up from sitting/lying positions • Talk with your care team to adjust other medications that affect blood pressure
Headache/muscle pain	• Acetaminophen as needed, avoid NSAIDs • Caffeine (small amount) • Ice compress
Diarrhea	Loperamide (Imodium)

Prostacyclin Pathway Medications

Cough/throat irritation (specific to inhaled therapy)

- Cough drops
- Drink very cold or warm liquid before treatments
- Swish and spit water after treatments
- Phenol-based oral spray before inhalation
- Talk to your care team about correct device positioning during treatment

Site pain/irritation (infusion-related)

- Acetaminophen, famotidine, fluticasone spray, hydrocortisone cream, lidocaine topical cream, PLO gel, menthol-containing topic cream
- Non-medication strategies: Ale vera gel ice compress

PHA Registry

PHAR is a registry that securely collects patient (deidentified) data such as demographics, medical history, diagnostic tests, medication and patient-reported quality-of-life.

Goals of PHAR

- Measure a patient's adherence to diagnostic and treatment guidelines
- Assess patient outcomes
- Improve the quality of care
- Data collected helps facilitate other PAH and CTEPH research studies

Who can participate…

- Newly diagnosed or established PAH
- CTEPH patients
- Pediatric PH: Due to developmental lung disease

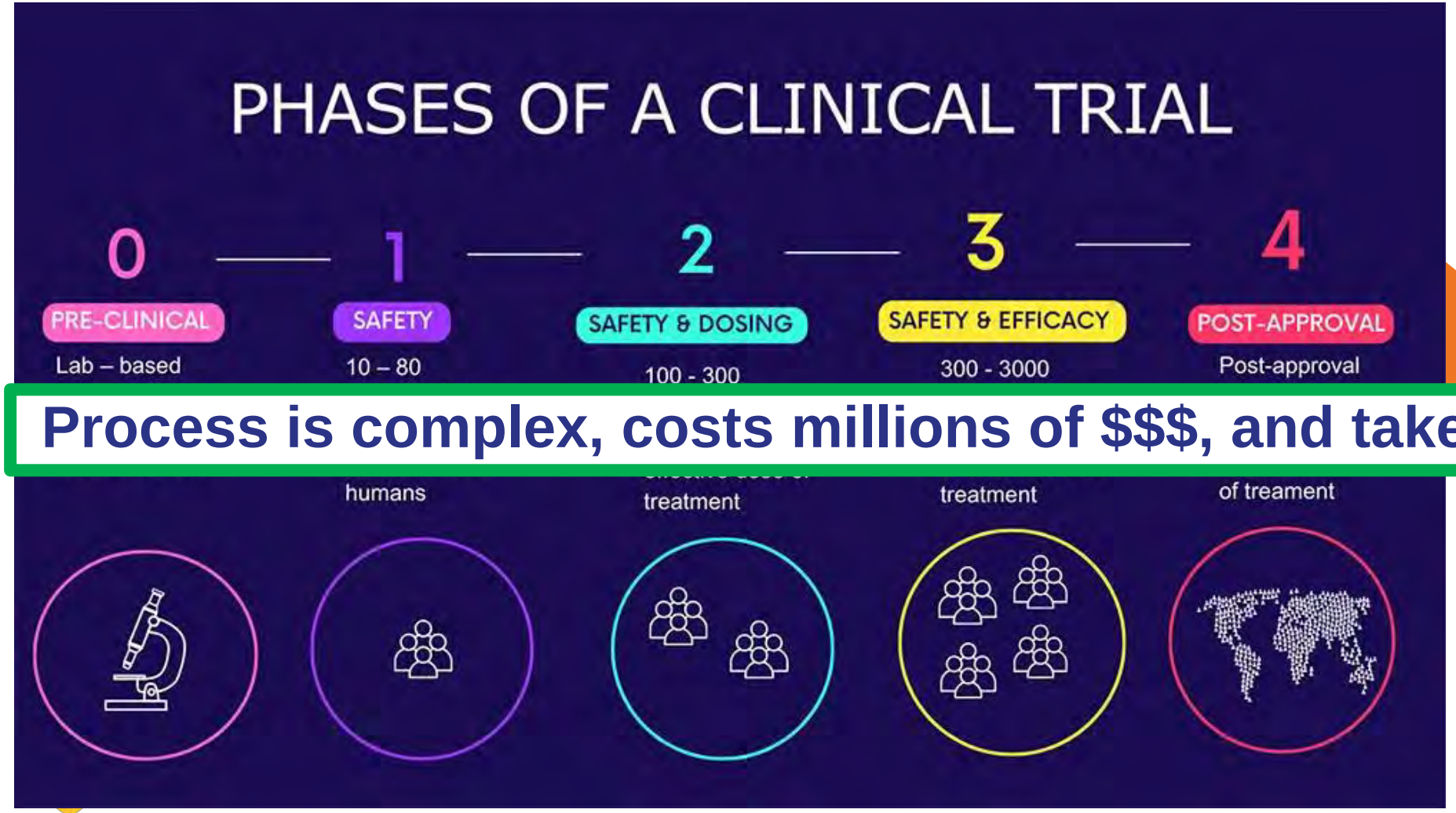
74 PHAR sites across the U.S.

Participating sites are PHA-accredited PH Care Centers (both CCCs & RCPs).

Goals for today

- Highlight some recent successes in research and in clinic trials which led to approval of new therapies
- Discuss findings of recent Phase 3 clinical trials of medications submitted to the FDA for approval
- Update on future pathways being studied
- What happens if the medications stop working

