caladrius BIOSCIENCES

# *Developing Regenerative Therapies that Reverse Chronic Disease*

David J. Mazzo, PhD
*President & Chief Executive Officer*

# Forward-looking statement

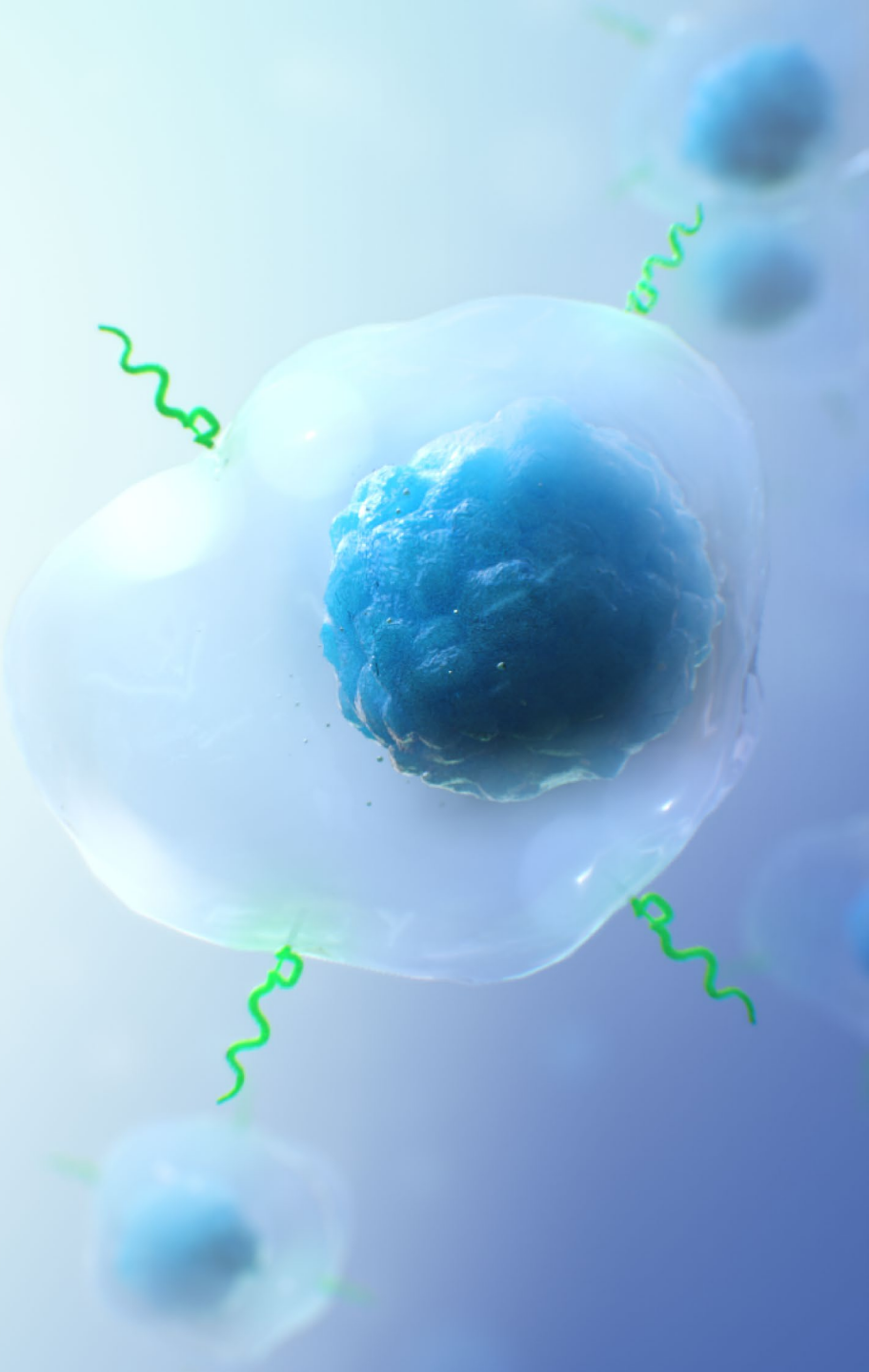
This Investor Presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements reflect management's current expectations, as of the date of this presentation, and involve certain risks and uncertainties. All statements other than statements of historical fact contained in this Investor Presentation are forward-looking statements. The Company's actual results could differ materially from those anticipated in these forward-looking statements as a result of various factors. Factors that could cause future results to differ materially from the recent results or those projected in forward-looking statements include the "Risk Factors" described in the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission ("SEC") on February 25, 2021 and in the Company's other periodic filings with the SEC. The Company's further development is highly dependent on, among other things, future medical and research developments and market acceptance, which are outside of its control. You are cautioned not to place undue reliance on forward-looking statements, which speak only as of the date of this Investor Presentation. Caladrius does not intend, and disclaims any obligation, to update or revise any forward-looking information contained in this Investor Presentation or with respect to the matters described herein.

# Caladrius investment highlights

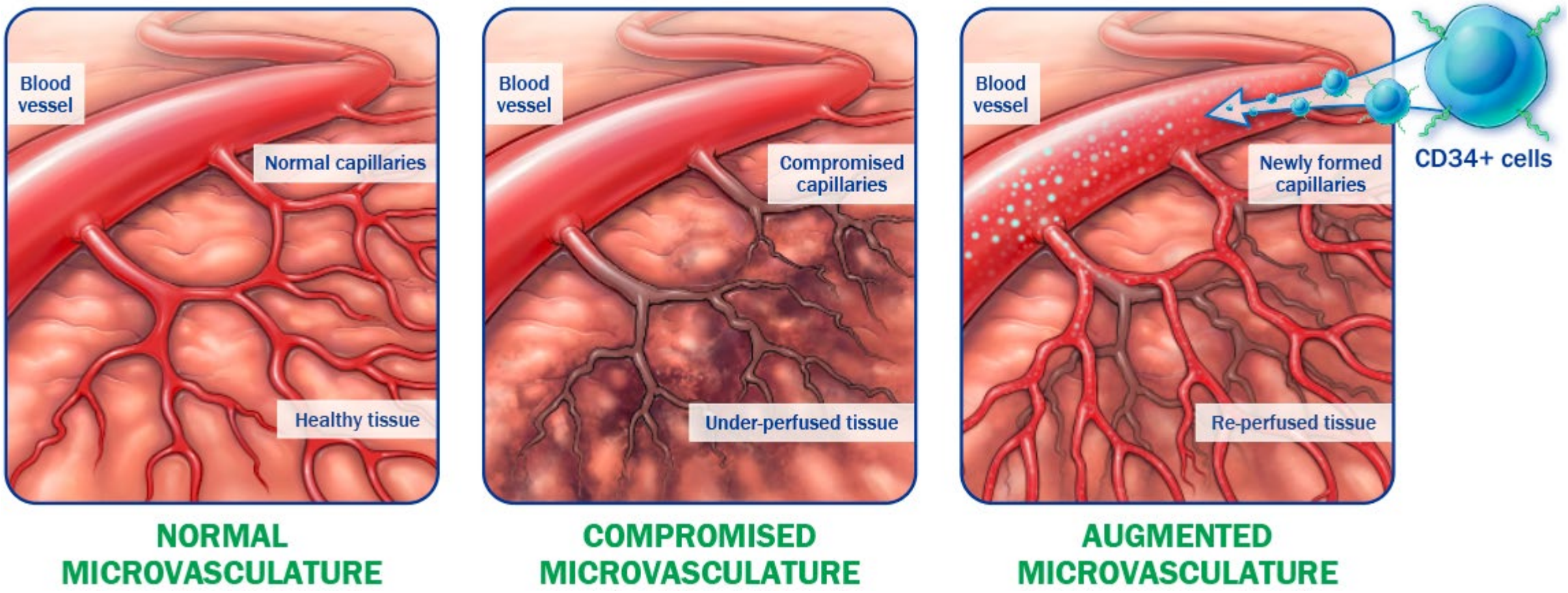
- CD34+ cell therapy platform yielding a multi-product development pipeline with 2 clinical programs having regenerative medicine “breakthrough” designation
- Proprietary field-leading technology in lucrative global indications backed by a strong IP portfolio
- Multiple potential value creating events in the next 12-24 months based on milestones across the pipeline
- Strong balance sheet; ~$106 million in cash & investments (6/30/2021) with no debt and cash runway projected to fund operations for several years
- Seasoned management with noteworthy domain expertise along with big pharma and emerging biotech experience

