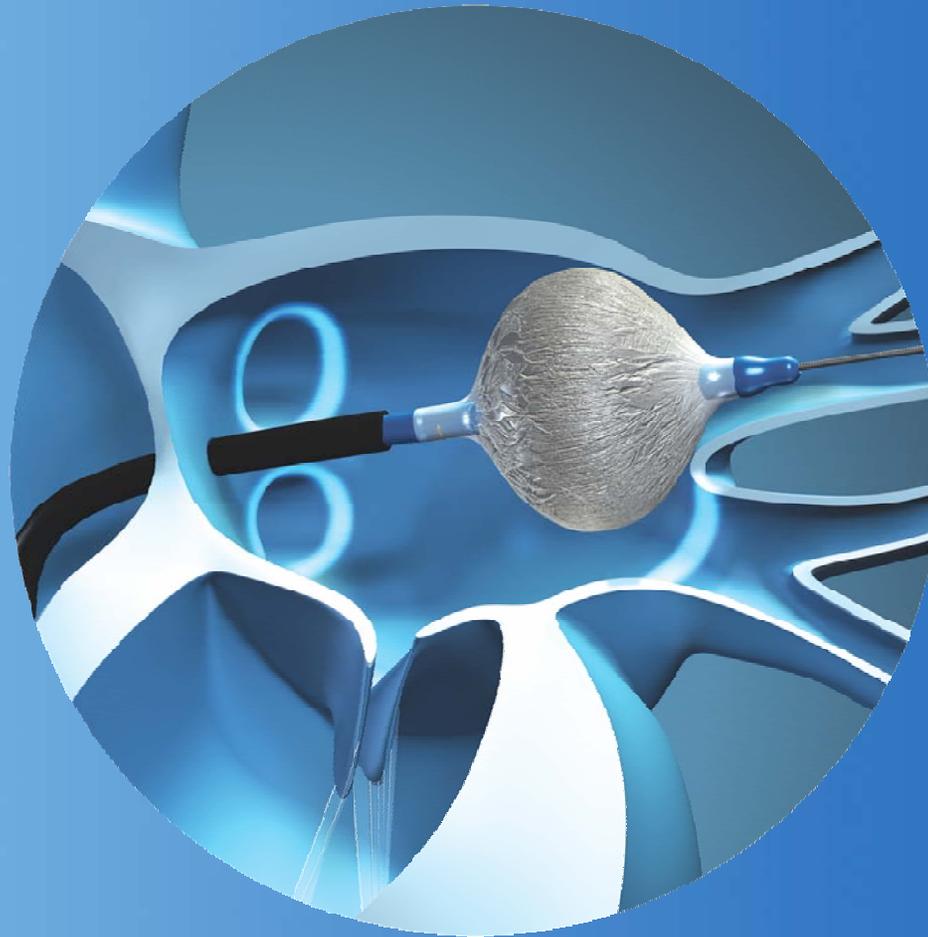


CryoCath Technologies Inc.

Montréal, Canada



Circulatory System Devices Panel

September 20, 2007

CryoCath Technologies Inc.

- Headquarters and manufacturing facilities located in Montréal, Canada
- Approximately 220 employees worldwide
- Sells cardiac cryoablation catheters in USA, EU and selected other countries
- Three 3 PMA approved products in the USA:
 - Freezor™ for the treatment of AVNRT
 - Freezor Xtra™ and Freezor Max™ for minimally invasive cardiac surgery, including the treatment of cardiac arrhythmias