Clinical Study Types/Phases

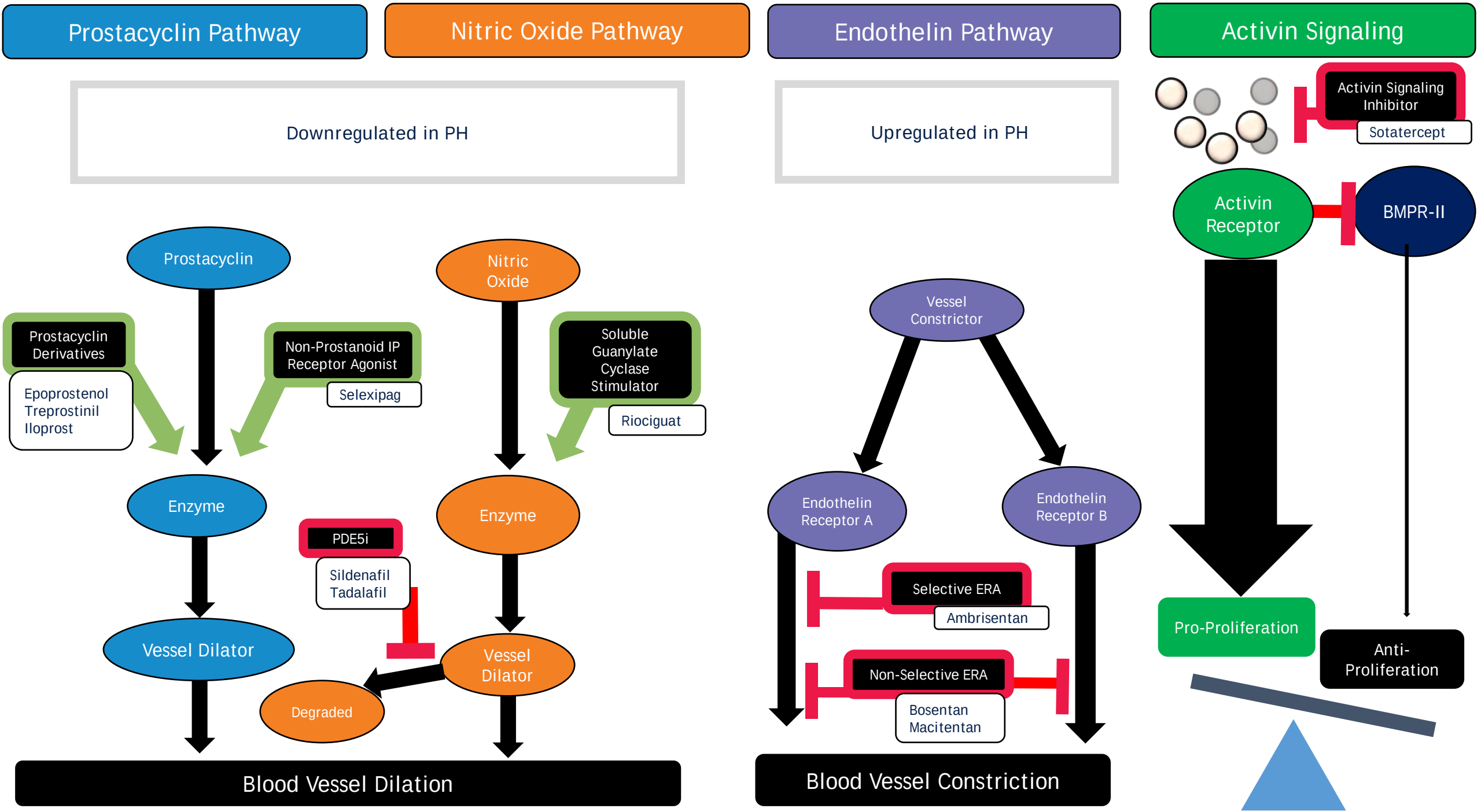


Overall Goals

Bring **new treatments** to patients that are:

✓ **Safe**

Process is complex, costs millions of $$$, and takes years of effort!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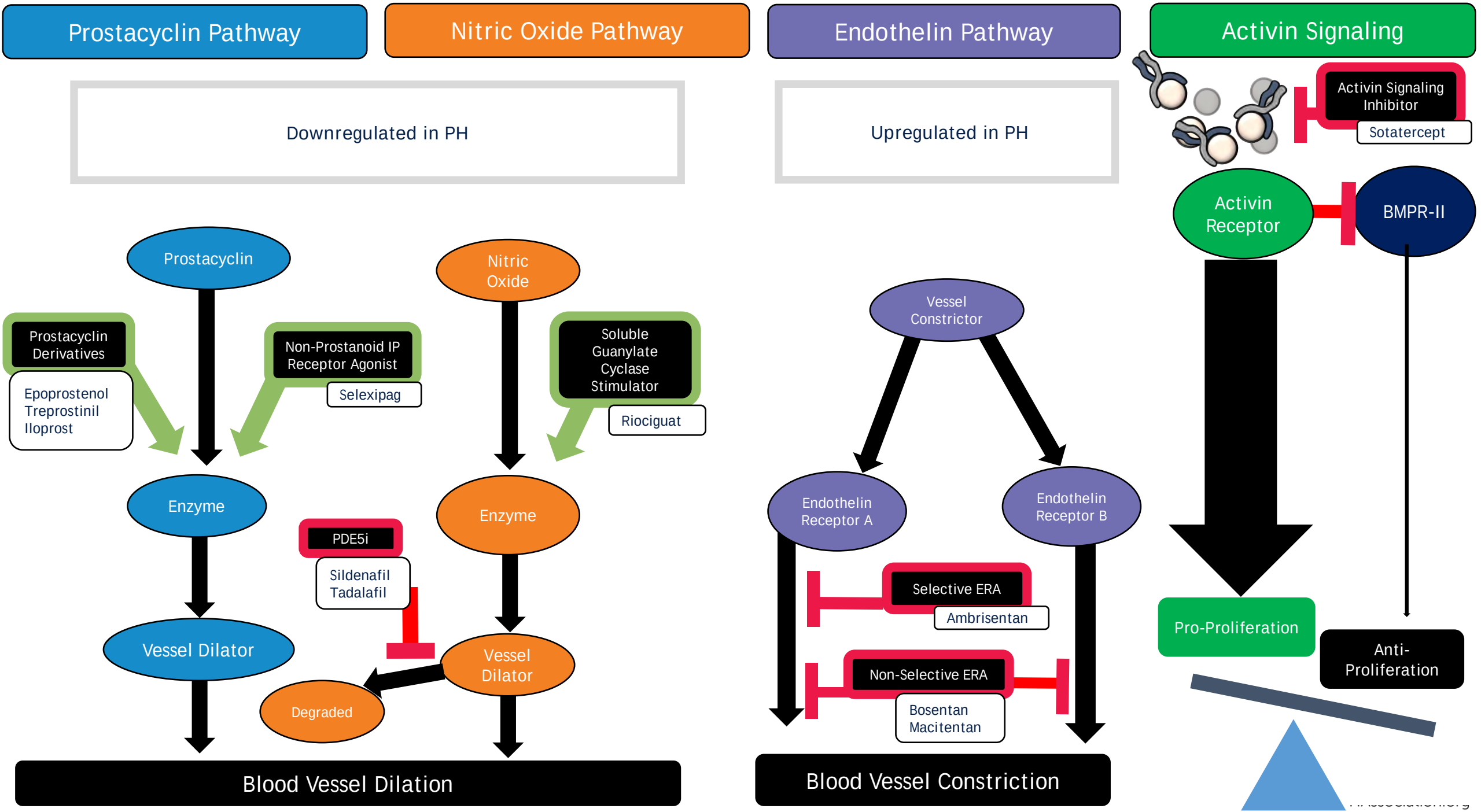
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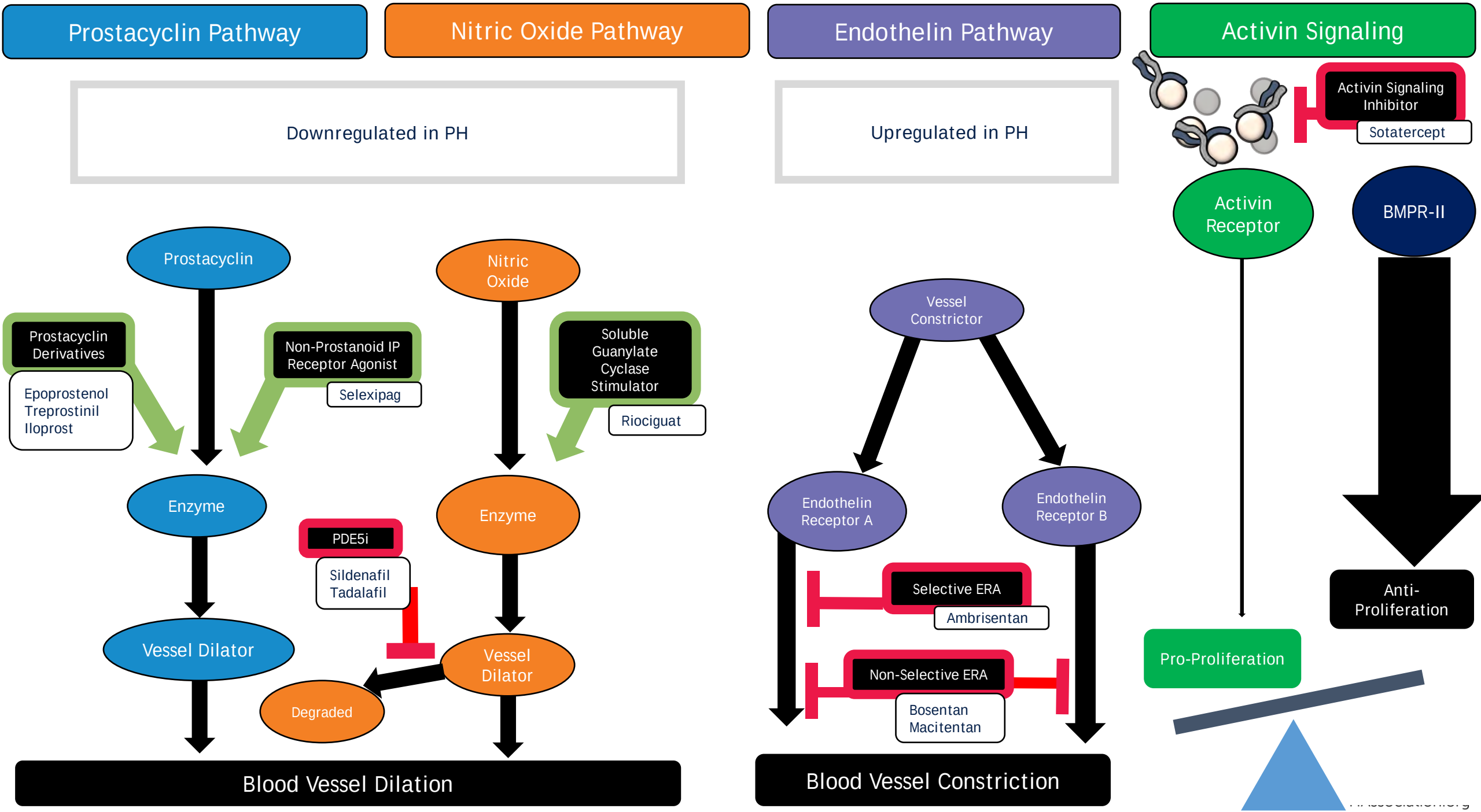
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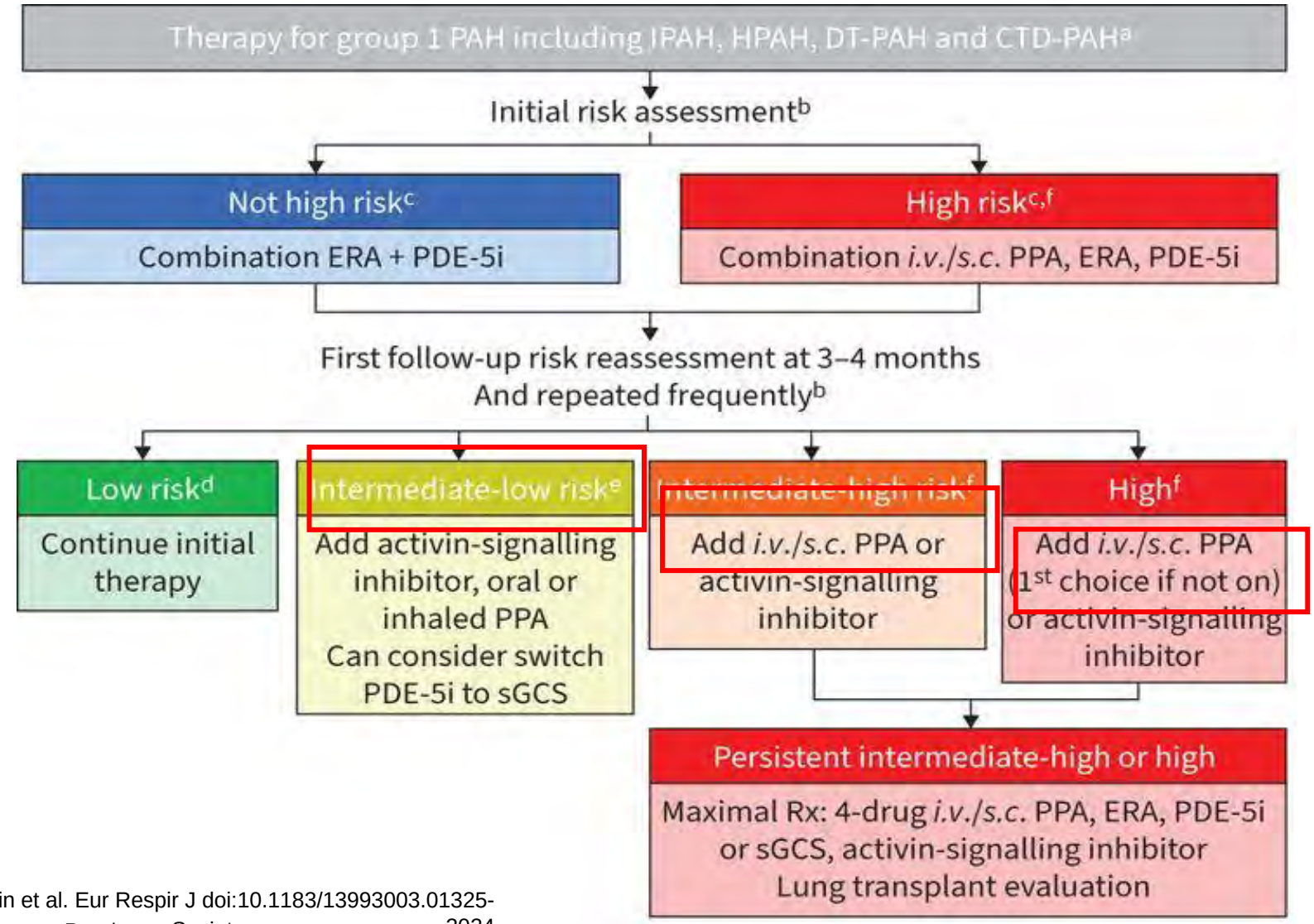
Treatment Approach



