# Launching the BAROSTIM NEO™ Global Registry

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BAROSTIM THERAPY SUMMIT

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BAROSTIM THERAPY™

# Agenda

- BAROSTIM NEO Global Registry Strategy
- Global Registry Designs
- Global Registry Status

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# Vision & Mission

BAROSTIMNEO™
GLOBAL REGISTRY

- Develop a better understanding of the long-term, real-world safety and efficacy profile of BAROSTIM THERAPY
- Collect data on every patient being commercially treated with BAROSTIM THERAPY, across all indications
- Novel registry design allows us to:
  - Study the effect of BAROSTIM THERAPY independently within each indication
  - Pool data across multiple indications to derive platform therapy conclusions

# Unique, modular structure permits a better understanding *across* the therapeutic platform

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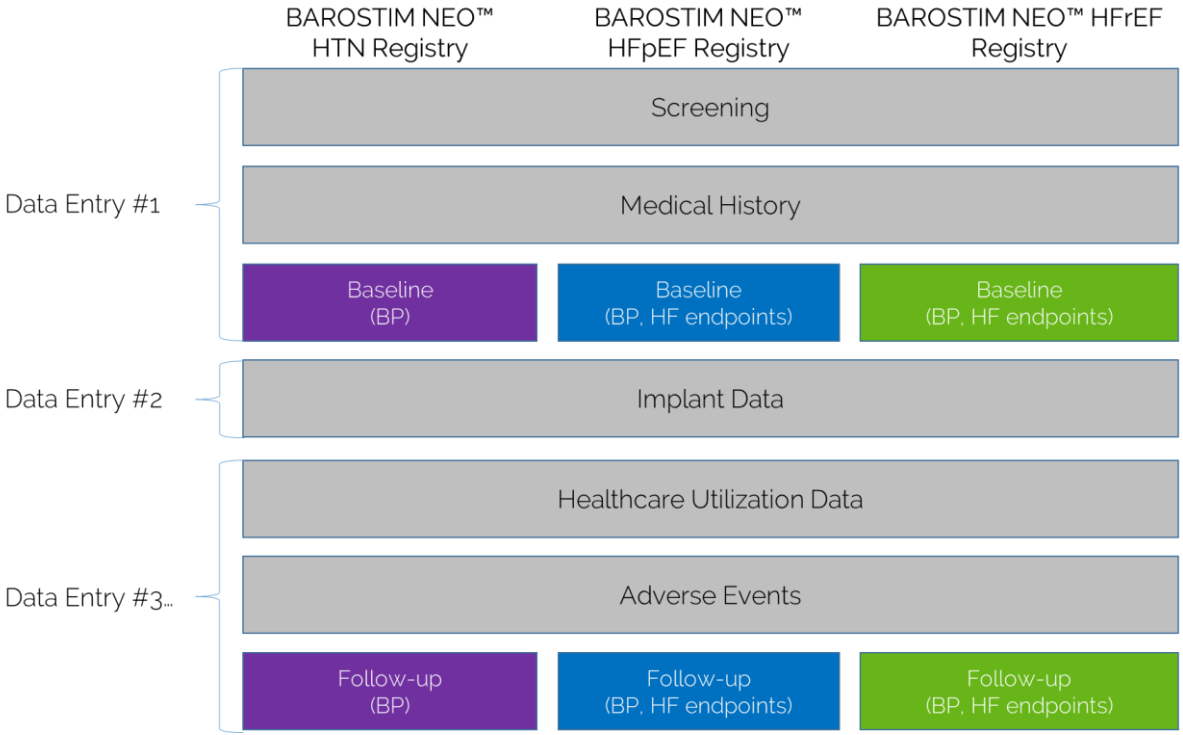
GLOBAL REGISTRY

Illustration:

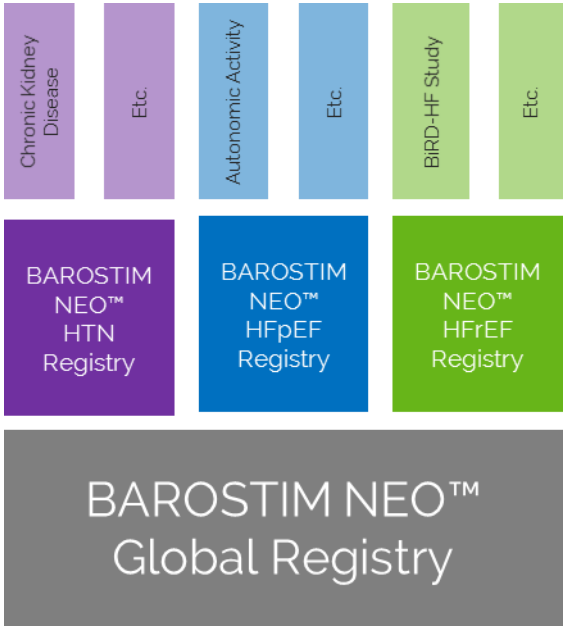


# BAROSTIM NEO Global Registry is the backbone for all post-market clinical research projects

BAROSTIM NEO™
GLOBAL REGISTRY

- Different projects are then built *on top of* the specific registry
- The BAROSTIM NEO Global Registry does not conflict with other post-market clinical projects– it is actually leveraged as a result of them
- Such a strategic approach means that CVRx is able to collect the same data from each patient being treated with BAROSTIM THERAPY, even though these patients are perhaps being followed in different clinical projects

