Making Proven Therapies Safer

Safe Harbor

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Investment Highlights

- Engineering safer oral product candidates for well-established, chronic markets
- Four clinical development programs underway with proof of concept established on three
- Product candidates provide attractive partnering opportunities
- Technology approach will continue to build pipeline

The Problem

- Approved drugs have serious safety problems identified post launch
  - 548 NCEs approved from 1975-1999
    - 56 acquired black box warnings or have been taken off the market *(JAMA 2002)*
- 90% of all drugs are cleared through cytochrome P450
  - Potential for drug-drug interactions
    - One of the leading causes of hospitalization and death in the United States
  - Adverse Drug Reactions *(JAMA 1994)*

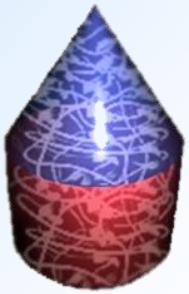
The ARYx Technology Solution

- ARYx's RetroMetabolic Engineering™ (ARM)

ARYx RetroMetabolic Engineering™ (ARM)

Identify Target Molecule	Design "Ideal" Metabolite	Create ARYx Product

• Oral: large, chronic market
• Do problems exist that we can fix?
  • P-450 clearance
  • Drug-Drug interactions
  • Off-target problems
	• Inactive
	• Non-toxic
	• Rapidly eliminated by non-P450 pathway
	• Water soluble
		• Retains desired efficacy
		• Safety problems eliminated
		• Breaks down into "ideal" metabolite



Generates New Intellectual Property
Composition of Matter Patents Issued on Three Lead Compounds

Product Pipeline

Large Commercial Opportunities; Well Protected by Patents

Product	Original Drug	Patent Coverage	Indication
ATI-5923 **Phase 2**	warfarin	2025	Anti-coagulation
ATI-7505 **Phase 2**	cisapride	2025	Multiple GI indications
ATI-2042 **Phase 2**	amiodarone	2020	Atrial fibrillation
ATI-9242 **Phase 1**	atypical antipsychotics	Patents pending	Schizophrenia

ATI-5923: Product Overview

Background on Original Drug (warfarin)

- "Gold standard" oral anticoagulant
- After 50 years still in the top 20 Rx'd overall
- #2 reason for drug-related hospitalization

Our Solution: ATI-5923

- Mode of action identical to warfarin - Selective VKOR Inhibitor
- Metabolized through non-p450 clearance pathway
- No drug-drug interactions
- More stable control of anticoagulation
- Coagulation status can be measured with INR

ATI-5923: Market Opportunity

Anticoagulants

- 3 major indications
  - AFIB: 2.4M (US)
  - Venous thromboembolism: 510,000 patients (US)
  - Mechanical heart valves: 340,000 patients (US)
- Approximately 80% of overall market considered for chronic use
- 33.6M prescriptions for warfarin written in 2006 (US) (estimated $376M in sales)

ATI-5923 Advantages versus Warfarin

- Superior time in therapeutic range and decrease in “dangerous” INR excursions
- Straightforward dosing schedule
- Reduced drug-drug interactions
- Not teratogenic

ATI-5923 Advantages versus DTIs and Xa’s

- Superiority to warfarin versus a “non-inferior” label
- Proven mechanism of action - physician familiarity
- Once a day dosing
- Monitorable with INR testing

Monitoring – An Important Therapeutic Tool

Patient Segments Where Monitoring and Control Is Important

- **Patients whom physicians prefer to monitor**
  - Patients for whom compliance is a concern
  - Elderly and polypharmacy patients
  - Patients with an unknown bleeding etiology
- **Patients who require monitoring**
  - Heart valve patients (particularly mechanical)
  - Patients with prior history of bleeding or clotting
- **Patients excluded from DTI and Xa trials**
  - Patients with severe renal impairment
  - Heart valve patients
  - Patients with high or low body weight