# CD34+ Cell Therapy

## Technology Overview



# CD34+ cells have a well characterized mechanism of action




- Naturally occurring endothelial progenitor cells that re-establish blood flow to under-perfused tissues[1,2]
- Possess pre-programmed pro-angiogenic and anti-inflammatory tissue repair properties[3,4]

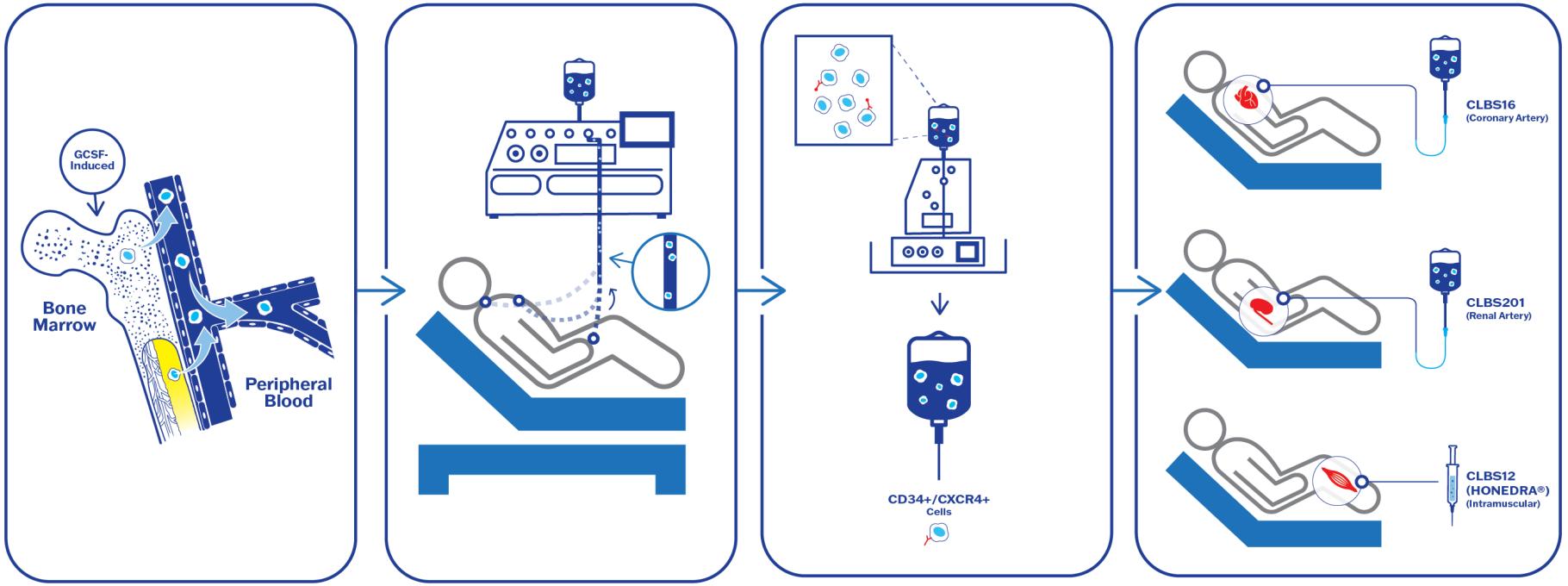
[1]Mackie, A.R. et al., *Tex Heart Inst J* 2011, 38(5), 474-485
[2]Kocher, A.A. et al., *Nat Med* 2001, 440-436
[3]Abd-Allah et al., *Cytotherapy 2015,* 17: 443-53
[4]Lo , B.C. et al., *Am J Respir Cell Mol Biol* 2017, 57: 651-61

# CD34+ cell therapy is extensively studied/clinically validated

- CD34+ cells have been studied clinically in a variety of ischemic disease indications by numerous investigators across many sites and countries
- CD34+ cells repeatedly demonstrated vascular repair in multiple organs
- Consistent and compelling results of rigorous clinical studies comprising >1,000 patients have been published in peer reviewed journals[1-4]
- A single treatment has elicited durable therapeutic effect
- No cell-related adverse events reported to date

[1] Povsic, T. et al. *JACC Cardiovasc Interv*, 2016, 9 (15) 1576-1585
[2] Losordo, D.W. et al. *Circ Cardiovasc Interv,* 2012; 5:821–830
[3] Velagapudi P, et al, *Cardiovas Revasc Med*, 2018, 20(3):215-219
[4] Henry T.D., et al, *European Heart Jour* 2018, 2208–2216

# Caladrius' CD34+ cell process is rapid/economical/scaled




**DAY -5 TO 0**
GCSF-induced mobilization of patient's CD34+ cells from the bone marrow to the peripheral circulation

**DAY 1**
Sample collection via apheresis at one of several access points at an outpatient center

**DAY 2**
**ISOLATION**, concentration and formulation of CD34+/CXCR4+ cells

**DAY 3 OR 4**
CD34+ cells returned to the **SAME PATIENT**; route of administration is indication-specific

- Drug induced mobilization eliminates need for surgical bone marrow aspiration
- No genetic manipulation or *ex vivo* expansion of cells
- Four days or less from donation to treatment

# Caladrius' CD34 technology has robust intellectual property

***Patent protection to 2031+***

**9**
U.S. patents granted

**28**
Foreign patents granted

## Key Claims

- Pharmaceutical composition of non-expanded CD34+/CXCR4+ cells
- Therapeutic concentration range
- Stabilizing serum
- Repair of injury caused by vascular insufficiency

# Caladrius' innovative CD34+ cell therapy pipeline[1,2]

| PRODUCT/INDICATION | DEVELOPMENT STAGE | KEY MILESTONE TARGETS |
|---|---|---|
| XOWNA® (CLBS16)<br>CORONARY MICROVASCULAR DYSFUNCTION | FREEDOM PHASE 2B TRIAL (**USA;** ONGOING) | - Complete enrollment: **3Q2022**<br>- Top-line data: **2Q2023** |
| HONEDRA® (CLBS12) ***SAKIGAKE DESIGNATED (JAPAN)***<br>CRITICAL LIMB ISCHEMIA + BUERGER'S DISEASE | REGISTRATION ELIGIBLE TRIAL (**JAPAN;** ONGOING) | - Complete enrollment: **TBD**<br>- Top-line data: **~2022**<br>- J-NDA filing: **1H2023**<br>- Approval:**~2023** |
| CLBS201<br>DIABETIC KIDNEY DISEASE | PHASE 2 (**USA;** INITIATION PENDING) | **6-patient run-in arm:**<br>- Initiate enrollment: **2H2021**<br>- Top-line data: **2Q2022**<br>**40-patient randomized arm:**<br>- To follow Data and Safety Monitoring Board clearance of the run-in arm |