Illustration:



# Agenda

- BAROSTIM NEO Global Registry Strategy
- BAROSTIM NEO Global Registry Designs
  - Hypertension
  - Heart Failure with Reduced Ejection Fraction
  - Heart Failure with Preserved Ejection Fraction
- BAROSTIM NEO Global Registry Status

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# Global Hypertension Registry
## SUMMARY

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GLOBAL REGISTRY

- Subjects may be considered for enrollment if they have been **recently implanted with the BAROSTIM NEO System** in accordance with CE-Mark approved criteria for resistant hypertension. Subjects must be enrolled within 30 days from implant.

- Up to **500 subjects** will be enrolled at up to **50 sites**.

- Data should be obtained from standard of care measurements taken **prior to implant**, at **enrollment/baseline**, and at **3, 6, and 12 months after** the device was implanted.

- After 12 months, data may be obtained in six month intervals for **up to three years after implant,** at which time each subject will be exited from the registry.

# Global Hypertension Registry
## OBJECTIVES

BAROSTIMNEO™
GLOBAL REGISTRY

- To describe change in the following measures at 3, 6, and 12 months, and long during long term follow-up, compared to pre-implant baseline:
  - **Systolic** blood pressure
  - **Diastolic** blood pressure
  - **Medication changes** over follow-up

- Evaluate **health care utilization** over follow-up, such as heart failure hospitalizations.

- Describe device programming and utilization

# Global Hypertension Registry
## ELIGIBILITY

BAROSTIM NEO™
GLOBAL REGISTRY

- Subjects must sign an Ethics Committee (EC) approved informed consent form for the registry to participate. Subjects can be included in the Hypertension Registry if they were implanted in the past 30 days and meet the CE-Mark approved indications and contraindications for BAROSTIM NEO in the treatment of resistant hypertension. These include:

- Indications:
  - Systolic blood pressure greater than or equal to 140 mmHg, and
  - Resistance to maximally tolerated therapy with a diuretic and two other antihypertension medications

- Contraindications:
  - Bilateral carotid bifurcations located above the level of the mandible
  - Baroreflex failure or autonomic neuropathy
  - Uncontrolled, symptomatic cardiac bradyarrhythmias
  - Carotid atherosclerosis that is determined by ultrasound or angiographic evaluation to be greater than 50%
  - Ulcerative plaques in the carotid artery as determined by ultrasound or angiographic evaluation

# Global HFrEF Registry

## SUMMARY

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GLOBAL REGISTRY

- The CVRx BAROSTIM THERAPY in Heart Failure with Reduced Ejection Fraction (HFrEF) Registry will be performed with subjects who have been **recently implanted with the BAROSTIM NEO System** in accordance with CE-Mark approved criteria for heart failure. Subjects must be enrolled within 30 days from implant.

- Up to **500 subjects** will be enrolled at up to **50 sites**.

- Data should be obtained from standard of care measurements taken **prior to implant**, at **enrollment/baseline**, and at **3, 6, and 12 months after the device was implanted**, at which time each subject will be exited from the registry.

# Global HFrEF Registry

## OBJECTIVES

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GLOBAL REGISTRY

- To describe change in the following measures at 3, 6 and 12 months compared to pre-implant baseline:
  - **NYHA Class**
  - **Six Minute Hall Walk**
  - **Echocardiogram measures**
  - **Biomarkers** (e.g. NT-pro BNP, eGFR, Troponin HsT, Cystatin C)

- Evaluate **health care utilization** over follow-up, such as heart failure hospitalizations.

- Describe device programming and utilization

# Global HFrEF Registry

## ELIGIBILITY

BAROSTIMNEO™
GLOBAL REGISTRY

- Subjects must sign an Ethics Committee (EC) approved informed consent form for the registry to participate. Subjects can be included in the Heart Failure with Reduced Ejection Fraction Registry if they were implanted in the past 30 days and meet the CE-Mark approved indications, and are not contraindicated, for the BAROSTIM NEO system in the treatment of heart failure.