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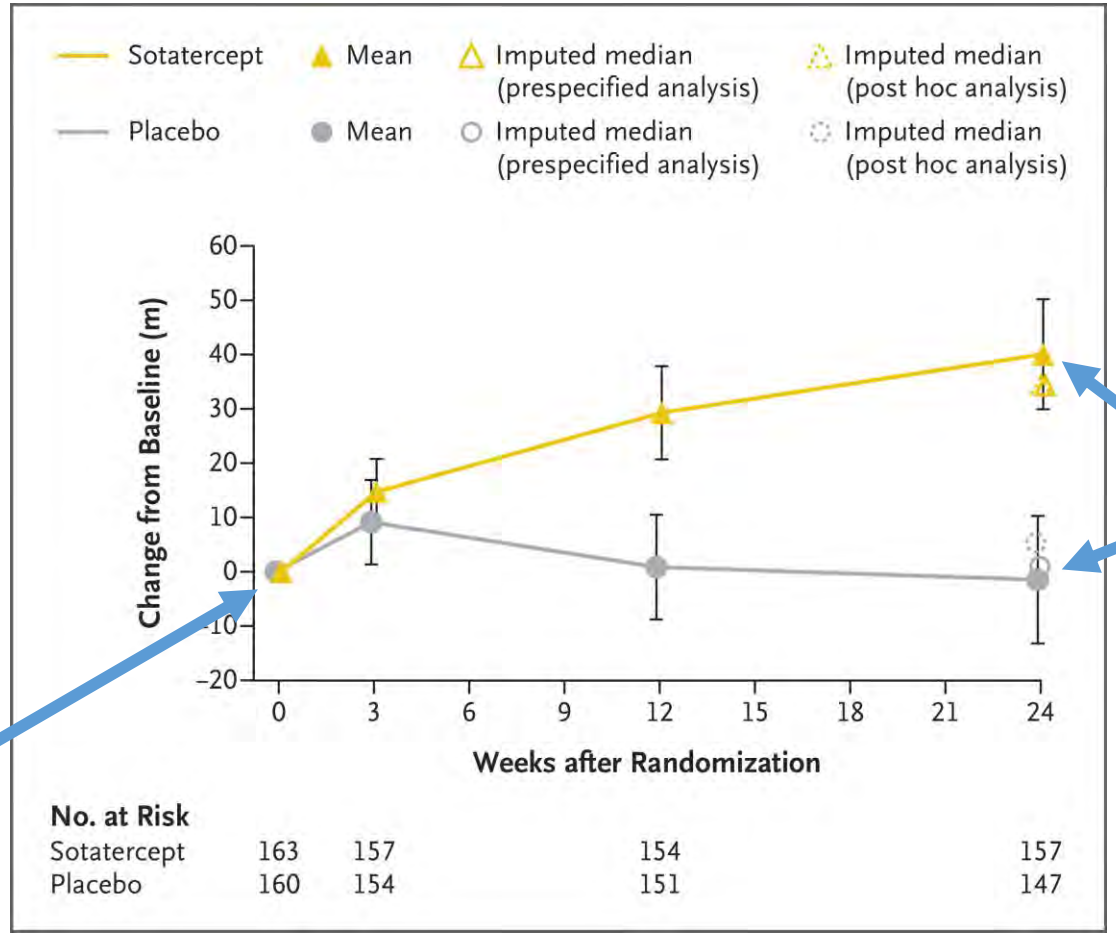
Sotatercept – STELLAR Trial