[1] Products are distinct and not interchangeable

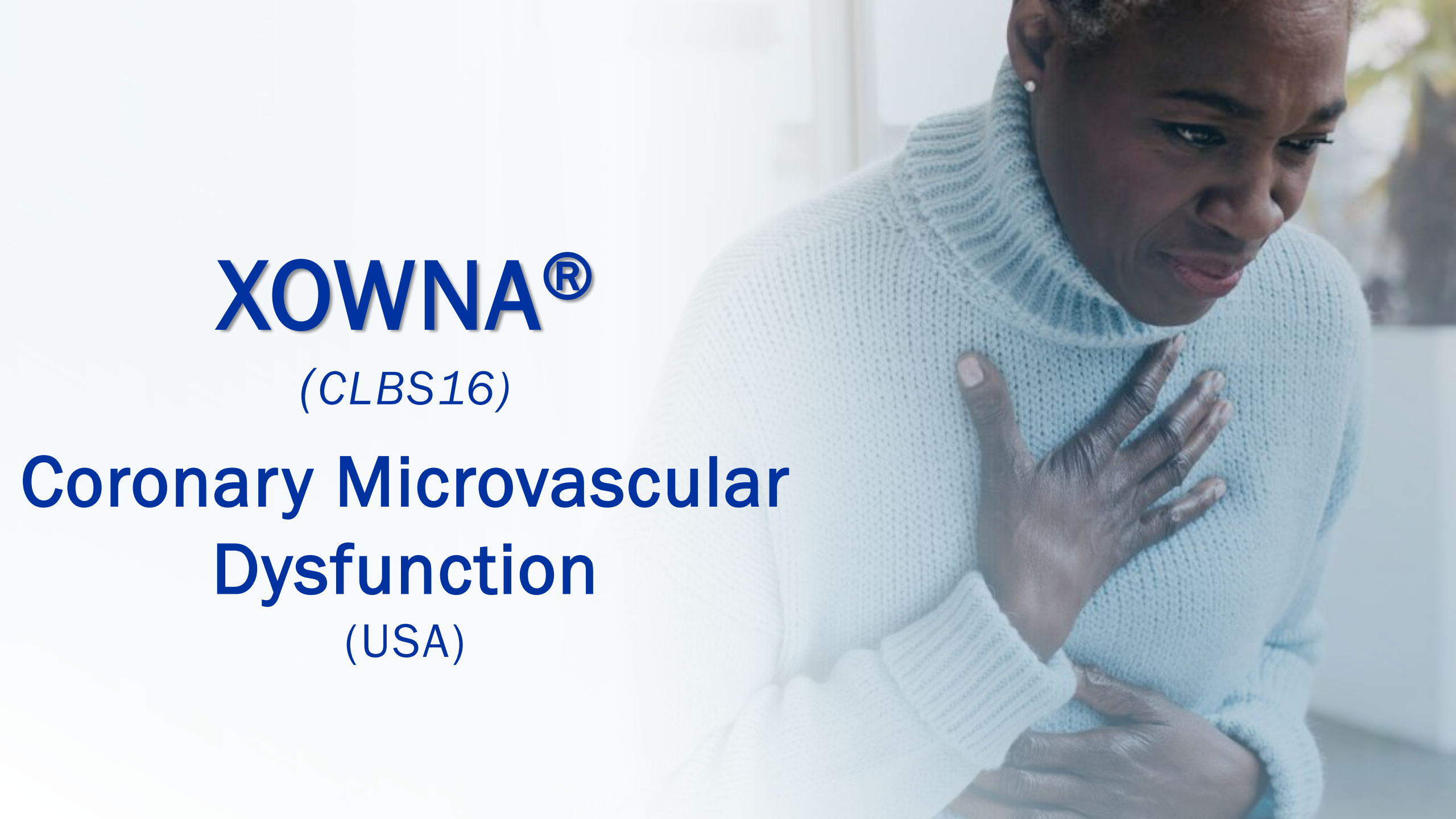
[2] Timing subject to COVID-19 pandemic influence

# XOWNA®

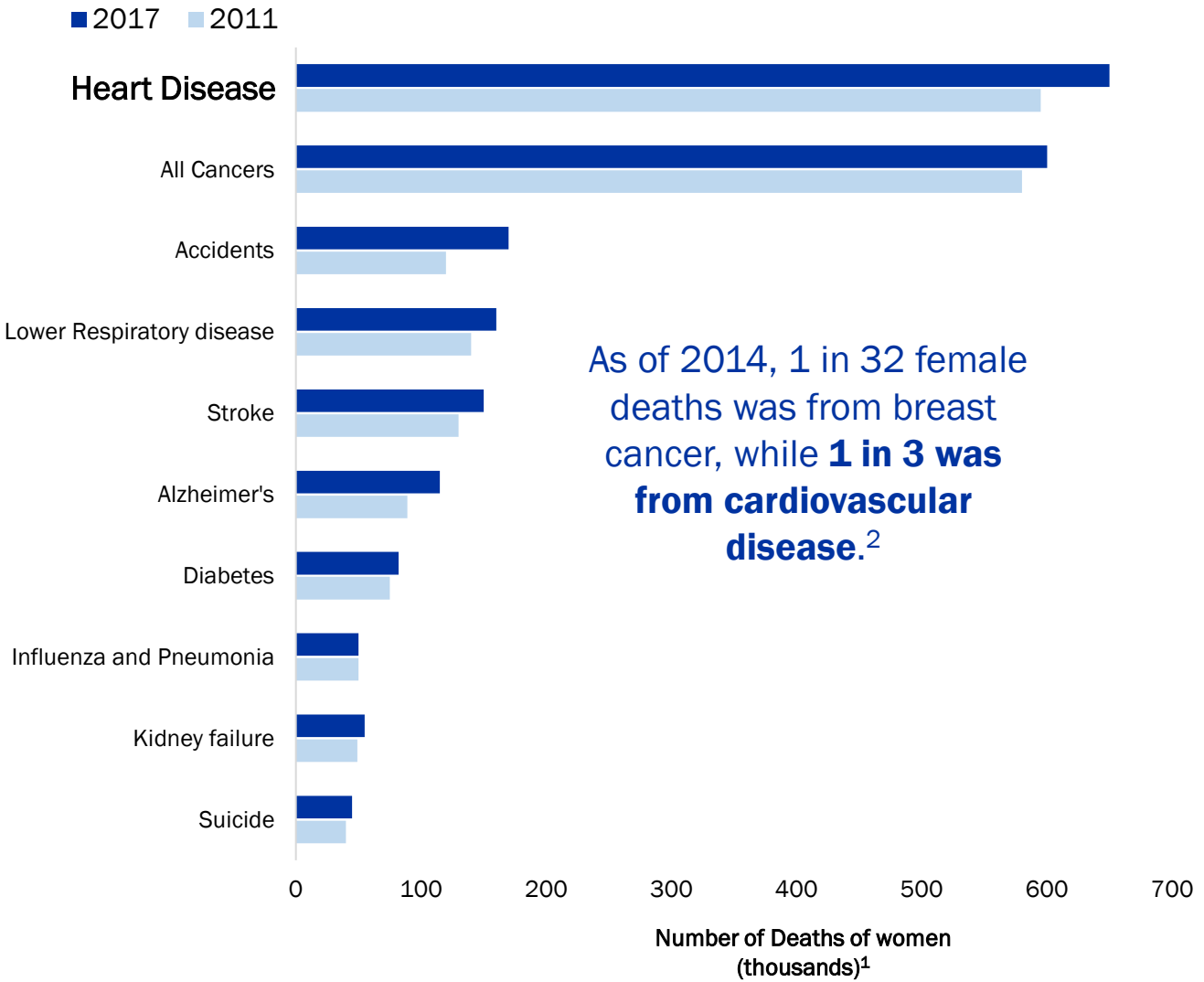
*(CLBS16)*

## Coronary Microvascular Dysfunction

(USA)



# CD34+ cell therapy targets unmet needs in cardiovascular diseases




As of 2014, 1 in 32 female deaths was from breast cancer, while **1 in 3 was from cardiovascular disease.**[2]

## ISCHEMIA Trial[3] results underscore the need for treatments beyond large vessel interventions

- The International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) enrolled 5,179 patients at 320 sites in 37 countries

**Conclusion:**
Interventional heart procedures *do not* reduce the overall rate of heart attack or death compared with medicines and lifestyle changes alone.