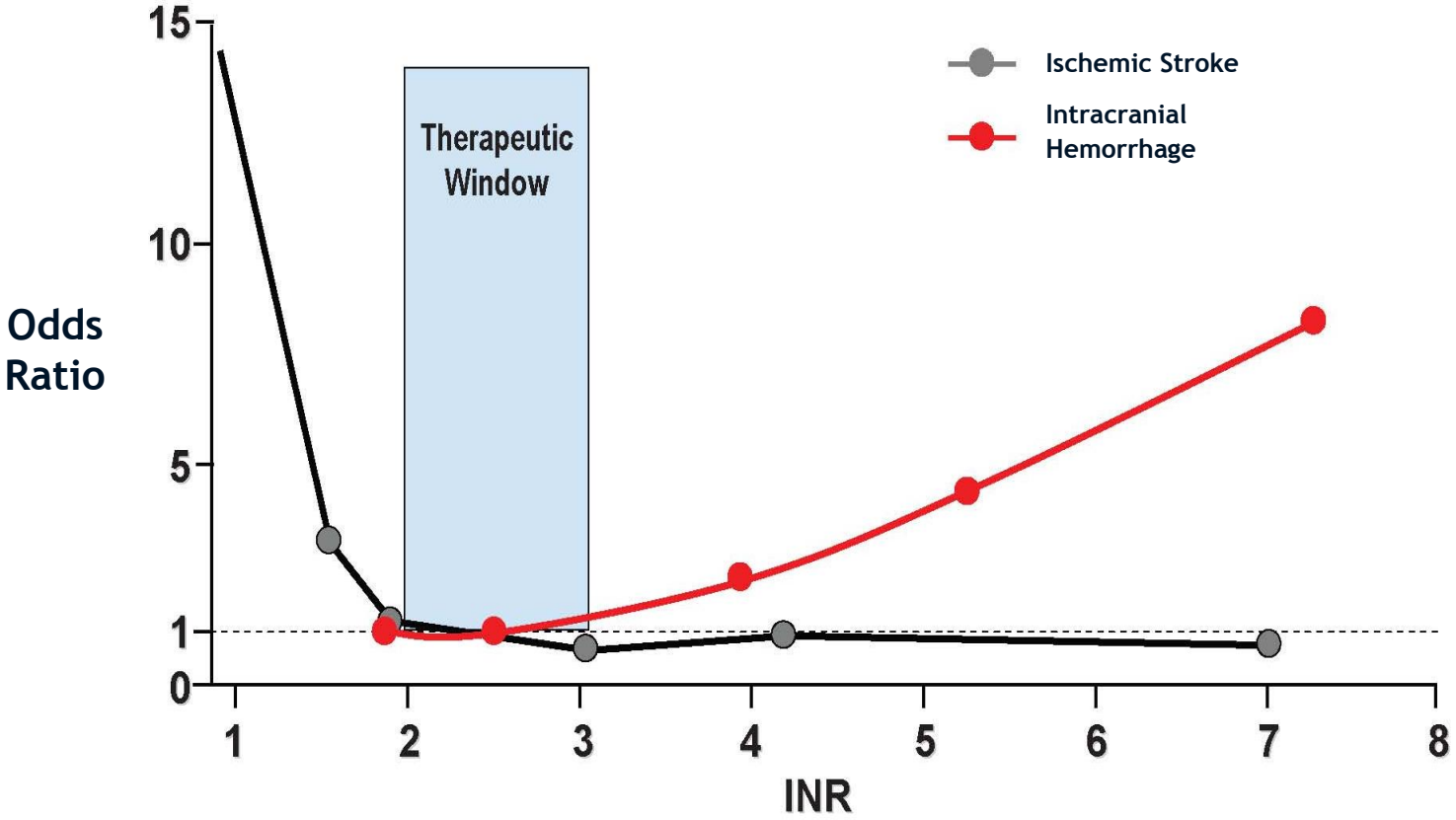
ATI-5923: Key FDA Feedback on Development Plan

Summary of written and verbal comments by FDA:

- INR is acceptable as surrogate endpoint in pivotal trials
  - Primary endpoint
  - Relevant outcome measure
- Demonstrate identical mode of action to warfarin
  - Clotting factor changes
- Superiority claim over warfarin possible
- ICH recommended safety data set is an adequate initial target

ATI-5923: Relationship Between Clinical Events and INR in Patients with AFIB

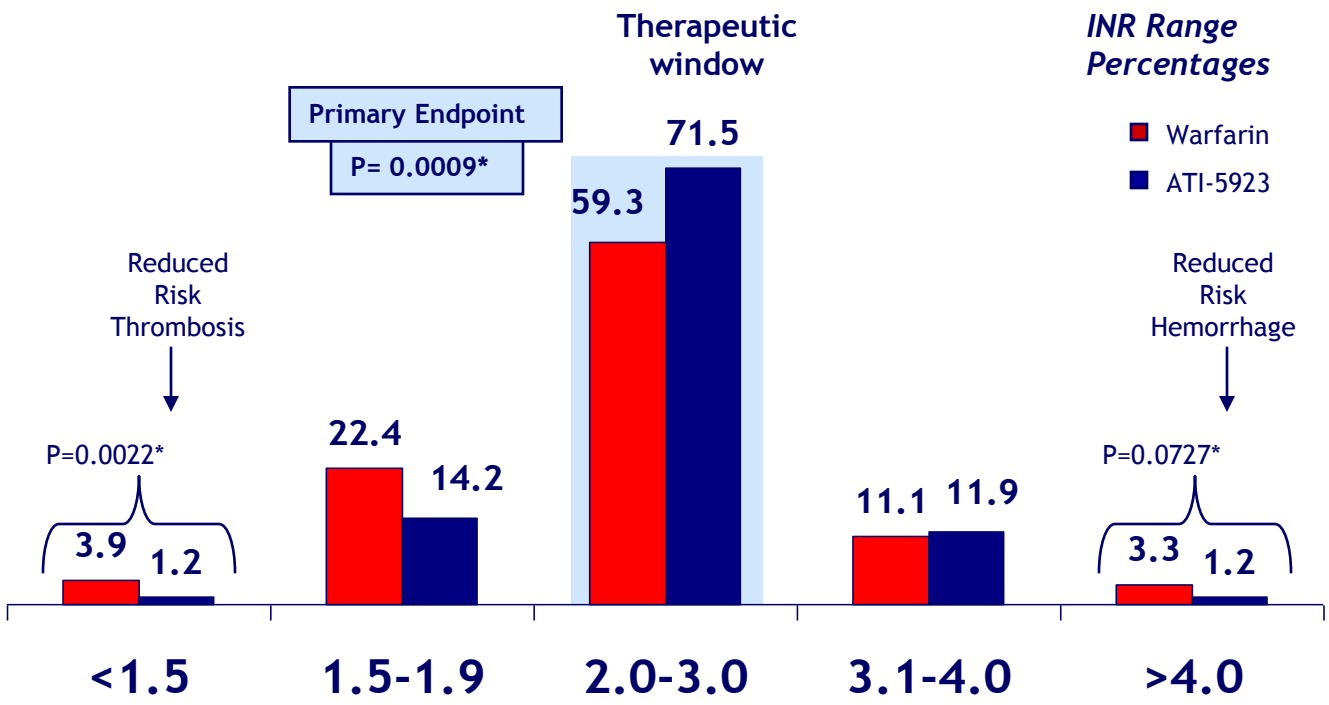
INR (International Normalized Ratio) is Globally Standardized and Commercially Available