The AF Ablation Toolbox

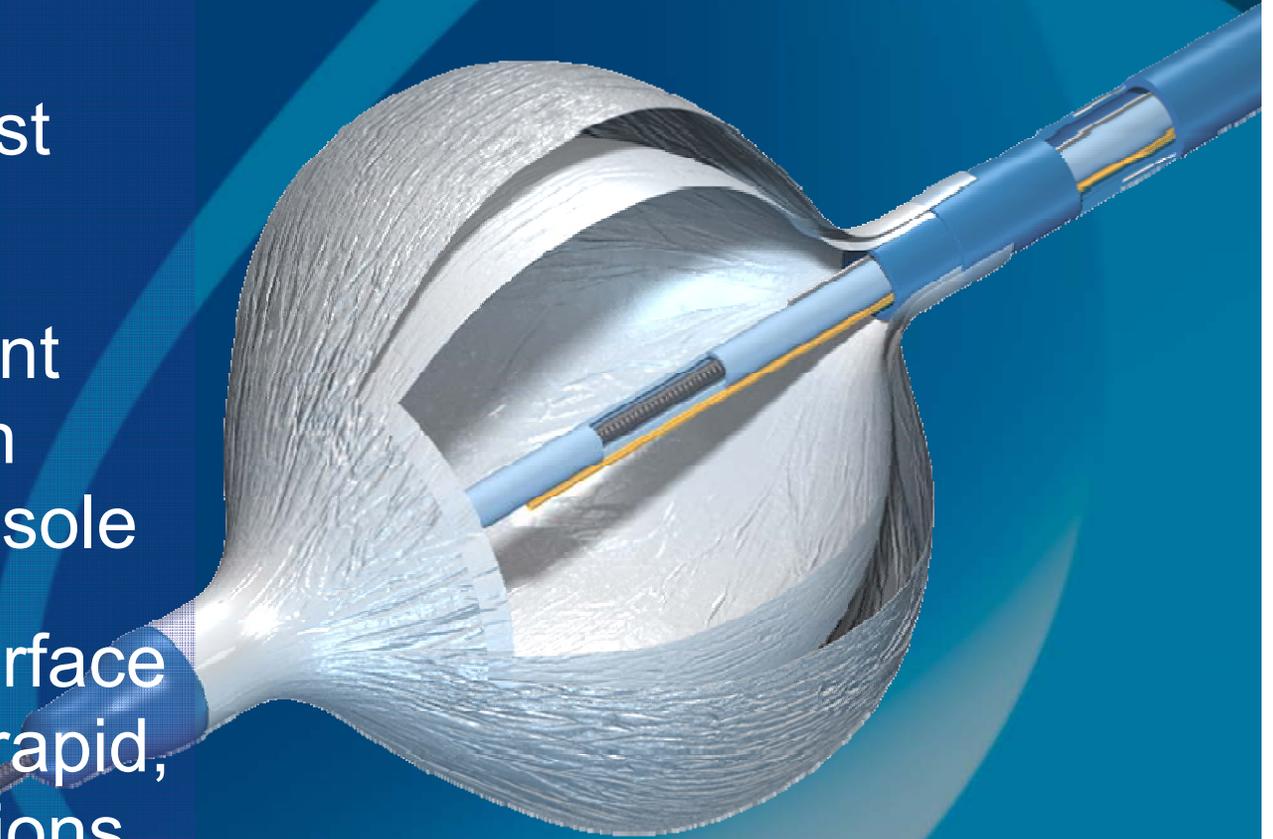
- **Arctic Front™**
for electrical isolation
of pulmonary veins
- **Freezor Max™**
for focal triggers and
cavo-tricuspid
isthmus ablation
- **Cryogenic console**
for delivery of
cryogenic fluid



Caution: Investigational Devices. Limited by U.S. law to investigational use.

Arctic Front™ Cryoballoon Ablation Catheter

- Double balloon system for highest level of safety
- Multiple redundant safety systems in catheter and console
- Entire balloon surface freezes to allow rapid, optimum cryolesions and easy positioning



Pivotal Study Design

- Control Group:
AFD Rx (propafenone, flecainide or sotalol)
- Experimental Group: Cryoablation +
AFD Rx (propafenone, flecainide or sotalol)
- RCT 2:1 Experimental to Control, with 3 month
Blanked F/U Period for both Groups
- Control failures can cross over after 6 months
- Experimental subjects allowed one reablation
during the blanking period

Inclusion / Exclusion Criteria

Key Inclusion Criteria:

- PAF
- Failed one or more of the 3 AFD drugs for effectiveness at a minimum dose
- ≥ 2 episodes of AF in 2 months prior to ablation
- LA ≤ 5 cm