[1] Centers for Disease Control and Prevention as cited in McKay, Betsy. "Heart-Failure Deaths Rise, Contributing to Worsening Life Expectancy." The Wall Street Journal, 30 Oct. 2019, Link to article.
[2] Kochanek, KD., et al. (2016). Deaths: final data for 2014. National vital statistics reports: from the Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System, 65(4), 1-122.
[3] ISCHEMIA Study Results, AHA Scientific Sessions November 2019. https://ischemiatrial.org/ischemia-study-results#slides

# Indication: coronary microvascular dysfunction (CMD)

- Deficient heart microvasculature ***without large vessel obstructive disease***
- Causes frequent, debilitating chest pain; not treatable by stents or bypass; responds poorly or not at all to available pharmacotherapies
- Afflicts women more frequently (2:1 to 3:1), especially younger women[1,2]
- Results in poor prognosis for patients[3]
  - Significantly elevated risk of all-cause mortality[4]
- Clinically diagnosed based on symptoms ***and*** demonstrated absence of large vessel obstructive disease
- Quantitatively diagnosed using Coronary Flow Reserve (CFR)[5]

[1] Coronary Microvascular Disease. (2015, July 31). In American Heart Association
[2] R. David Anderson, John W. Petersen, Puja K. Mehta, et al., Journal of Interventional Cardiology, 2019: 8
[3] Loffler and Bourque, Curr Cardiol Rep. 2016 Jan; 18(1): 1
[4] Kenkre, T.S. et al., Circ: CV Qual & Outcomes 2017, 10(12) 1-9
[5] Collins, P., British heart journal (1993) 69(4), 279–281

# CMD represents a large unmet medical need

- ~112 million people globally are affected by angina[1]
- ~8.3 million people in the U.S. suffering from coronary artery disease (CAD)[2]
- 10% - 30% of angina patients have no significant CAD on invasive coronary angiography[3,4]
- 50% - 65% of patients with angina without obstructive CAD are believed to have CMD[5]

**Applicable CMD population in the U.S. potentially treatable by XOWNA® ranges from ~415,000 to ~1.6 million patients[6]**

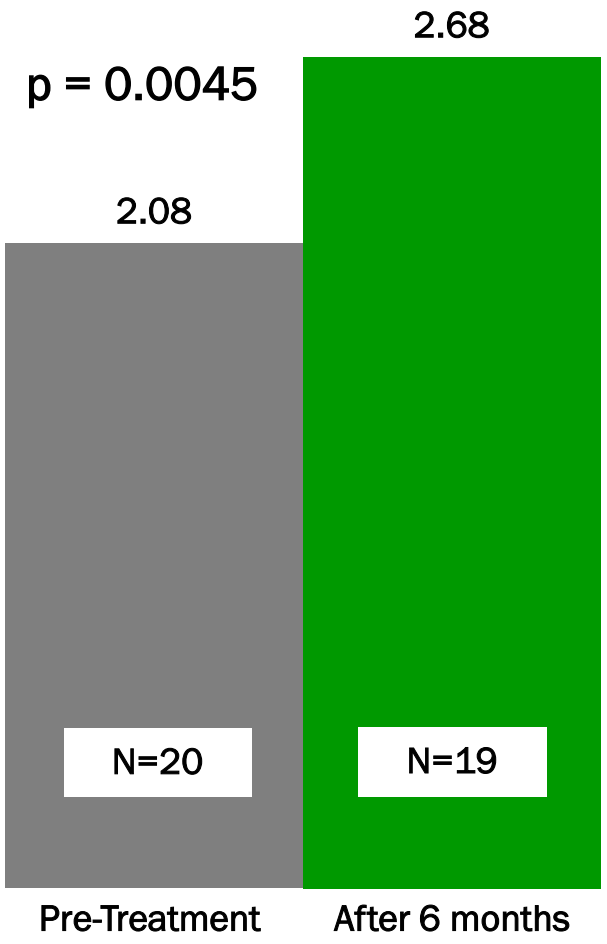
[1] Kunadian V, et al. European Heart Journal. 2020; 0:1-21
[2] Cleveland Clinic/AHA (American Heart Association)
[3] Farrehi PM, et al. Am J Manag Care. 2002;8:643–648
[4] Bradley SM, et al. J Am Coll Cardiol. 2014;63:417–426
[5] Marinescu MA, et al. JACC Cardiovasc Imaging. 2015;8:210-220
[6] Tunstall-Pedoe H. (ed.) WHO, Geneva, 2003, pp. 244, Swiss Fr 45, ISBN: 92-4-156223-4.

# ESCaPE-CMD: Phase 2a interventional, proof-of-concept trial

| | |
|---|---|
| **Endpoints** | ▪ Therapeutic effect and the evaluation of adverse events; including changes from baseline to 6 months for coronary flow reserve, angina frequency, CCS angina class, quality of life |
| **Study Size** | ▪ 20 subjects (U.S. centers - Cedars Sinai, Los Angeles & Mayo Clinic, Rochester) |
| **Dose** | ▪ Up to 300 x $10^6$ CD34+ cells |
| **Mode of administration** | ▪ Single intracoronary infusion |
| **Timing** | ▪ Positive complete results presented at SCAI Scientific Sessions (May 2020) |

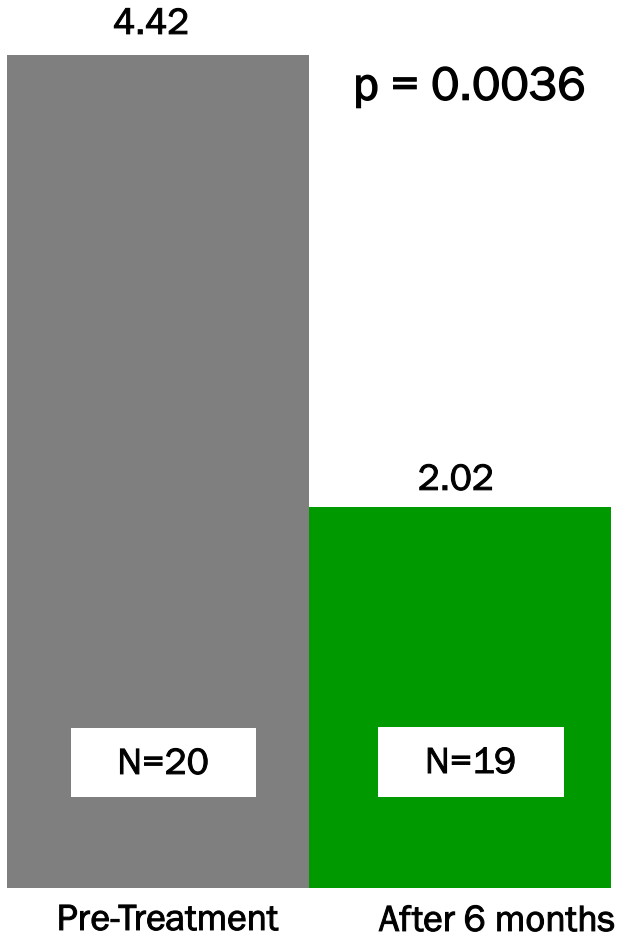
# XOWNA® ESCaPE-CMD results are unique and compelling