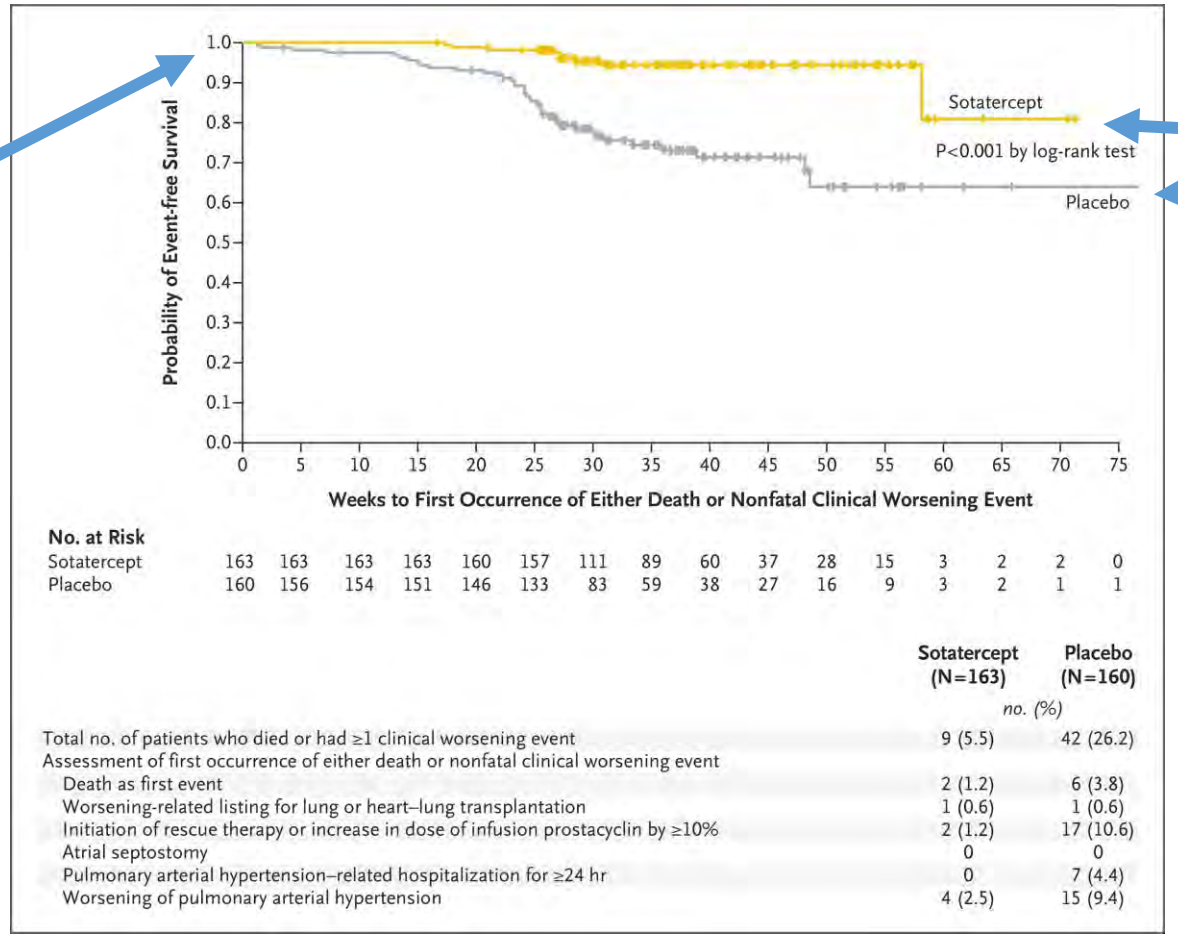
At Start

24 weeks of therapy

Hoeper MM N Engl J Med 2023

Sotatercept – STELLAR Trial

At Start



No. at Risk

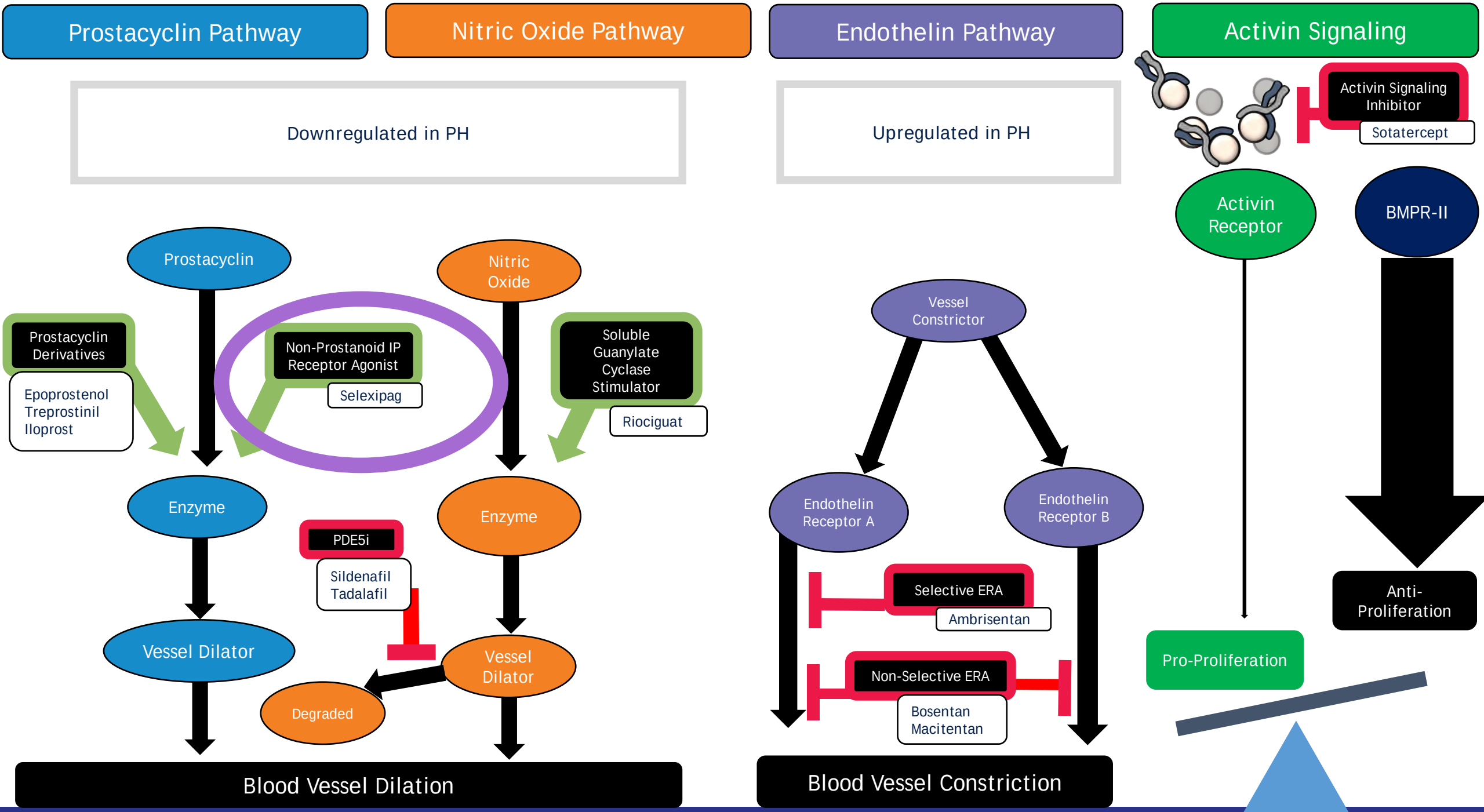
Sotatercept	163	163	163	163	160	157	111	89	60	37	28	15	3	2	2	0
Placebo	160	156	154	151	146	133	83	59	38	27	16	9	3	2	1	1

	Sotatercept (N=163)	Placebo (N=160)
	no. (%)	
Total no. of patients who died or had ≥1 clinical worsening event	9 (5.5)	42 (26.2)
Assessment of first occurrence of either death or nonfatal clinical worsening event		
Death as first event	2 (1.2)	6 (3.8)
Worsening-related listing for lung or heart–lung transplantation	1 (0.6)	1 (0.6)
Initiation of rescue therapy or increase in dose of infusion prostacyclin by ≥10%	2 (1.2)	17 (10.6)
Atrial septostomy	0	0
Pulmonary arterial hypertension–related hospitalization for ≥24 hr	0	7 (4.4)
Worsening of pulmonary arterial hypertension	4 (2.5)	15 (9.4)

After therapy

What else is coming?