Key Exclusion Criteria:

- Persistent and chronic AF
- Any prior LA ablation
- Amiodarone in 6 months prior to ablation
- Presence of pacemaker or ICD
- Cardiac pathology, valve prosthesis, EF $< 40\%$

Follow-up Schedule and Key Assessments

- Follow-up at 1 (safety), 3, 6, 9 (telephone) and 12 months
- Weekly and symptom-driven TTMs with concurrent compliance monitoring and callbacks
- 24 hour Holter monitoring at baseline, 6 and 12 months
- MRI / CT of PVs at baseline, 6 and 12 months
- Additional assessments for phrenic nerve function, neurologic events, cognitive function changes and quality of life impacts

Key Study Outcome Measures

Effectiveness:

- **Primary:** freedom from CTF (Chronic Treatment Failure = Detectable AF after 90 day blanking)
- **Acute:** isolation of ≥ 3 pulmonary veins (experimental subjects only)

Safety:

- **Primary:** MAFEs (Major AF Events) = CV deaths, key hospitalizations, MI or stroke
- **Procedural:** CPEs (Cryoabl'n Procedure Events) = key device and procedural SAEs (experimental subjects only)

Trial Progress

- October '06: first patient enrolled under conditional approval
- April '07: approval for significant expansion
- August '07: unconditional approval
- Two Canadian centers also enrolling
- Status:
 - Nearing halfway mark for enrollment
 - Rate \approx 1 subject / site / month

Enrollment issues

- “Screened to Enrolled” conversion rate is highly variable, ranging from 1 – 20% between centers
- Subject resistance to control randomization occurs but is not major difficulty given crossover option, desirability of cryoablation
- Some subjects lost due to insurer refusal (BCBS)
- Adequate AF documentation, intolerance AAD failures and amiodarone use within 6 months are common reasons for exclusion

Discussion (1): OPC for Procedural AEs

- FDA's acceptance of a two-part safety assessment which separates out ablation procedural events (CPEs) from long term disease and drug events (MAFEs) is innovative and clinically relevant
- However, there are no comparably monitored AF IDE studies and therefore there are few reliable data on which to base OPC estimates
- Existing publications have variable reporting and monitoring standards and referral practices, and may have significant negative detection biases for AEs
- On what should Sponsors base their OPC estimates?

Discussion (2): Interim Analyses

- AF ablation studies are designed with rough estimates of key study parameters, which can lead to sample size and other design errors
- Prespecified interim analyses together with adaptive methods for sample size re-estimation allow trials with results exceeding plan estimates to complete enrollment early and trials found to be underpowered to be expanded
- Can new guidance be offered which encourages and specifies acceptable forms of interim analysis and adaptive design for AF ablation trials?

Discussion (3): Complexity and Continuity

- Currently conforming study designs randomized against anti-arrhythmics are complex, combining the difficulties of both drug and device studies
- This leads to “administrative failures” which obscure safety and effectiveness assessments
- Non-informative failures are bad for everyone
- We strongly urge that any proposed study design changes lead to greater simplicity and flexibility
- Significant changes in guidance should not be retroactively applied to previously approved studies

Discussion (4): 1° Effectiveness Statistic

- The key outcome measure is recurrence of AF, a time-to-event measure exactly as in AF drug trials
- The standard statistic is log rank test or equivalent
- FDA is requiring a test of independent proportions, which is less efficient and less informative
- Close clinical follow-up backed by weekly and symptom-driven TTMs with successful compliance programs give sufficiently detailed data to allow the use of time-to-event data for the primary hypothesis
- We urge discussion and resolution of this key issue

Conclusion

- CryoCath is conducting an AF Guidance-conforming pivotal IDE trial and nearing the halfway mark for enrollment
- Enrollment difficulties exist but are fairly typical for an RCT device trial and these are being resolved by Investigator communications and site-specific interventions and support
- Clarity on safety OPC estimates, the use of interim analyses, simplification of trial design requirements and establishment of standard outcome statistical methods would help us complete future studies