1. Hylek EM et al. *Ann Intern Med.* 1994;120:897
2. Hylek EM et al. *N Engl J Med.* 1996;335:540

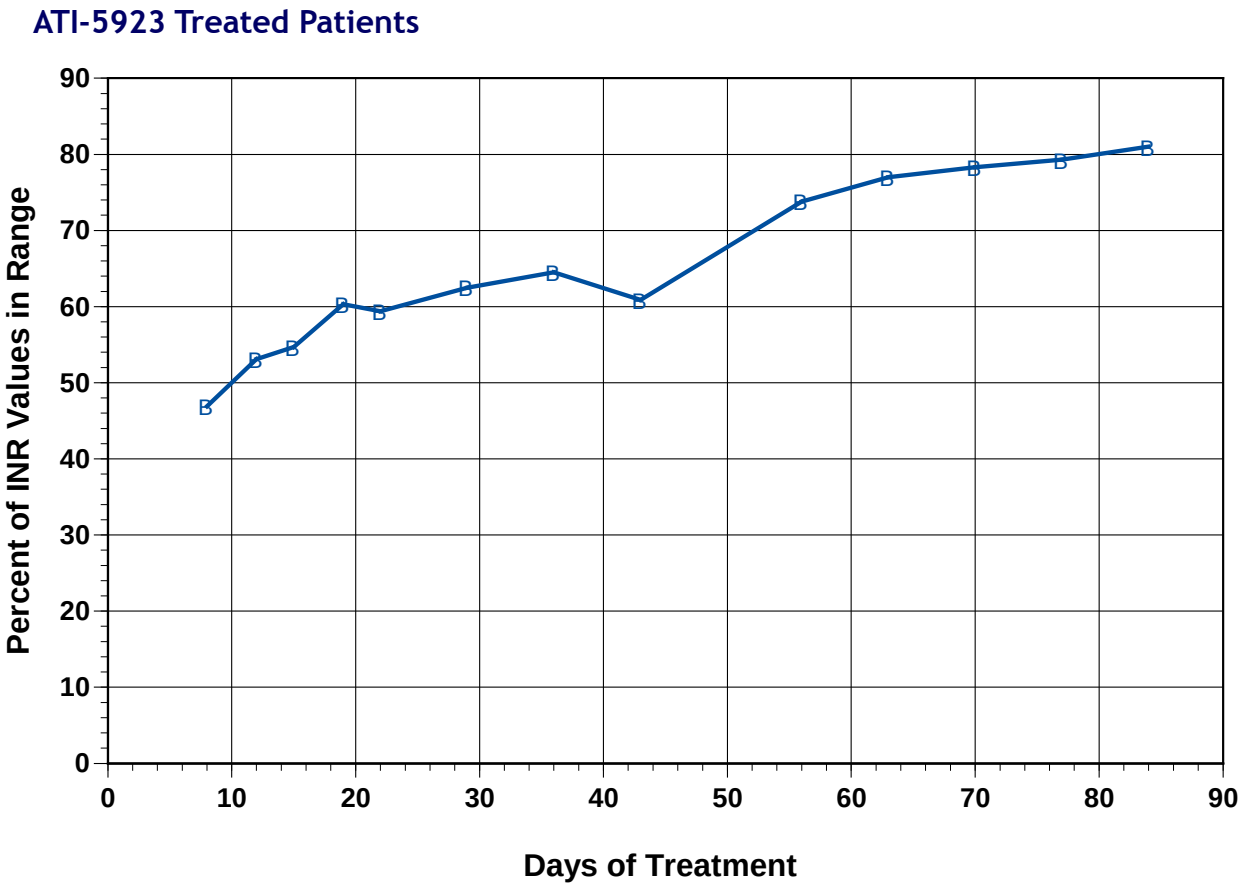
ATI-5923: Completed Phase 2 Study (CLN-504) - *Trial Results*

Interpolated INR Values for warfarin vs ATI-5923 (n=64)
Titration Weeks 1-3 Excluded