Phase 3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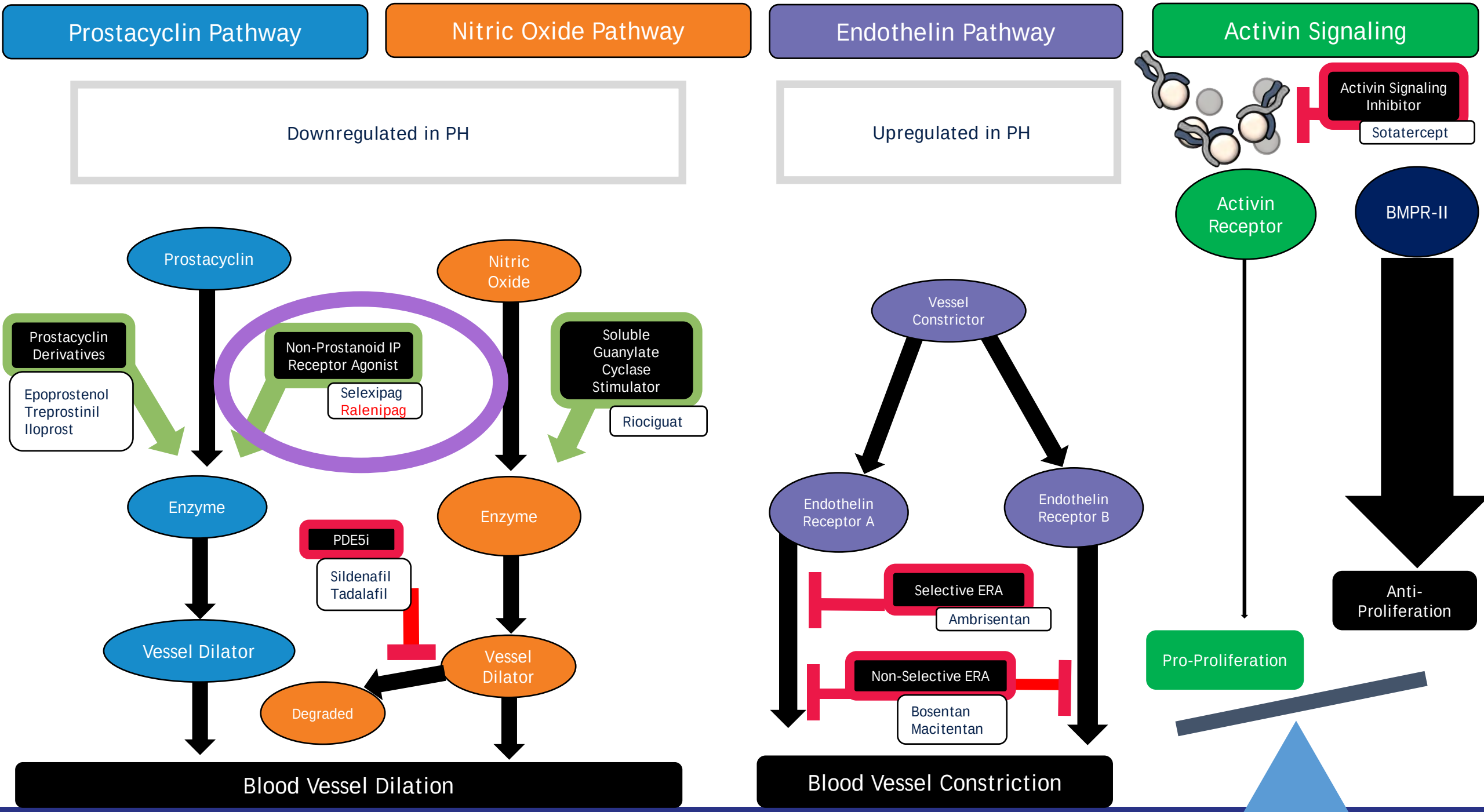
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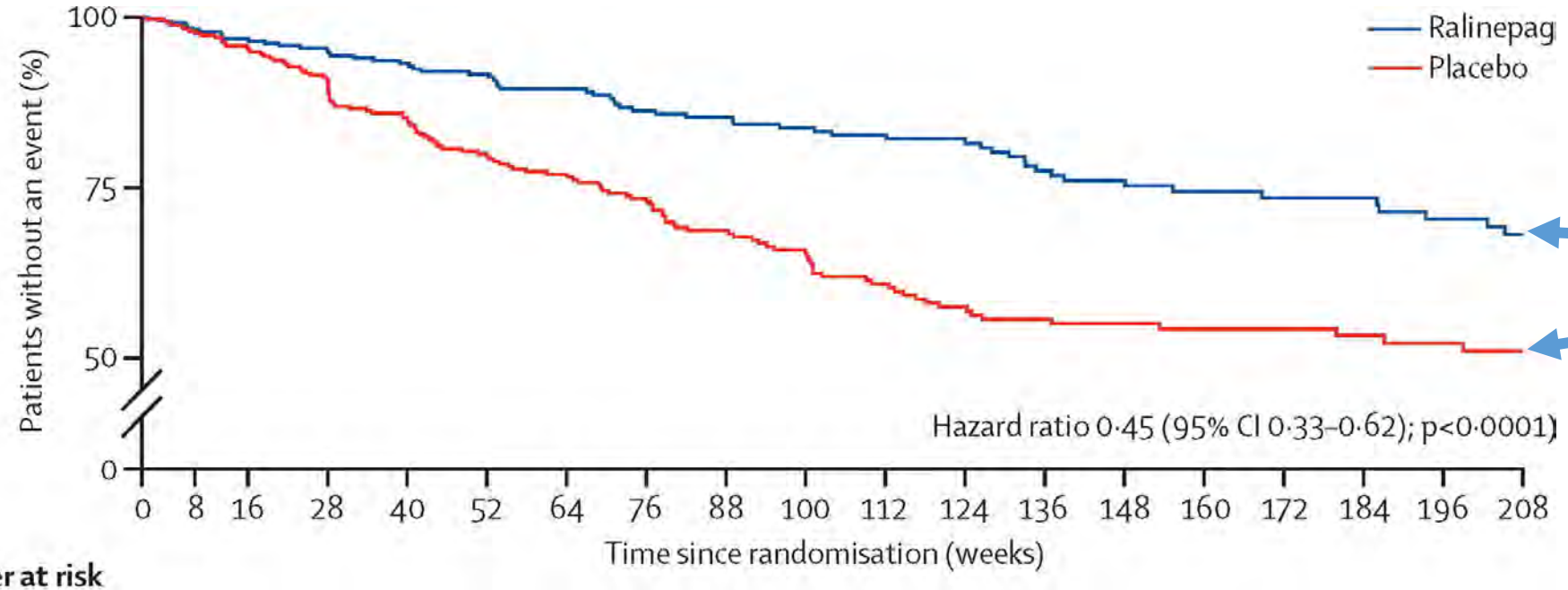
Ralenipag – Advance Outcomes

At Start



After therapy

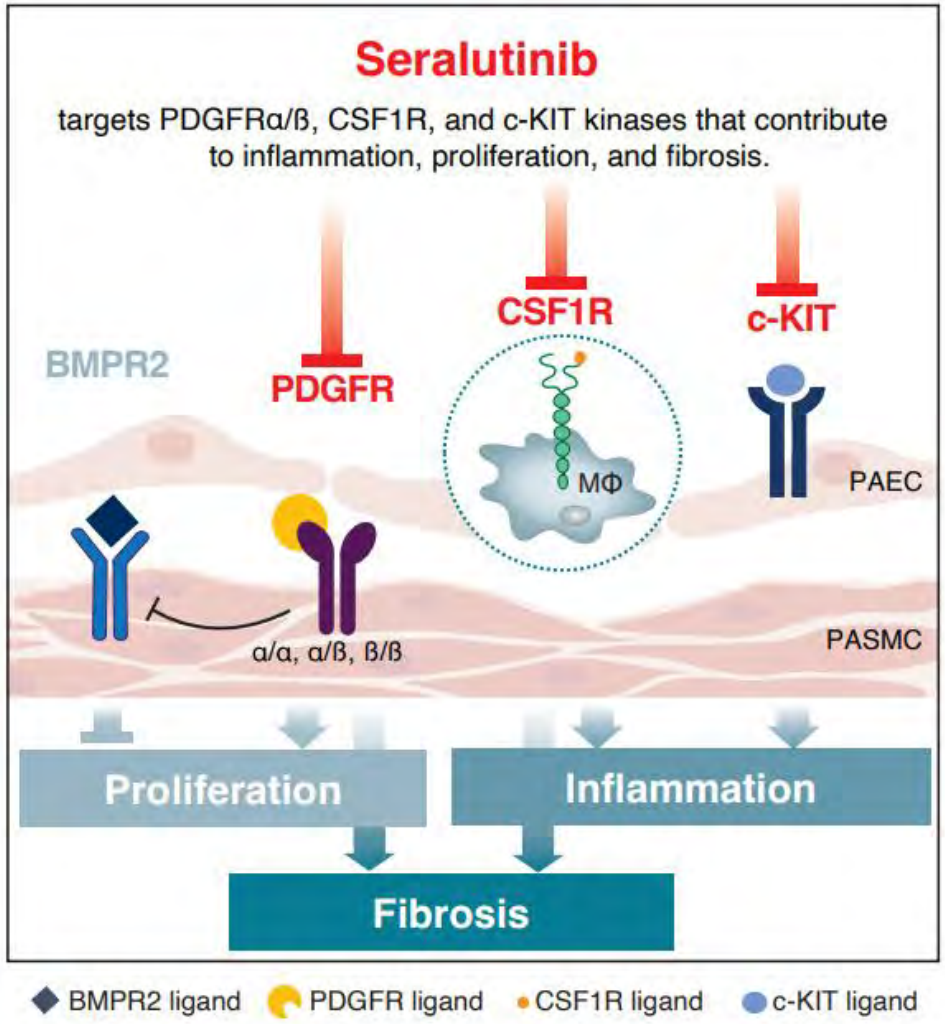
Number at risk (censored)																			
Ralinepag	350 (0)	311 (33)	286 (55)	261 (74)	238 (92)	220 (107)	204 (118)	185 (129)	172 (140)	158 (151)	144 (163)	135 (171)	111 (188)	98 (199)	90 (206)	76 (218)	72 (222)	66 (225)	59 (230)
Placebo	337 (0)	327 (3)	313 (9)	283 (24)	246 (45)	217 (57)	197 (70)	180 (79)	150 (97)	135 (106)	112 (119)	99 (126)	86 (136)	75 (146)	69 (151)	59 (161)	52 (167)	45 (173)	43 (174)

