Challenges in Development of Innovative Device

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Disclosure Statement of Financial Interest

I, Robert Thatcher, DO have a financial interest/arrangement or affiliation with 4C Medical Technologies, Inc. that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.
What is EFS?

Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies

Guidance for Industry and Food and Drug Administration Staff

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For questions regarding this document, contact CDRH’s Andrew Farb, 301-796-6343, Andrew.Farb@fda.hhs.gov or Dorothy Abel, 301-796-6366, Dorothy.Abel@fda.hhs.gov, or CBER’s Office of Communication, Outreach and Development at 1-800-835-4709 or 301-827-1800.
Why EFS?

*Allows for early clinical evaluation of device*

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**Proof of principle and initial clinical safety data**

Clinical experience is necessary because nonclinical testing methods are not available or adequate to provide the information needed to advance the developmental process.

**Sooner introduction of the needed treatment to patients**

Risk to patients associated with the lack of treatment available may be higher than risk associated with participation in EFS.
EFS Can Obtain Initial Insights Into:
In Preparation Of Pivotal Study Design

Assess device-specific aspects of the procedure

- Whether the device can be successfully delivered, implanted or used
- The clinical safety of the device (e.g., evaluation of device-related serious adverse events)

Define procedural details/flow/steps

- Operator technique challenges with device use

Define patient selection

- Patient characteristics that may impact device performance (e.g., anatomical limitations)
EFS: Driver of Medical Device Innovation

- FDA recognizes the value of encouraging medical device innovation to address clinical needs and improve patient care, particularly when alternative treatments or assessments are unavailable, ineffective, or associated with substantial risks to patient safety.

- FDA developed guidance to facilitate the early clinical evaluation of medical devices in the United States under the IDE regulations, using risk mitigation strategies that appropriately protect human subjects in EFS.
The First Potential HBD EFS

The treatment of moderate to severe MR in patients who are considered high risk for mortality and morbidity during open-heart surgery.
Estimated Prevalence of Mitral Regurgitation (MR) in Japan (2017)

- Older age is an independent determinant of all forms of valve disease that arise with considerable frequency in elderly people.\(^1\)
- The estimated prevalence of Moderate/Severe MR drastically increases with age:
  - from 0.5% (aged 18 to 44 years) to 9.3% (aged ≥75 years)\(^{1-2}\)

With the projected shift to an older population, the burden of valvular diseases will probably increase substantially in the future.\(^1\)
New Treatment Options Needed for MR Patients

>2 MILLION Japanese people suffer from MR\(^1,2\)

MR affects nearly 1 in 10 Japanese aged 65\(^+\)

50% of all symptomatic MR patients are NOT ELIGIBLE for open-heart surgery due to the procedure risk.\(^3\)

Dynamic, Irregular and Variable
Anatomy of Mitral Valve

Difficult sizing and anchoring device due to various shapes and sizes of mitral valve annulus

4C Valve Potential Benefits

- Supra-annular placement preserves native mitral valve and left ventricle (LV)
  No risk of LVOT obstruction
  No sub-valvular mitral valve apparatus interaction
- Expands treatable patient population
  MR mechanism agnostic
  Suitable for any anatomy
- Provides transseptal or transapical delivery options
  Ease of use
4C Delivery System Flexibility

Supra-annular design does not require fitting in the native annulus & allows transseptal delivery, minimally invasive approach

**TRANSSEPTAL**
Crossing the septum to gain access to the left atrium

**TRANSAPICAL**
Surgical entry through the chest, left ventricle, and into the left atrium

4C Valve Hemodynamic Assessments: Doppler Assessment
4C Valve Hemodynamic Assessments: LV Gram Assessment
4C Medical EFS Design

- **Purpose:** to assess safety and performance of the 4C valve for the treatment of moderate to severe MR in patients who are considered high risk for mortality and morbidity during open-heart surgery.

- **Endpoints will include:**
  - Technical success
  - Device success
  - Procedural success
  - Change in MR grade
  - Change in NYHA class

- **Global Enrollment:** 20-30 patients at up to 10 sites
  - Japan and United States
  - Harmonization by Doing (HBD)

With the help of HBD, the goal is to conduct an EFS study in both Japan & USA
Thank You!