## Coronary Flow Reserve [1]



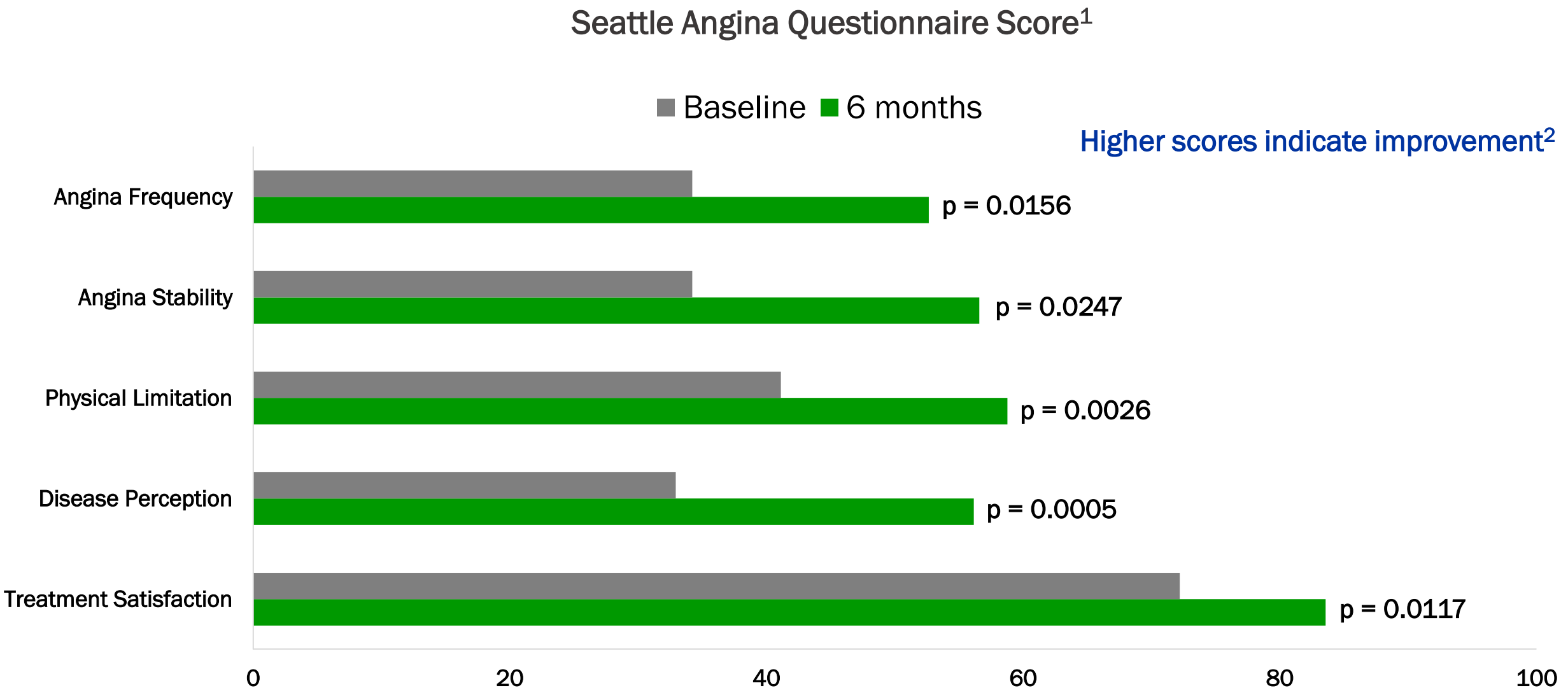

- CFR ≤2.5 indicates CMD
  - CFR of 2 = 3-4 x increase in MACE at 3 years[1]
- CFR ≥2.5 is in “normal” range
- Results after a single intracoronary administration of XOWNA®

## Daily Angina Frequency [2]




[1] Murthy et al, Circulation, 2014
[2] Henry, D. T., SCAI 2020 Scientific Sessions

# XOWNA® ESCaPE-CMD results are unique and compelling




[1] Henry, D. T., SCAI 2020 Scientific Sessions
[2] Spertus, J.A. et al, JACC Vol. 25, No. 2 February 1995: 333-341

# XOWNA®: ESCaPE-CMD summary

- Statistically significant improvement in heart function and symptoms
- No evidence of cell related adverse events
- First therapy to potentially reverse CMD after a single administration; a potential breakthrough in the treatment of CMD
  - Expected to lead to a decreased risk of MACE, including CV-related death
- Supports microvascular repair mechanism of CD34+ cells

# FREEDOM trial: Phase 2b double-blind, placebo-controlled

| | |
|---|---|
| **Endpoints** | ▪ Change from baseline in angina frequency [Baseline to 3 and 6 months]<br>▪ Change from baseline in total exercise time [Baseline to 6 months]<br>▪ Change from baseline in health-related quality of life [Baseline to 3 and 6 months]<br>▪ Change from baseline in peak coronary flow reserve [Baseline to 6 months] |
| **Study Size** | ▪ 105 subjects (~15 sites in the USA) |
| **Dose** | ▪ 1 x $10^6$ to 300 x $10^6$ CD34+ cells (XOWNA®) or placebo |
| **Mode of administration** | ▪ Single intracoronary infusion |
| **Timing**<br>**(Assuming no further COVID-19 impact)** | ▪ Study initiated 4Q2020<br>▪ Complete Enrollment: 3Q2022<br>▪ Top-line Data Target: 2Q2023 |

# HONEDRA®

*(CLBS12)*

## Critical Limb Ischemia

(Japan)

SAKIGAKE designated – Japan

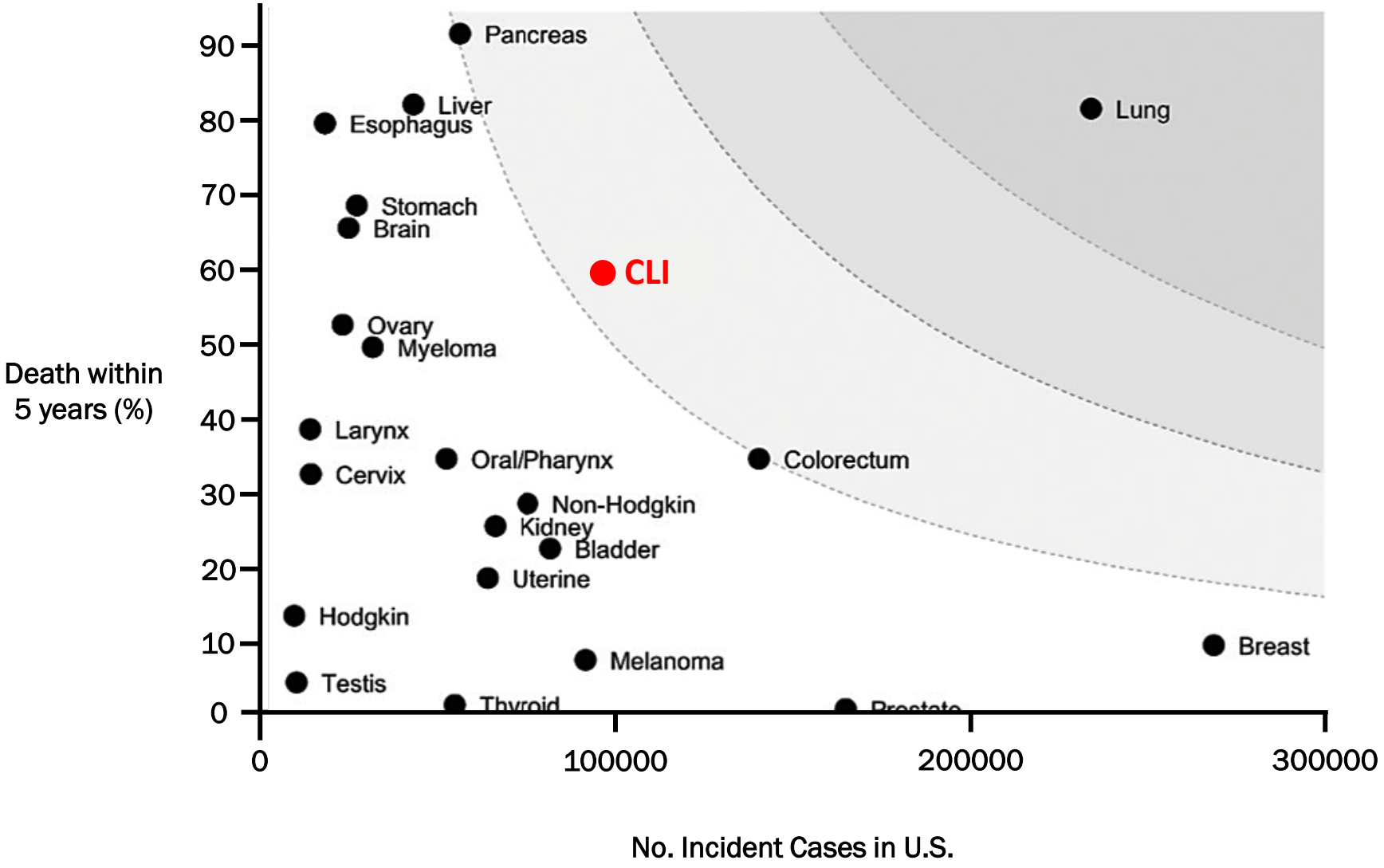
Orphan Drug designated
(Buerger's disease) - USA

Advanced Therapeutic Medicinal
Product (ATMP) designated – EU

# Indication: critical limb ischemia (CLI)

- Severe arterial obstruction impeding blood flow in the lower extremities
  - Often found as a co-morbidity in diabetes patients
  - Includes severe rest pain and non-healing ulcers
- Buerger's disease (inflammation in small and medium arteries) a form of CLI associated with a history of heavy smoking (orphan population)
- Patients with no-option CLI have persistent symptoms even after bypass surgery, angioplasty, stenting and available pharmacotherapy
- CLI patients are at high risk of amputation and increased risk of death
- Multi-hundred-million-dollar opportunity in Japan