Events

Death
24 hour hospitalization
Partenteral Prostacyclin
Decrease in 6MWD
Additional PAH therapy
Worsening WHO FC
Unsatisfactory clinical response

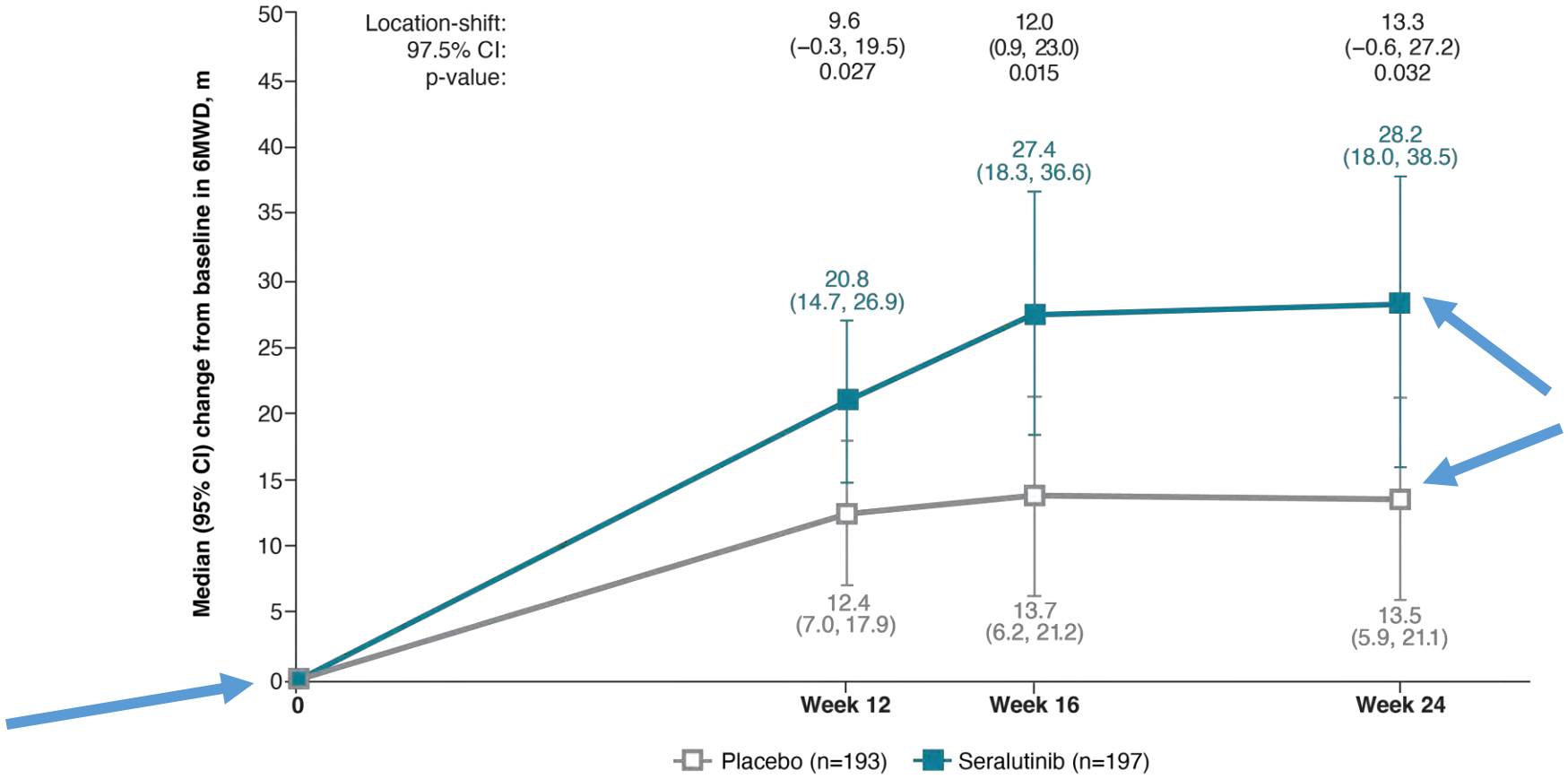
Mclaughlin et al. Lancet 2026

Seralutinib – New Pathway



Frantz Lancet Repir Med 2024
Gossamer Press Release

Seralutinib – Phase 3

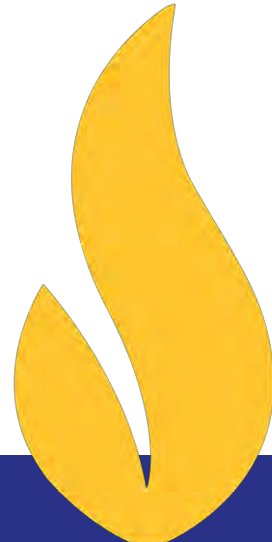


24 weeks of therapy

At Start

Provided by Gossamer Bio

What else is coming?