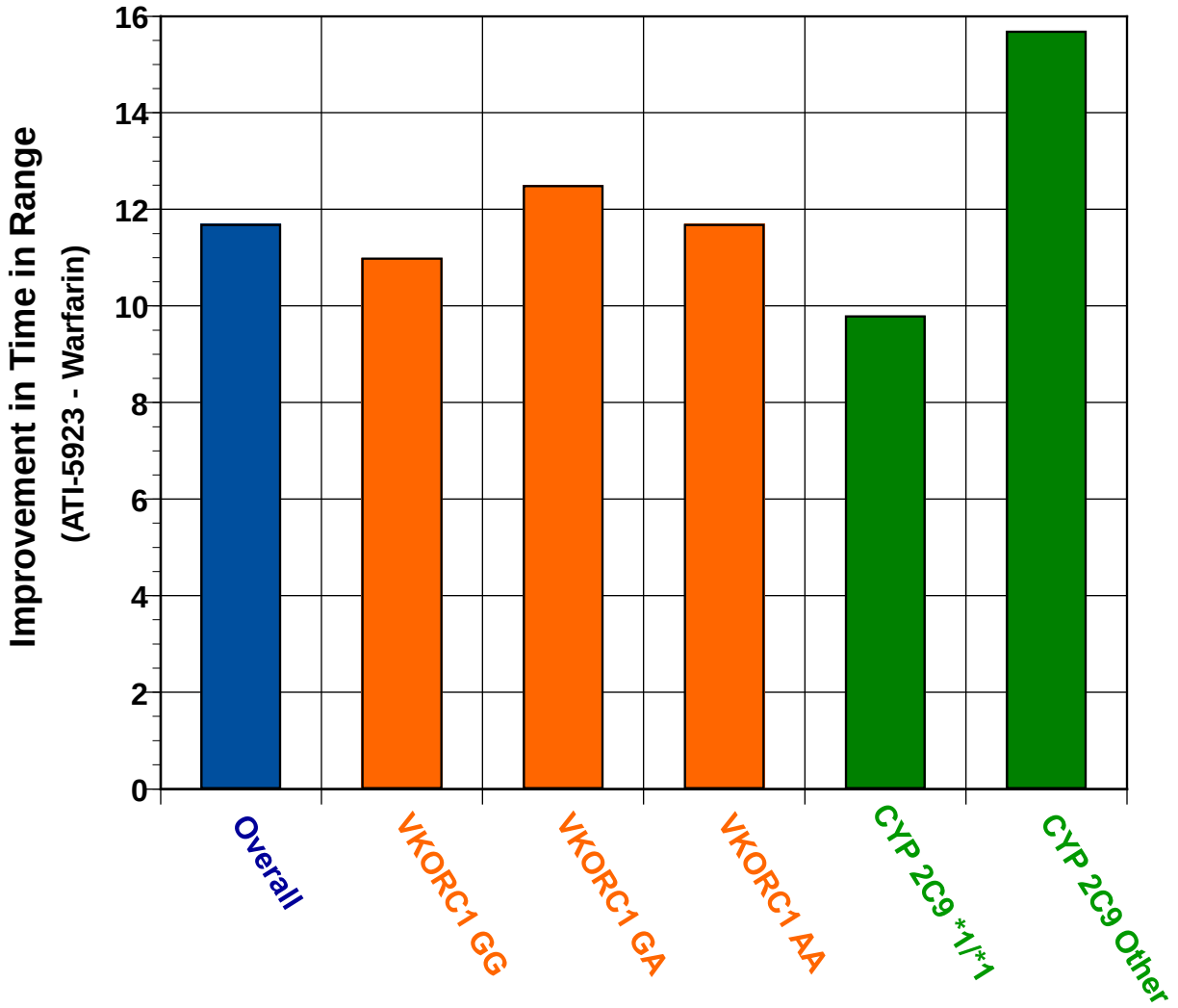


* Wilcoxon Signed-Rank Test

CLN-504 – INR Time in Range Improves Over Time



CLN-504 – Consistent Effect Across Multiple Genotypes



Legend:

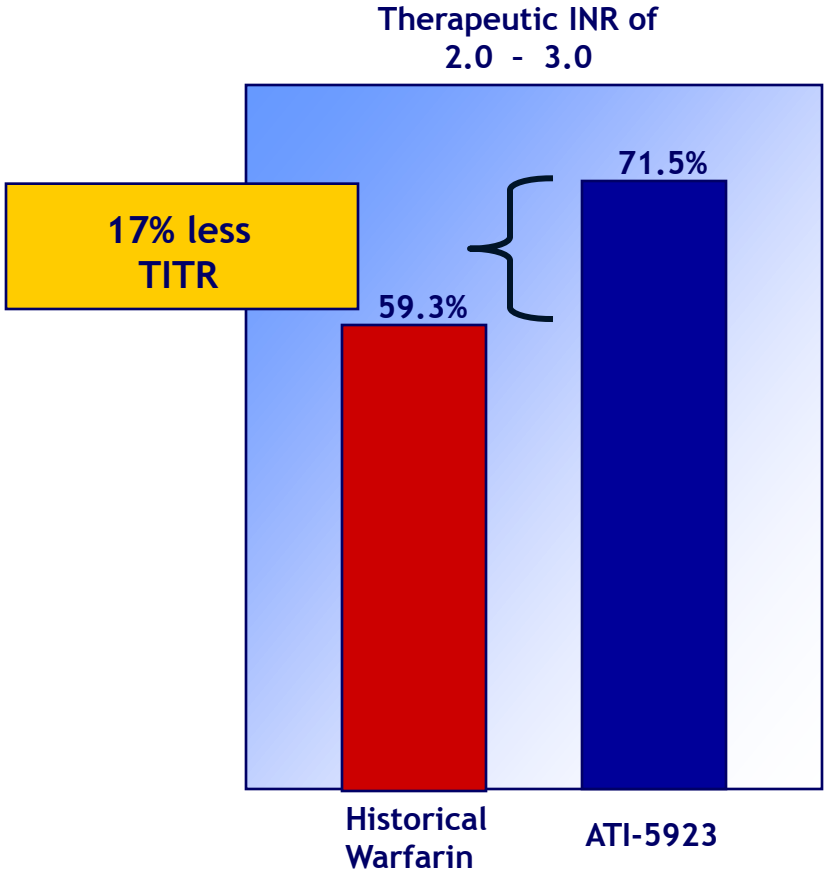
► VKORC1 Genotypes; warfarin:
Sensitive = AA
Intermediate = GA
Least sensitive = GG