# CLI: higher mortality rate and incidence than most cancers




Mustapha, J. A., Katzen, B. T., et al. (2019, May). Endovascular Today, 18(5), 80-82

# HONEDRA® targets patients based on the Rutherford Scale

## CLI amputation rates increase with increasing Rutherford score (disease severity)[1]

**Rutherford ("R") scale**

**R 6:** Functional foot no longer salvageable

**R 5:** Minor tissue loss non-healing ulcer; focal gangrene with diffuse pedal ischemia

**R 4:** Debilitating rest pain

**R 1-3:** Mild to severe claudication

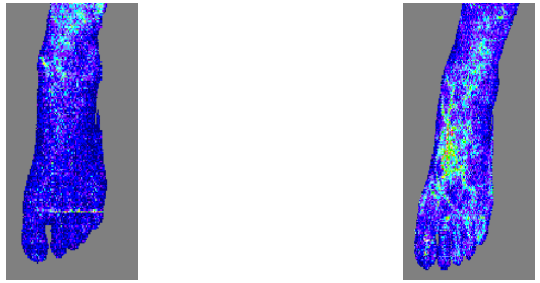
HONEDRA® targets patients with **R4** or **R5** disease

[1] Reinecke H., European Heart Journal, 2015 Apr 14;36(15):932-8

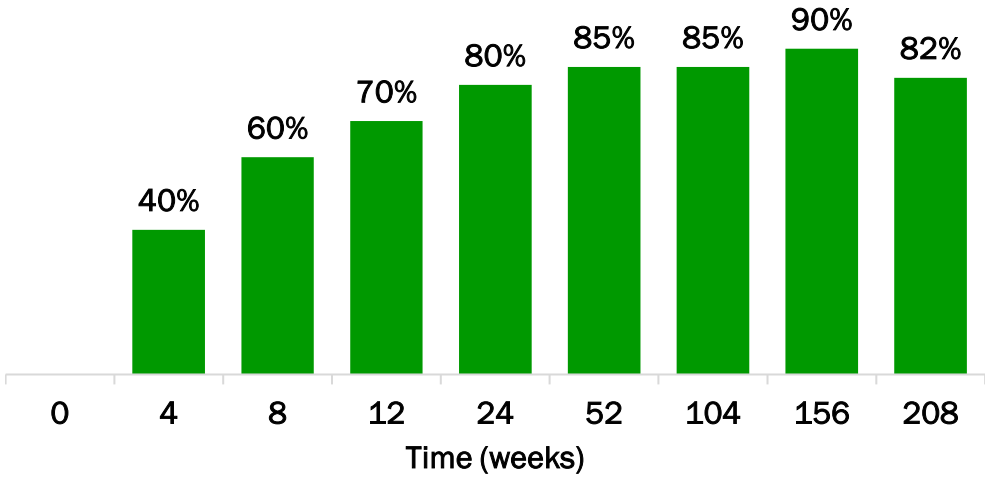
# Single treatment of CD34+ cells reversed CLI (Phase 2 data)

## Actual CLI Patient Laser Doppler Image

Pre-treatment Post-treatment (week 12)

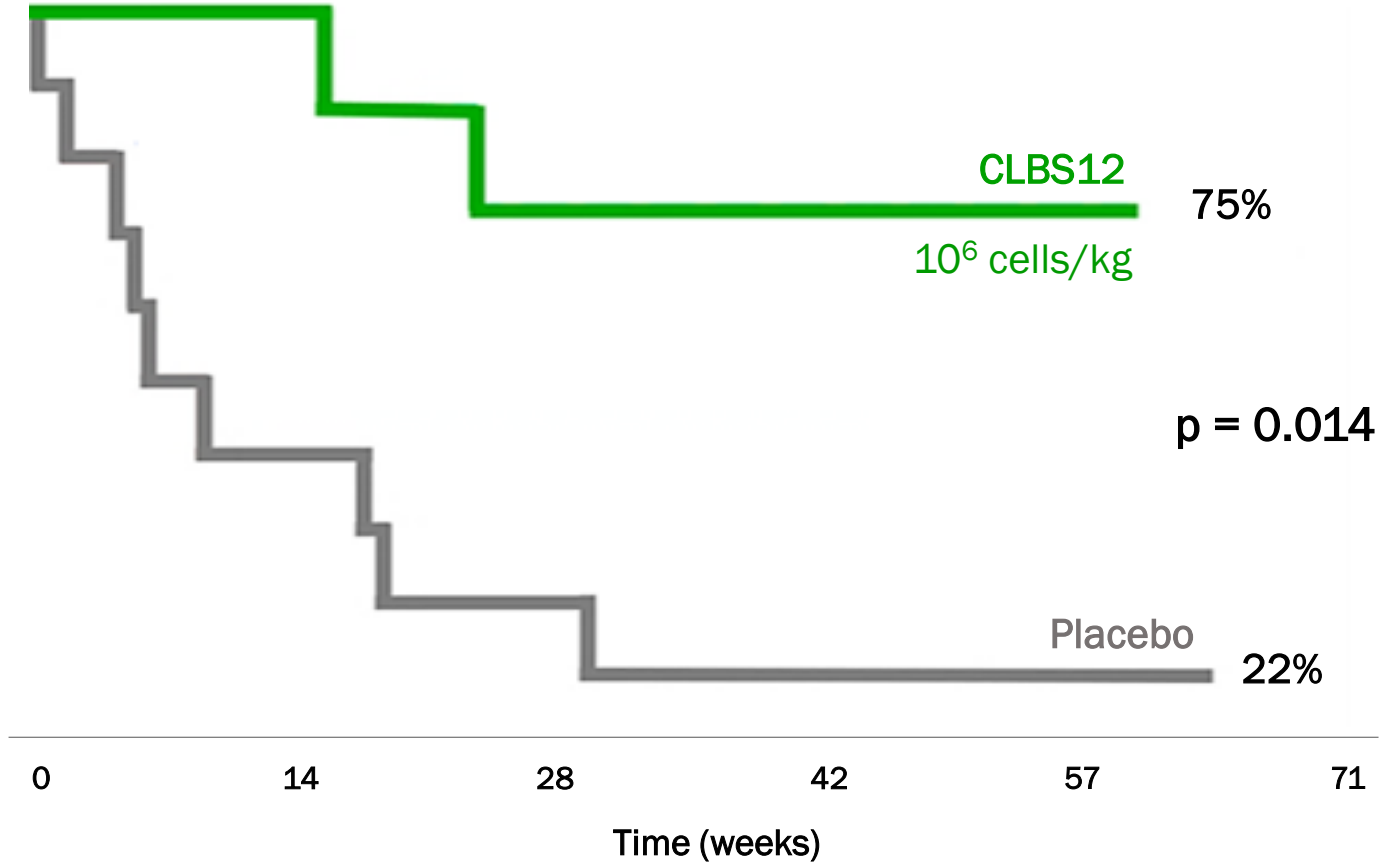


## % of Patients (CLI + BD) Achieving CLI-free Status (Japan; n=27)[1]




*~80% of patients achieved sustainable remission within 6 months of a single treatment; durable for at least 4 years*

## Probability of Amputation-Free Survival (USA; n=28)[2]




[1] Kinoshita et al, Atherosclerosis 224 (2012) 440-445
[2] Losordo, D.W. et al, Circulation 2012; 5(6):821-830

# HONEDRA® registration-eligible study (Japan)

| | |
|---|---|
| **Primary Endpoint** | ▪ Continuous CLI-free (2 consecutive monthly visits, adjudicated independently) |
| **Study Size** | ▪ 30 subjects with no-option CLI + 7 Buerger's disease pts.; all Rutherford category 4 or 5; recruited across 12 centers in Japan |
| **Dose** | ▪ Up to $10^6$ cells/kg of HONEDRA® (CLBS12) to the most seriously affected limb (target limb) |
| **Control/Comparator** | ▪ Standard of Care: wound care plus drugs approved in Japan<br>  ▪ Including antimicrobials, antiplatelets, anticoagulants and vasodilators |
| **Mode of administration** | ▪ Intramuscular, 20 injections in affected lower limb in a single treatment |
| **Timing** | ▪ Enrollment completion/results target : TBD (COVID-19 impact dependent)<br>▪ Earliest approval target: ~2023 |