New oral prostacyclin receptor agonist
- Ralenipag – once a day

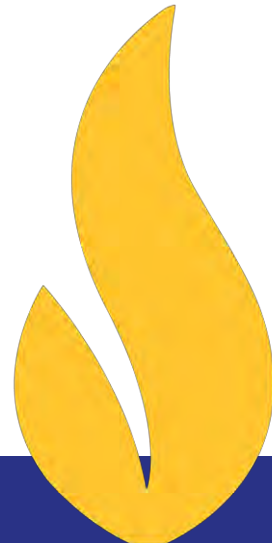
New Inhaled Treprostinil (Currently 4 times a day)
- Soft Mist Inhaler (SMI) - no new drug application needed
- L606 – twice a day – Phase 3
- TPIP – once a day – Phase 3 – PAH and PH-ILD

New pathways
- Seralutinib – Pending FDA review
- IKT001 – imatinib pathway – Phase 3
- VI-0106 – tacrolimus – Phase 3
- APL-9796 – Phase 2
- ROC-101 – Phase 2
- REGN13335 – Phase 2
- CS1 – Phase 2
  NS-863 – Phase 2
- Tiprelestat (Elafin) – Phase 2

PH from lung disease
- L606 – PH-ILD – Phase 3
- TPIP – PH-ILD - Phase 3
- Mosliciguat – PH-ILD – Phase 2 complete ☺
- Frespaciguat – PH-COPD – Phase 2 complete
- TX000045 – PH-ILD
- LAM-001 – PH-ILD
- ROC-101 – PH-ILD
- Mirivadelgat (FP-045) – PH-ILD
- NS-863 – PH-ILD
- APL-9796 – PH-ILD

PH from heart disease
- Sotatercept - Phase 2 complete ☺
- TX000045 – PH-HFpEF
- TNX-201 – PH-HFpEF

What happens if medications don’t work?

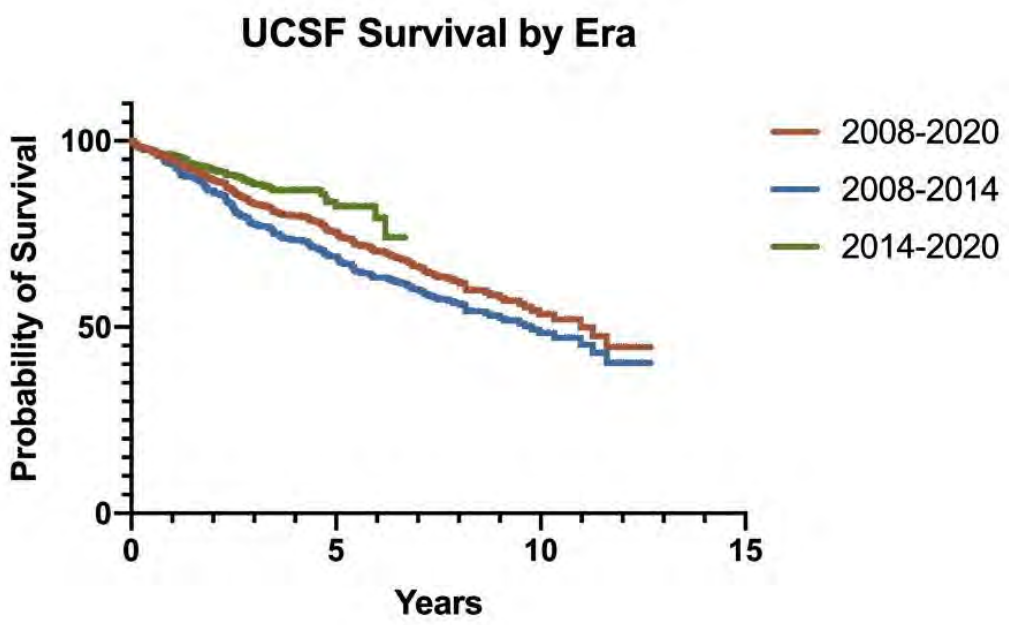


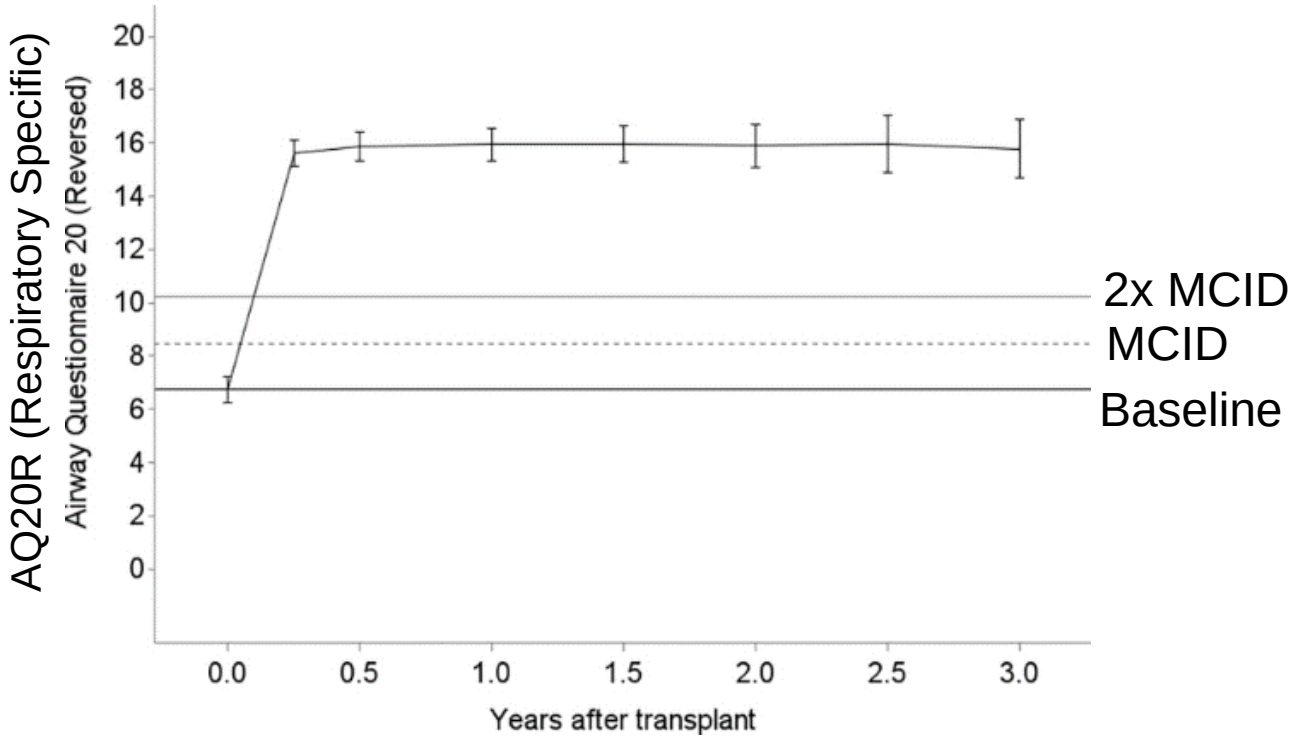
Two primary aims of lung transplantation

Transplant as an Option: The “window”

- Overall goal – similar to treatment of PAH, best possible longevity and quality of life
- Always want to get the *most milage* possible from native lungs
- Transplant should be considered when:
  - All medical treatment options have been exhausted
  - Declining/high risk despite maximum medical therapy
  - Anticipated life expectancy < 2 years (>50% probability)
  - Highly selected on case-by-case basis – no other life limiting illness, reasonable expectation of success with transplant

Two primary aims of lung transplantation





ISHLT Registry 2019
Singer Am J Transplant 2017