► CYP 2C9 Genotypes; warfarin:
Normal metabolizers = *1
Slow metabolizers = *2, *3

Increased Time in Targeted INR Affects Outcomes

A 10% decrease in time in therapeutic range results in[1]:

- a 29% increase in mortality risk
- a 10% increase in ischemic stroke risk
- a 12% increase in all thromboembolic events



1 Jones et al. Heart 2005 (91) 472-477.

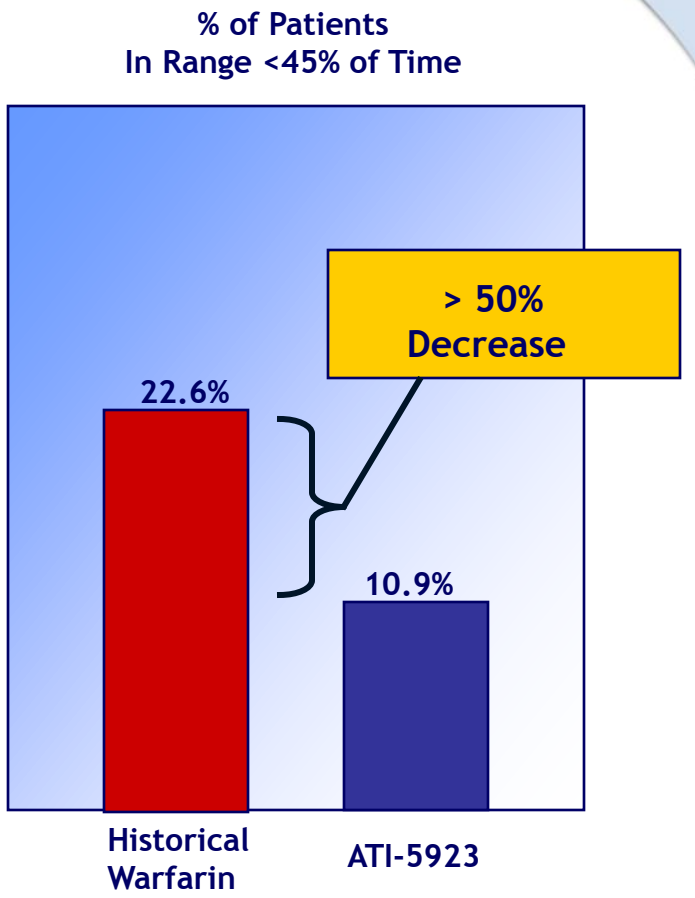
Increased Time in Targeted INR Affects Outcomes

Patients who have an INR in the targeted therapeutic range <45% of the time are at increased risk of recurrent thromboembolism or risk of major bleeding[1]

- **25% annual incidence in patients in therapeutic range <45% of the time**

versus

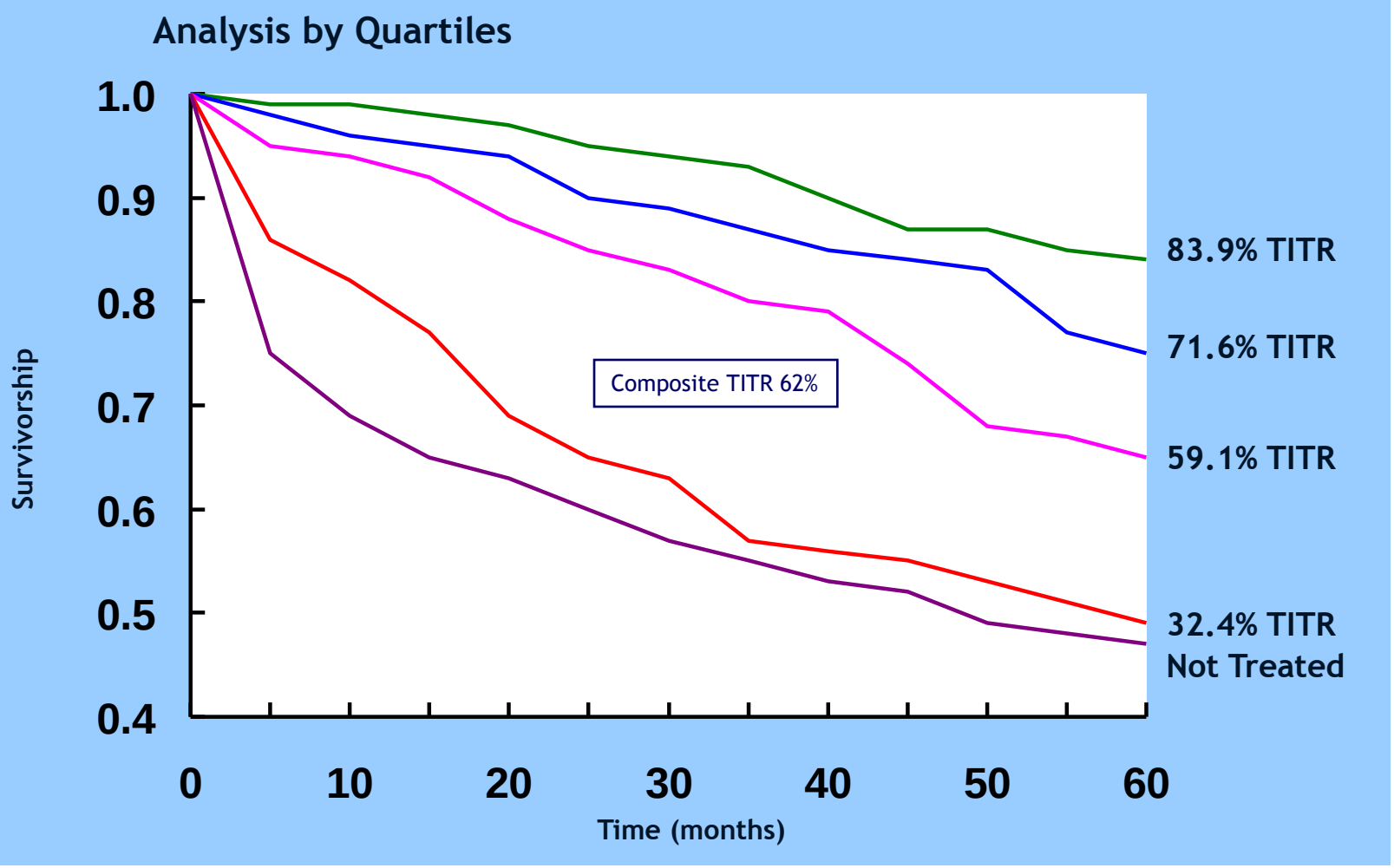
- **6.6% annual incidence for all other patients**