- Indications:
  - Heart failure, defined as New York Heart Association (NYHA) functional Class III and left ventricular ejection fraction (LVEF) ≤ 35% despite being treated with the appropriate heart failure guideline directed therapy

- Contraindications:
  - Bilateral carotid bifurcations located above the level of the mandible
  - Baroreflex failure or autonomic neuropathy
  - Uncontrolled, symptomatic cardiac bradyarrhythmias
  - Carotid atherosclerosis that is determined by ultrasound or angiographic evaluation to be greater than 50%
  - Ulcerative plaques in the carotid artery as determined by ultrasound or angiographic evaluation

# Global HFpEF Registry
## SUMMARY

BAROSTIMNEO™
GLOBAL REGISTRY

- The CVRx BAROSTIM THERAPY in Heart Failure with Preserved Ejection Fraction (HFpEF) Registry will be performed with subjects who have been **recently implanted with the BAROSTIM NEO System** in accordance with CE-Mark approved criteria for **resistant hypertension and have evidence of HFpEF** per the registry enrollment criteria. Subjects must be enrolled within 30 days from implant but prior to therapy activation.

- Up to **70 subjects** will be enrolled at up to **10 sites**.

- Data should be obtained from standard of care measurements taken **prior to implant**, at **enrollment/baseline**, and at **3 and 6 months after the device was implanted**, at which time each subject will be exited from the registry.

# Global HFpEF Registry

## OBJECTIVES

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- Primary:
  - To describe **change in office cuff systolic blood pressure** at 6 months compared to preimplant baseline.

- Secondary:
  - To describe changes in the following measures at 6 months compared to pre-implant baseline:
    - Global **longitudinal strain**
    - **LA volume index**
    - **E/E' ratio**
    - **Other echocardiographic measures**, including LVMI
    - **NYHA Class**
    - **NT-pro-BNP**, as routinely collected as standard of care
    - **Other biomarkers of end organ damage** routinely collected as standard of care (e.g., eGFR, Troponin T, etc.)
  - Evaluate **health care utilization** over follow-up, such as heart failure hospitalizations.
  - Describe device programming and utilization.

# Global HFpEF Registry

## ELIGIBILITY: INCLUSION CRITERIA

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- Sign an Ethics Committee (EC) approved informed consent form for the registry.
- Implanted with the BAROSTIM NEO System in accordance with CE-Mark approved indications and contraindications for resistant hypertension within 30 days prior to enrollment.
- BAROSTIM THERAPY not yet chronically activated.
- Pre-implant echocardiogram with left ventricular ejection fraction ≥ 50% within 30 days prior to implant.
- On stable, maximally-tolerated, guideline-directed cardiovascular medications for at least 30 days prior to enrollment.
- Objective evidence of heart failure according to the following criteria:
  - Hospitalization for heart failure within 12 months prior to enrollment OR
  - Echocardiographic evidence of diastolic dysfunction (LA Volume Index >34 ml/m2 OR E/e >13) within 30 days prior to enrollment OR
  - NTproBNP > 220 pg/mL or BNP > 80 pg/mL (in atrial fibrillation, NTproBNP > 600 pg/mL or BNP > 200 pg/mL) within 30 days prior to enrollment

# Global HFpEF Registry

## ELIGIBILITY: EXCLUSION CRITERIA

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- Heart failure secondary to a reversible or treatable condition such as, cardiac structural valvular disease, acute myocarditis and pericardial constriction.

- Heart failure secondary to right ventricular failure or right ventricular myocardial infarction.

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# Site & Patient Enrollment Status

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GLOBAL REGISTRY

| | SITES ACTIVATED | PATIENTS ENROLLED |
|---|---|---|
| Hypertension | 11 | 33 |
| HFrEF | 11 | 5 |
| HFpEF | 3 | 0 |

# Site & Patient Enrollment Opportunity

BAROSTIMNEO™ GLOBAL REGISTRY

| | SITE ACTIVATION OPPORTUNITY | PATIENT ENROLLMENT OPPORTUNITY |
|---|---|---|
| Hypertension | 39 | 467 |
| HFrEF | 39 | 495 |
| HFpEF | 7 | 70 |

If your site is **not yet active and you would like to participate**, please reach out to the respective chair:

- Global Hypertension Registry: Prof. Reuter /Prof. Koziolek
- Global HFrEF Registry: Prof. Müller-Ehmsen
- Global HFpEF Registry: Prof. Pieske

If your site is **already active**, please continue to enroll every patient treated with BAROSTIM THERAPY!

# Goal for April 2018

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GLOBAL REGISTRY

- Next BAROSTIM NEO Global Registry Investigator Meeting will be at Spring DGK 2018 Meeting
- By Spring DGK 2018, the goal is to have a total of 150 patients enrolled in the BAROSTIM NEO Global Registry
- Let's go!!

# Thank you.

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