# Extraordinary HONEDRA® results in Buerger's disease (JPN)

- Surgery not viable; existing pharmacotherapies do not prevent amputation[1]
- Cohort enrollment complete
- Results will contribute to the efficacy evaluation of the full study population

**Approximately 60% of patients achieved CLI-free status**

*(Natural patient evolution is continual deterioration for all patients)*

[1] Cacione DG, et al, Pharm. treatment of Buerger's Disease, Cochrane Database of Systematic Reviews, 2016, (3) CD011033

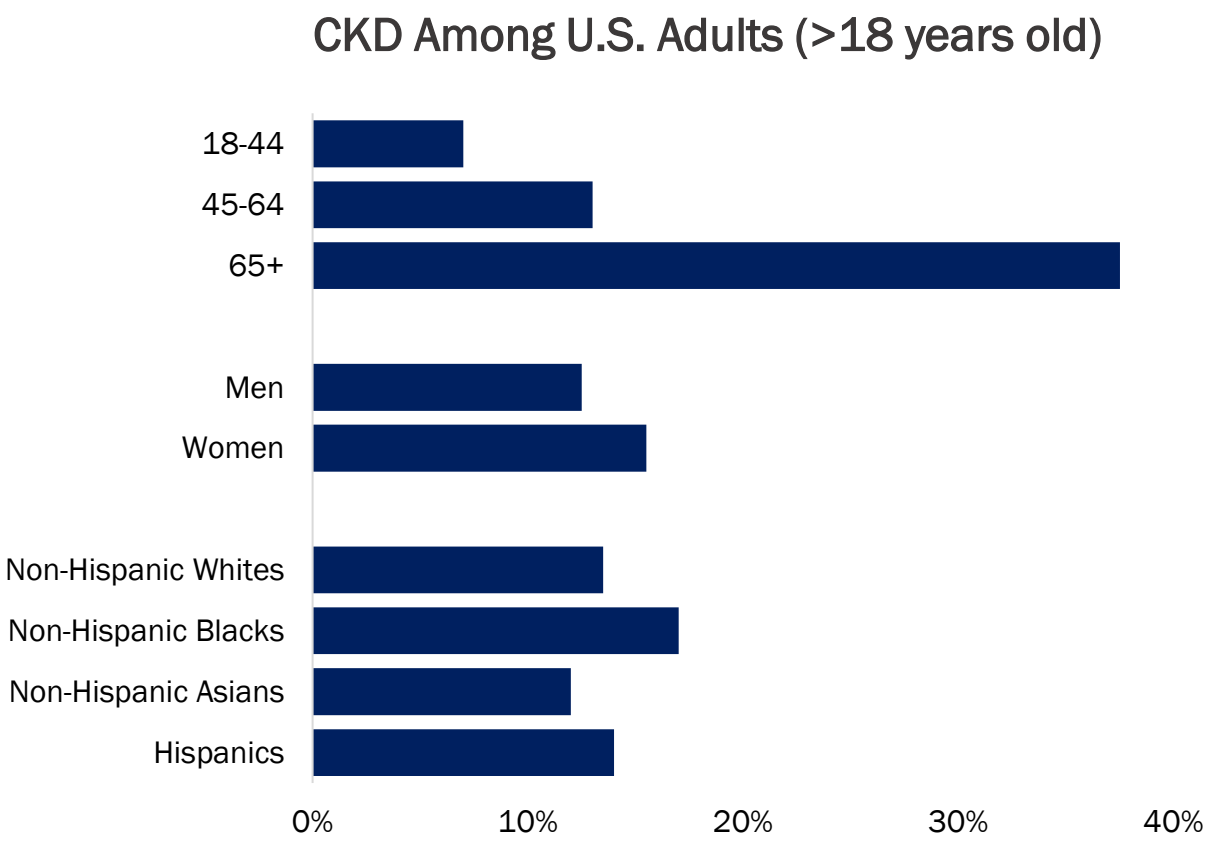
# CLBS201

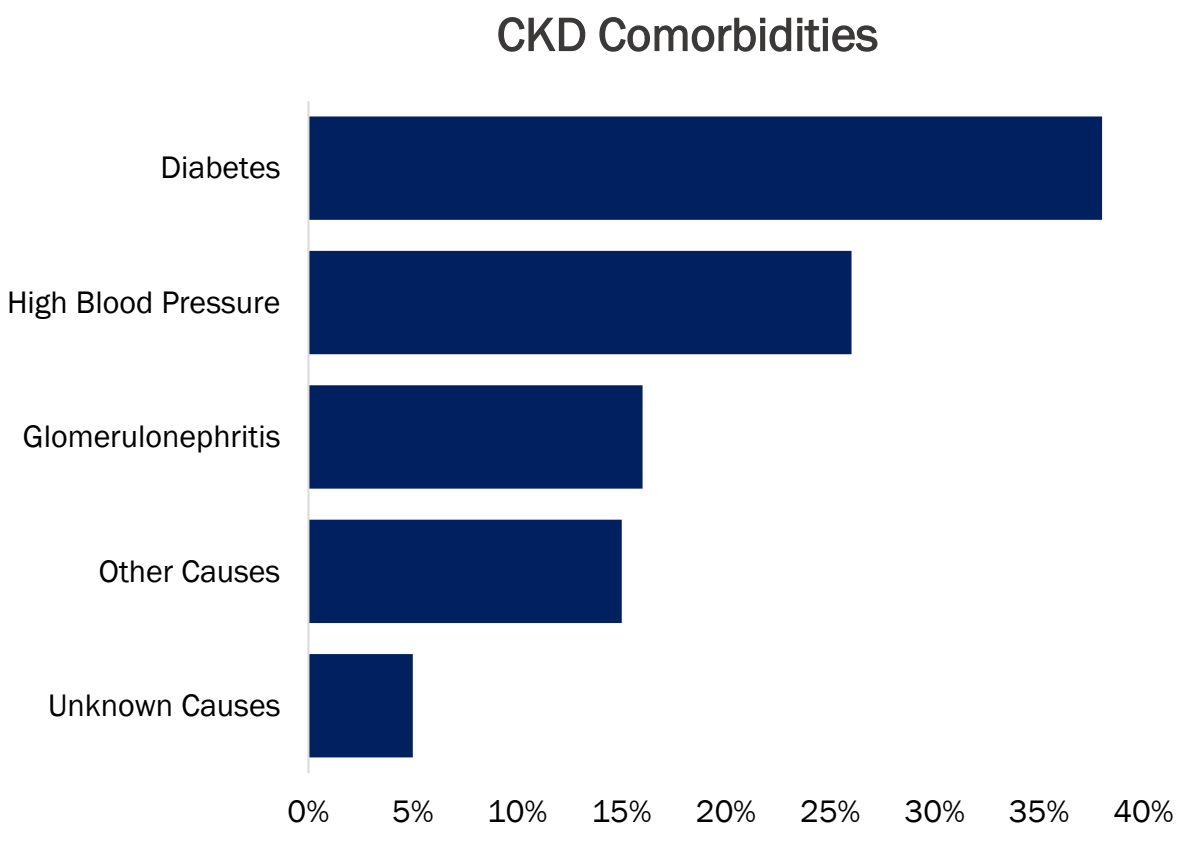
## Diabetic Kidney Disease

(USA)

# Chronic kidney disease: risk factors and comorbidities

- An aging population is at greatest risk of chronic kidney disease (CKD) with diabetes and hypertension being typical comorbidities
  - 1 in 3 adults are diabetic and 1 in 5 adults are hypertensive

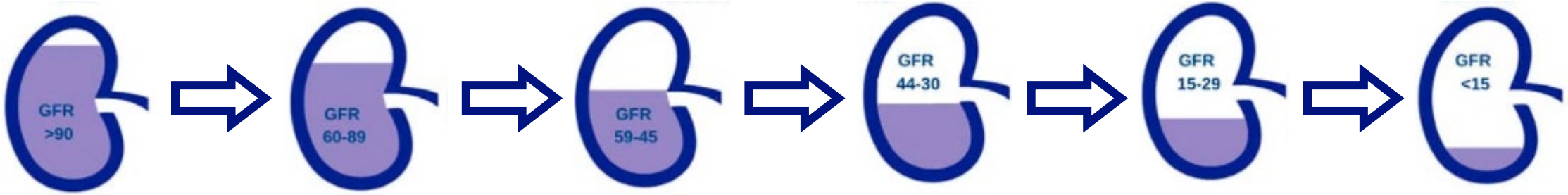



Centers for Disease Control and Prevention. Chronic Kidney Disease in the United States, 2019. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention; 2019.