1. Veeger et al. British Journal of Haematology 2005 (128) 513-519.

Time in Range (TITR) Correlates to Life Expectancy

Interpolated Analysis



Source: Currie et al Heart 2006 (92) 196-200.

ATI-5923: Next Planned Study (Phase 2)

ATI-5923 Versus Warfarin

- **600 Patient-Study in Patients Requiring Anticoagulation**
  - Direct comparison to warfarin
  - Double blind placebo controlled trial
  - Time to stable dose
  - Time in range
  - Clinical outcomes
  - Superiority to warfarin
  - Multiple pathologies enrolled

ATI-7505: Product Overview

Background on Original Drug (cisapride)

- Approved in US for Nighttime GERD; used in multiple GI indications
- $1 billion at time of market withdrawal (2000)
- hERG channel interaction
- QTC prolongation and cardiovascular liability

Our Solution: ATI-7505

- Novel selective 5HT4 agonist with prokinetic effects
- Upper and lower GI tract activity
- No QTc prolongation to-date; over 600 patients treated with no cardiovascular liability exhibited
- Metabolized through non-P450 clearance pathway
- No drug-drug interactions

The Need for a Good Prokinetic Agent Still Exists

Functional Dyspepsia

- Estimated 35-44M people (US) suffer from functional dyspepsia
- According to Rome III, postprandial distress syndrome (PDS) defined by:
  - Postprandial fullness,
  - Early satiety, or
  - Upper abdominal bloating

Gastroparesis

- Estimated 5M patients suffer from gastroparesis (US)
- High prevalence in diabetic patients

GERD

- $17B spent worldwide each year
- Estimated 10% of population experiences symptoms daily
- Estimated 20-25% of patients (6.0-7.5M in US) do not obtain adequate relief from stomach acid-reducing treatments

Lower GI Indications (Chronic Constipation and IBS)

- Estimated 36-57M people (US) affected by chronic constipation
  - 33% of those see a physician
- Estimated 5.5M adults (US) suffer from IBS with constipation
- Estimated 28M adults (US) suffer from IBS with intermittent constipation

