
Metabasis Therapeutics, Inc.
Innovative Therapies Targeting Chronic Diseases

Forward-Looking Statements

This presentation includes forward-looking statements that are based on our management's current beliefs and assumptions and on information available to our management on the date of the presentation.

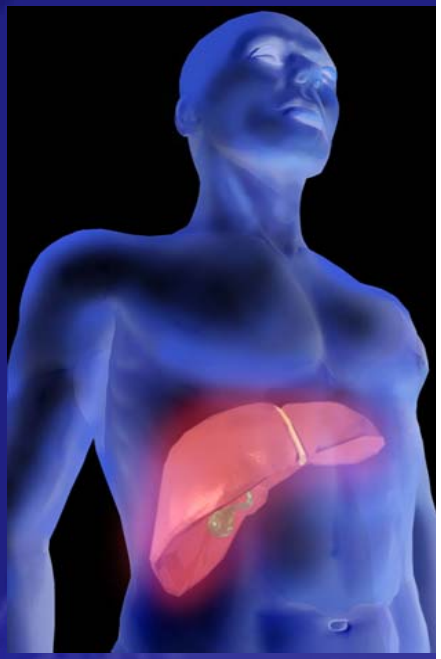
This presentation was given during the week of March 17, 2008 and is only valid as of that date.

Forward-looking statements involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements.

Please see the sections entitled "Risk Factors" and "Forward-Looking Statements" in Metabasis' Quarterly Report on Form 10-Q for the quarter ended September 30, 2007 for a more detailed description of these risks and uncertainties as well as additional information regarding forward-looking statements.

Building a Leading Biopharmaceutical Company

- Unique proprietary technology and know-how
  - Expertise on liver and liver pathways
  - Proprietary technologies
- Strong pipeline
  - Two clinical stage product candidates in our core focus area of metabolic disease
  - Two clinical stage product candidates targeting liver diseases
  - Several metabolic disease candidates approaching recommendation for development
- Experienced team
  - Accomplished discovery group -- all product candidates discovered internally
  - Metabolic disease focused development team
- Key upcoming milestones



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Pipeline Overview

Metabolic Diseases

Product Candidates	Disease/Condition	Mechanism	Partner	Our Commercial Rights	Status
MB07803	Diabetes	FBPase Inhibitor	None	Worldwide	Phase 2a
MB07811	Hyperlipidemia	TRβ Agonist	None	Worldwide	Phase 1b
Undisclosed	Hyperlipidemia	TRβ Agonist	None	Worldwide	Preclinical
Undisclosed	Diabetes	Glucagon Antagonist	None	Worldwide	Preclinical
Undisclosed	Diabetes/ Hyperlipidemia	AMPK Activators	Merck	Royalties, North America Co-promotion Option	Preclinical

Liver Diseases

Product Candidates	Disease/Condition	Mechanism	Partner	Our Commercial Rights	Status
MB07133	Primary Liver Cancer	Prodrug of activated cytarabine	None	Worldwide	Phase 1/2 completed
Pradefovir	Hepatitis B	Prodrug of adefovir	None	Worldwide	Phase 2b completed
Undisclosed[1]	HCV	Undisclosed	Merck Idenix	Royalties	Discovery

[1]Metabasis liver targeting technology applied to partners' candidate compounds.

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Core Metabolic Disease Pipeline

- MB07803 - FBPase Inhibitor for the Treatment of Type 2 Diabetes
- MB07811 - TRβ Agonist for the Treatment of Hyperlipidemia
- Metabolic Disease Candidates Approaching Development

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MB07803

Novel Treatment for Diabetes

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FBPase Inhibitors – A Novel Approach for Treating Diabetes

- Excess production of endogenous glucose in patients with diabetes is a well-known and recognized abnormality
  - Driven mainly by gluconeogenesis pathway
  - Controlling excess production is a goal of many current therapies
- FBPase inhibitors directly inhibit the gluconeogenesis pathway
  - FBPase is a key regulatory enzyme
  - Unlike most other oral anti-diabetics, act independent of insulin

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FBPase Inhibitors – A Novel Approach for Treating Diabetes

- Major market opportunity
- Potential to be administered alone or in combination with other anti-diabetic agents – PPAR, SU, DPP-IV, etc.
  - Metformin therapy failures
    - Primary
    - Secondary
  - Metformin contraindicated (elderly, renal insufficient)
  - First-line therapy
  - Type 1 diabetes