# CKD: multiple stages progressing toward kidney failure

- The stages of CKD are determined by glomerular filtration rate (GFR)[1]
- GFR is measured to determine the level of creatinine in the blood (serum creatinine)
- As kidney function worsens, the level of creatinine increases and GFR decreases
- In 2015-2016, 14%-15% of U.S. adults had evidence of CKD stages 1-4; of these, ~15 to 18 million had evidence of CKD stage 3 or 4[2]




**STAGE 1** Normal function

**STAGE 2** Mild loss of function

**STAGE 3A** Mild to Moderate loss of function

**STAGE 3B** Moderate to Severe loss of function

**STAGE 4** Severe loss of function

**STAGE 5** Kidney failure

[1] 2020 Dallas Nephrology Associates
[2] Centers for Disease Control and Prevention. Chronic Kidney Disease Surveillance System—United States.

# Scientific rationale for CLBS201 trial

- CKD is often associated with progressive microvasculature damage and loss, resulting from its common comorbidities of hypertension and diabetes[1]
- The pathophysiology of CKD denotes compromised renal microvasculature[2]
- Preclinical studies show that microcirculation replenishment improves kidney function
- CD34+ cells are promoters of new capillary growth, improving the microvasculature

# CLBS201 clinical strategy

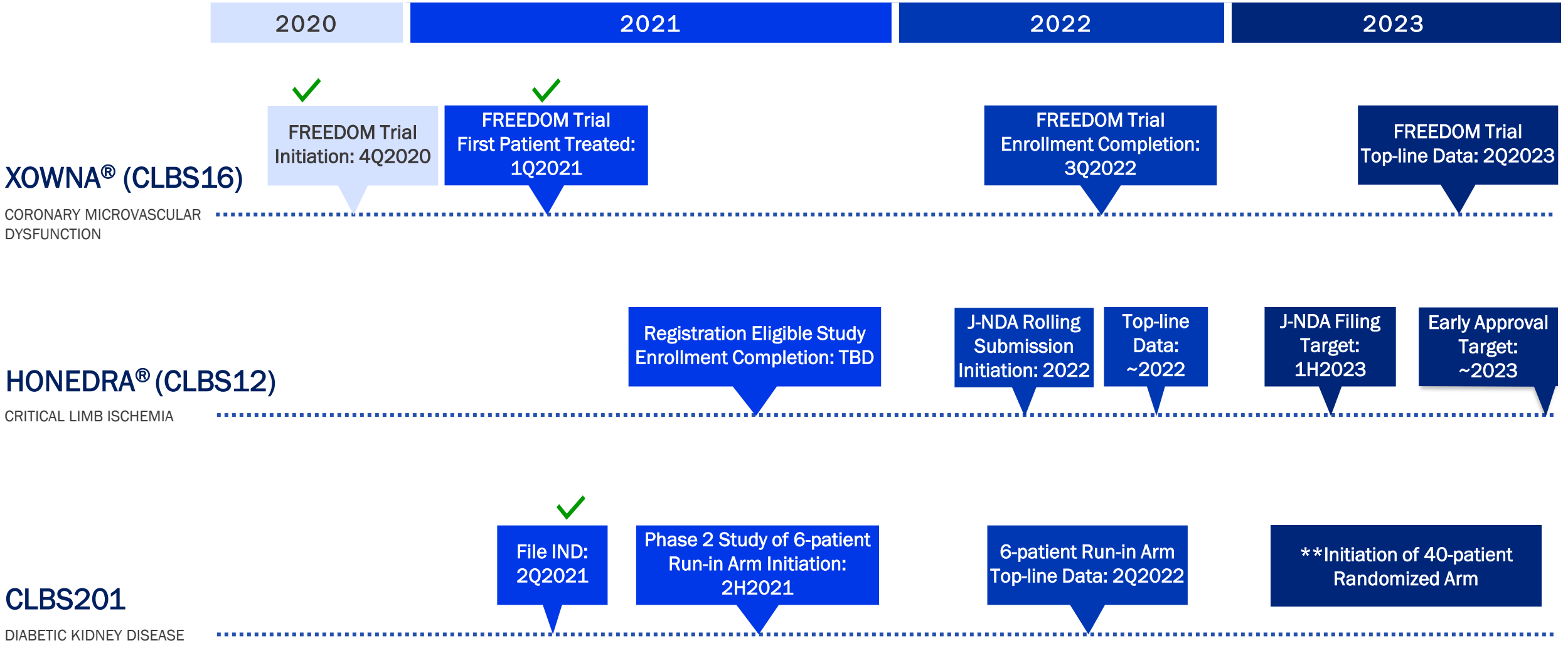
- To demonstrate that regeneration of the kidney microcirculation using CD34+ cell therapy will safely improve or stabilize kidney function [as measured by GFR]
- To show that progression to kidney failure and hemodialysis can be slowed or prevented

[1] Chade AR. (2017) Small Vessels, Big Role: Renal Microcirculation and Progression of Renal Injury. Hypertension; 69(4):551-563.
[2] *Zuk, Anna & Bonventre, Joseph. (2016). Annual Review of Medicine. 67. 293-307. 10.1146/annurev-med-050214-013407.*

# CLBS201: Planned Phase 2 proof-of-concept study

| | |
|---|---|
| **Primary Endpoint** | ▪ Change in eGFR compared to baseline, assessed at 6 months |
| **Study Size** | ▪ 6 patient open-label run-in arm (safety) followed by ~40 subjects (stage 3b diabetic kidney disease) randomized arms |
| **Dose** | ▪ $1x10^6$ – $300x10^6$ cells, half per kidney, administered as a one-time infusion |
| **Design** | ▪ Placebo-controlled with a total of 12-months follow-up |
| **Mode of administration** | ▪ Single intra-arterial injection into each renal artery |
| **Timing** | <u>6-patient run-in arm:</u><br>▪ Initiation target: 3Q2021<br>▪ Top-line data target: 2Q2022<br><u>40-patient randomized arm:</u><br>▪ To follow Data and Safety Monitoring Board (DSMB) clearance of the run-in arm |

# Caladrius timeline of key development milestones*




✓ Completed

*Timing subject to COVID-19 pandemic influence

**Contingent on DSMB clearance of run-in arm

# Caladrius key financial information

| | |
|---|---|
| Cash & Investments:<br>As of June 30, 2021 | $106 million |
| Six months ended June 30, 2021 Operating Cash Burn[1]: | $14.0 million |
| Cash Runway Based on Current Plan: | Sufficient capital to fund operations beyond multiple key data readouts (>2023) |
| Debt as of June 30, 2021: | $0 |
| Common Shares Outstanding:<br>As of June 30, 2021 | 59.5 million shares |
| Options Outstanding as of June 30, 2021:<br>Exercise Price: $1.48 - $3.50 = 346,000 shares<br>Exercise Price: > $3.50 = 659,000 shares | 1.0 million shares |
| Warrants Outstanding as of June 30, 2021:<br>Weighted Average Exercise Price: $2.84 | 21.4 million shares |

[1] Excludes $1.4 million in net proceeds from sale of New Jersey NOLs

# Caladrius investment highlights

- CD34+ cell therapy platform yielding a multi-product development pipeline with 2 clinical programs having regenerative medicine “breakthrough” designation
- Proprietary field-leading technology in lucrative global indications backed by a strong IP portfolio
- Multiple potential value creating events in the next 12-24 months based on milestones across the pipeline
- Strong balance sheet; ~$106 million in cash & investments (6/30/2021) with no debt and cash runway projected to fund operations for several years
- Seasoned management with noteworthy domain expertise along with big pharma and emerging biotech experience

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**Investor Relations Contact:**

*John D. Menditto*

Tel: (908) 842-0084

jmenditto@caladrius.com