ATI-7505: Clinical Summary

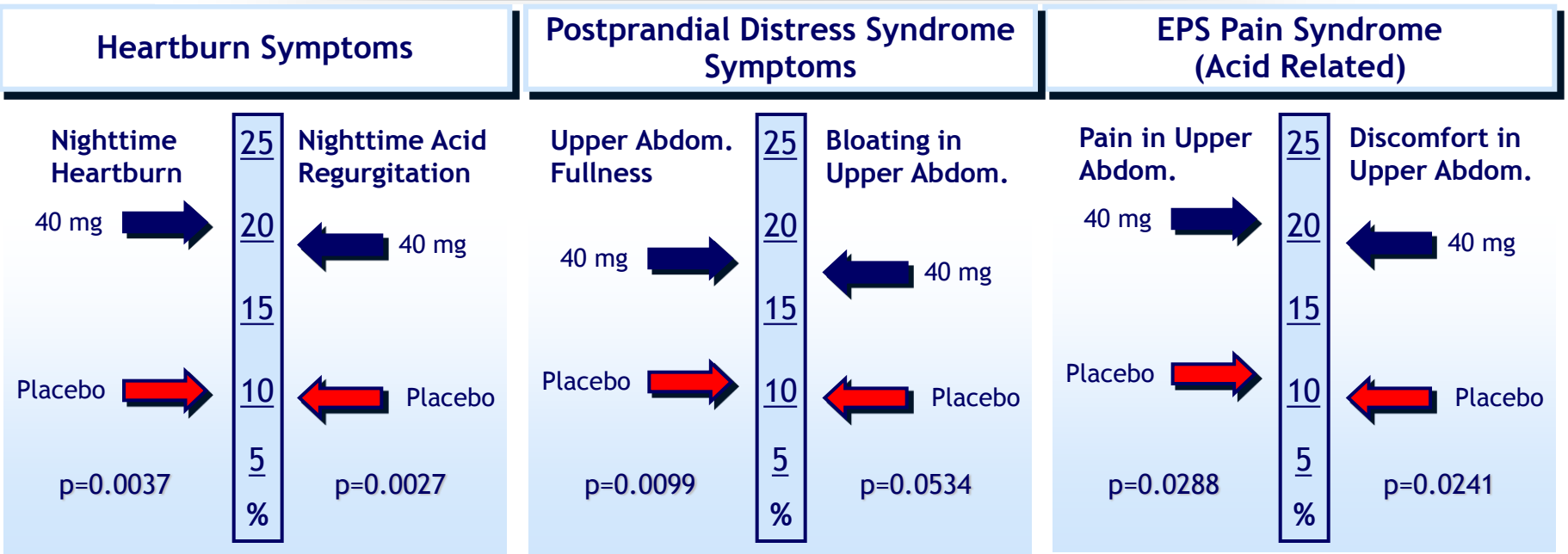
STUDY	RESULTS
Phase 1- Safety	Safe and well tolerated: no QTc signal
Phase 1- Motility	Gastric emptying accelerated (p=0.038) Colon transit accelerated (p=0.031)
Phase 2- pH Study	Reflux episodes of >5 minutes reduced (p=0.0007)
Phase 2- EE GERD Efficacy	Healing of EE grade A patients: (57% 40 mg qid; 41% 12 mg qid; 33% placebo)
Phase 2- sGERD Efficacy	Increase in symptom-free days in functional dyspepsia (Increase of 57% p=0.011)

ATI-7505: sGERD Phase 2 Study

Trial Design

- 50 centers across the US
- 404 patients with sGERD (no erosions) enrolled
- Primary endpoint of "adequate relief of heartburn symptoms" in last week of treatment not achieved, but a path forward identified

Trial Results (Proportion of symptom-free days from Baseline in % Points)



ATI-7505: P&G Clinical Plan

- Aggressively move forward in 2 indications
  - Lower GI indication – Chronic Constipation (400 patients)
  - Upper GI indication – Functional Dyspepsia-PDS (900 patients)
  - Parallel development
- Perform definitive QTc study in 1H 2008
  - Confirm cardiovascular safety
- Continue to explore other potential indications

ATI-7505: Collaboration with Procter & Gamble Pharmaceuticals

- World-wide development and commercialization deal
  - $25M non-refundable up front fee
  - $391M in remaining milestone payments
  - Tiered royalties
  - 1,000+ person salesforce, with 250 targeting gastroenterologists and endocrinologists
    - Asacol – IBD
    - Actonel – Osteoporosis
  - ARYx option to co-promote in the US (GE's and Endo's)

ATI-7505 Co-promotion Option

Strategic Value to ARYx

- Forward integrate commercially to specialized physicians
- Focus on metabolic/GI disease
- Specialty salesforce (80-120 sales people)
- Bridge to commercialization of other products
- Research programs support commercialization strategy
  - Metabolic program
  - GI program

ATI-2042: Product Overview

Background on Original Drug (amiodarone)

- Amiodarone, the "Gold-standard" for the treatment of AFIB
- Not labeled for AFIB in US
- Numerous safety issues due to drug accumulation

Our Solution: ATI-2042

- Preserved pharmacology – K^+, Na^+, Ca^+, and ß receptors
- Enhanced Safety - metabolism optimized and improved relative to amiodarone
- Significantly shorter biological half-life
- Avoids safety issues due to organ accumulation
- Cleared through an additional non-P450 pathway - Drug-Drug interactions avoided

ATI-2042: Atrial Fibrillation

Large Potential Market

- Most common form of cardiac arrhythmia
- Affects >6.4M people (US, Europe and Japan)
- Approximately 2.4M AFIB patients diagnosed (US)
- Estimated 2M patients treated (US) in 2006
- Estimated to be responsible for >75,000 strokes per year (US)

Amiodarone Usage

- Estimated 60% of AFIB patients (US) receive anti-arrhythmic therapy
  - Remainder receive “rate therapy”
- Estimated 1/3 (600,000) of AFIB patients treated (US) for arrhythmia receive amiodarone