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FBPase Inhibitors

- MB07803 is a 2nd generation FBPase inhibitor designed to improve on the 1st generation compound CS-917
  - CS-917 was licensed to and developed by Daiichi Sankyo
    - Shown safe and effective in two Phase 2a clinical trials conducted in patients with established disease but failed to significantly reduce HbA1c levels in a three-month Phase 2b clinical trial
      - Safe and well-tolerated
      - No evidence for tachyphalyxis
      - HbA1c level in study unexpectedly low ~7.6% compared to ~ 8.5% in previous studies
      - HbA1c significantly reduced in subgroup of patients with more established disease
      - PK/PD model suggests that doses tested were sub-maximal for efficacy
  - Development of CS-917 was discontinued in favor of MB07803

MB07803 - 2nd Generation FBPase Inhibitor

- MB07803 - Orally-active FBPase inhibitor designed to improve on CS-917
  - Superior preclinical profile
    - Expected to be once a day treatment
    - Improved pharmacokinetic profile
    - Increased potential to engage the mechanism
  - Superior PK profile in humans
  - Being developed independently by Metabasis

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MB07803 – Novel Treatment for Type 2 Diabetes

- Have completed multiple Phase 1 clinical trials
- 28-day, Phase 2a, Proof-of-Concept clinical trial in progress
  - Recently completed enrollment with 105 patients
  - Enrolling patients with both newly diagnosed diabetes and more advanced disease
  - Good safety and tolerability to date
    - Well above projected efficacious dose range
  - Final results expected Q2, 2008

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MB07811

Novel Treatment for Hyperlipidemia

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MB07811 – Novel Treatment for Hyperlipidemia

- Being independently developed by Metabasis
- Orally-active, clinical stage product candidate
- First-in-class agent – liver-targeted β selective thyroid receptor agonist
- Expected to be administered alone or in combination with statins
- Unique profile – activity in addition to LDL-C lowering

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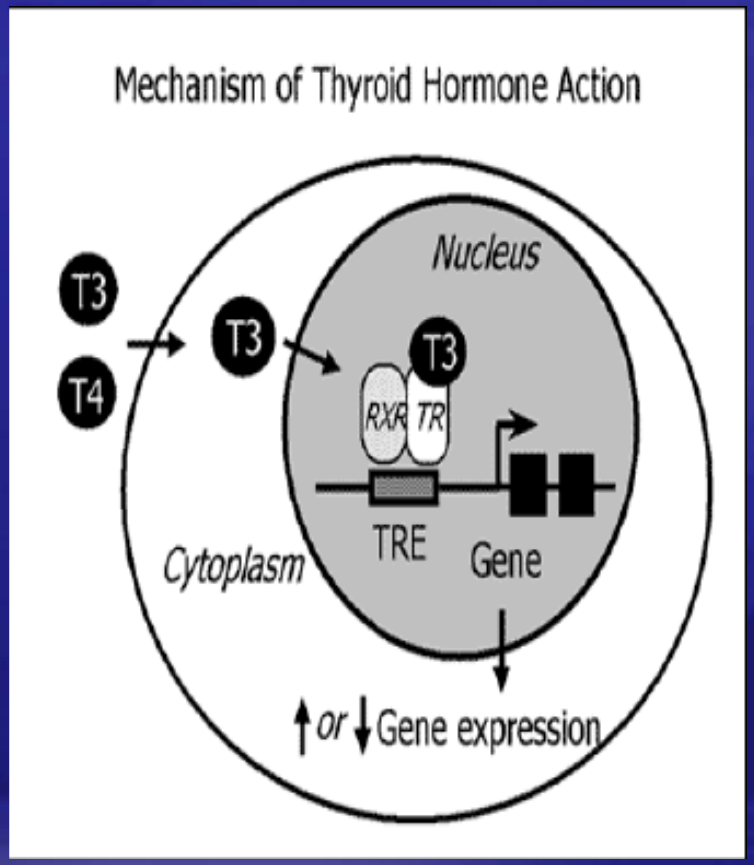
Thyroid Hormone Action - Known Mechanism for Reducing Cholesterol



- Efficacy (Liver)
  - Reduced total cholesterol
  - Reduced atherogenic lipoproteins LDL-C, Lp(a)
  - Reduced triglycerides
    - Plasma
    - Liver
- Safety (non-Hepatic)
  - Cardiovascular
    - heart rate, cardiac hypertrophy, contraction, conductance
  - Thyroid stimulating hormone suppression
  - Muscle wasting
  - Bone loss