ATI-2042: CLN-208 Phase 2 Study

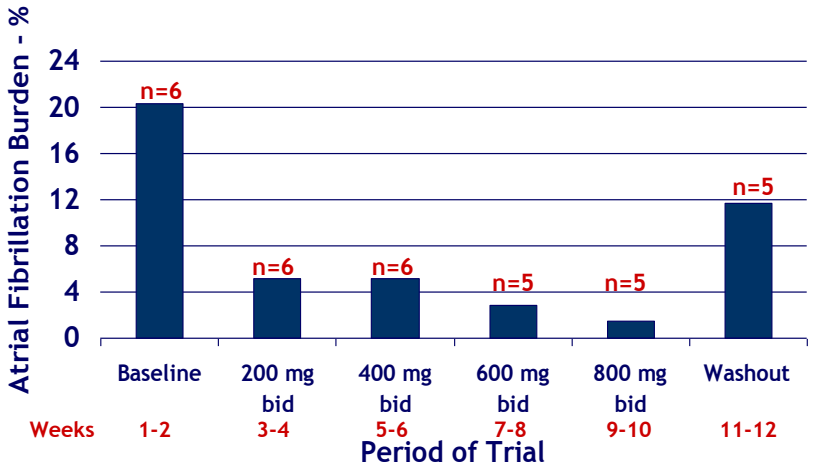
Trial Design

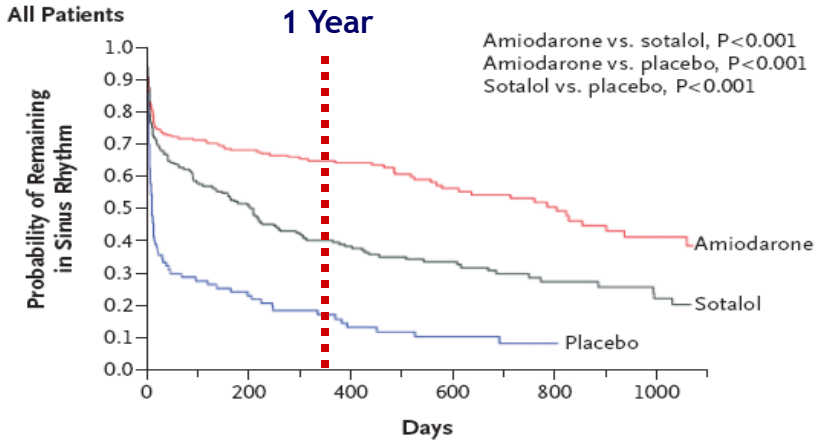
- Open-label dose-escalation in 6 patients for an 8-week period
- Endpoint: establish reduction in percent of time spent in atrial fibrillation
- Implanted pacemakers monitored the duration and severity of the episodes of atrial fibrillation and logged

Trial Results

Amiodarone: more effective than propafenone or sotalol for AFIB

ATI-2042 CLN-208 Trial





Source: SAFE-T trial (1) - Canadian trial had similar results (2)

(1) B.N. Singh et al. M. Ezekowitz, NEJM; 2005;352:1861-72

(2) D. Roy et al., NEJM, 2000;342:913-920

ATI-2042: Clinical Strategy/ Development - Phase 2

- Randomized, double-blind, placebo-controlled study currently enrolling patients in North America and Europe
- Targeted to test the safety and efficacy of ATI-2042 in paroxysmal atrial fibrillation patients who have an implanted dual-chamber pacemaker with recording capabilities
- Doses of 200 mg bid, 400 mg bid and 600 mg bid, or placebo, are being administered for a 12-week treatment period
- Results from this trial are expected by ~YE 2008
- Goals:
  - Establish proof-of-concept by mirroring results of CLN-208
  - Determine the appropriate dosing regimen to be used in Phase 3

ATI-9242: Product Overview

Background on Class of Drugs (atypical antipsychotics)

- $16.2 billion in revenues in 2007 with five dominant products
- All products used in multiple indications
- Lack of efficacy and safety issues result in frequent discontinuation of use
- Treatment issues vary and exist for all products
  - Metabolic issues
  - QT Prolongation
  - Suicide ideation
  - Mortality in elderly
  - Limited efficacy on positive symptoms
  - Lack of efficacy on negative symptoms

Our Solution: ATI-9242

- Molecular scaffold selected not associated with blood dyscrasias
- ATI-9242 designed to be “Best in Class” of the atypicals
  - Best in Class for efficacy (positive and negative symptoms, cognition)
  - Best in Class for safety (metabolic, diabetes, suicide ideation, QT)

Upcoming Milestones

- ATI-7505 (P&G)
  - Complete ATI-7505 definitive QTc study — 1H 2008
  - Complete ATI-7505 Phase 2 trial in chronic constipation — 2H 2008
  - Complete ATI-7505 Phase 2 trial in functional dyspepsia — 1H 2009
- ATI-5923
  - Initiate ATI-5923 Phase 2 trial (CLN-505) in AFIB — 1H 2008
  - Complete ATI-5923 Phase 2 trial (CLN-505) in AFIB — 1H 2009
- ATI-2042
  - Complete ATI-2042 Phase 2 trial in AFIB (CLN-205) — ~YE 2008
- ATI-9242
  - Filed IND for ATI-9242 and Phase 1 study initiated — 1H 2008

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- Product candidates provide attractive partnering opportunities
- Technology approach will continue to build pipeline

Management Team

• **Paul Goddard, Ph.D.** Chairman & Chief Executive Officer	*Elan Pharmaceuticals, Neurex, SmithKline Beecham*
• **Peter Milner, M.D.** President, Research & Development	*CV Therapeutics*
• **John Varian** Chief Operating Officer & Chief Financial Officer	*Genset, Elan Pharmaceuticals, Neurex*
• **Pascal Druzgala, Ph.D.** Chief Scientific Officer	*Advanced Therapies, Xenon Vision*
• **Daniel Canafax, Pharm.D.** Chief Development Officer	*XenoPort, MedImmune*
• **David Nagler** Vice President of Corporate Affairs	*Genentech*

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