Little to no separation between therapeutic dose and dose that causes side effects – a narrow therapeutic index (TI)

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Metabasis Technology Improves a Recognized Mechanism

- Lipid effects mediated by TRβ receptor in liver
  - TRβ selective agonist improves TI
    - Recent data has shown efficacy potential of approach
    - TI may still be relatively narrow
- MB07811 targets a novel TRβ selective agonist to the liver by using:
  - Metabasis' proprietary HepDirect® prodrug technology to target active agent to the liver
  - Other structural features to reduce uptake of active agent in non-hepatic tissue

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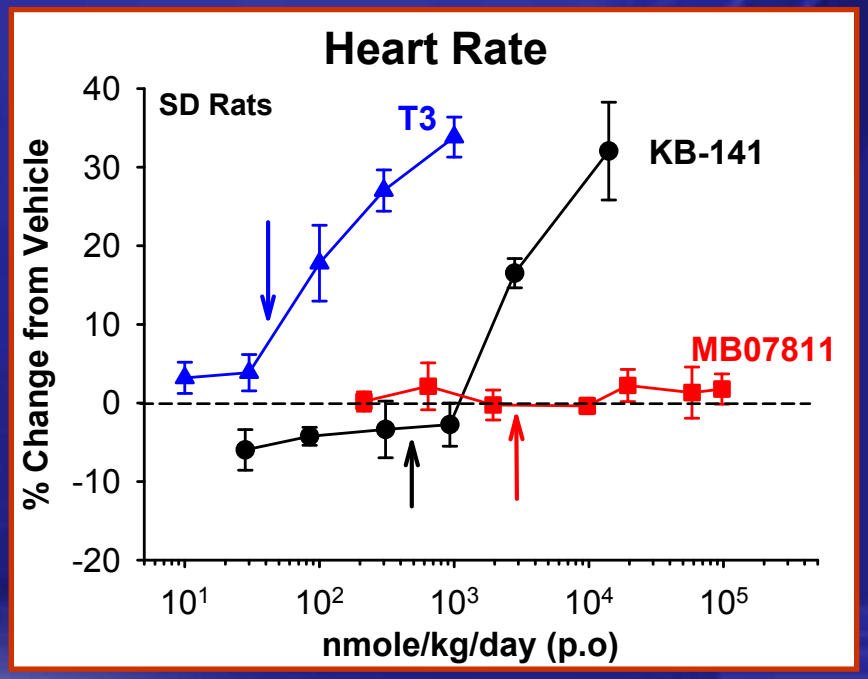
MB07811 – Evidence of Improved Therapeutic Index

- Liver targeting expected to greatly widen the therapeutic index
  - Demonstrated in numerous animal studies from rodents to primates

7 days, Rat



Arrows represent 3x cholesterol lowering ED_{50}

	TI
T3	< 1x
KB-141	~ 3x
MB07811	> 77x

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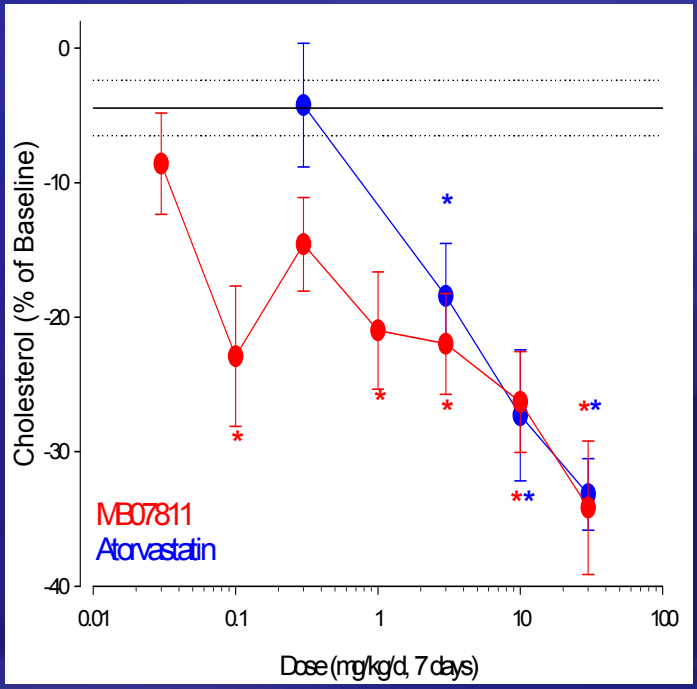
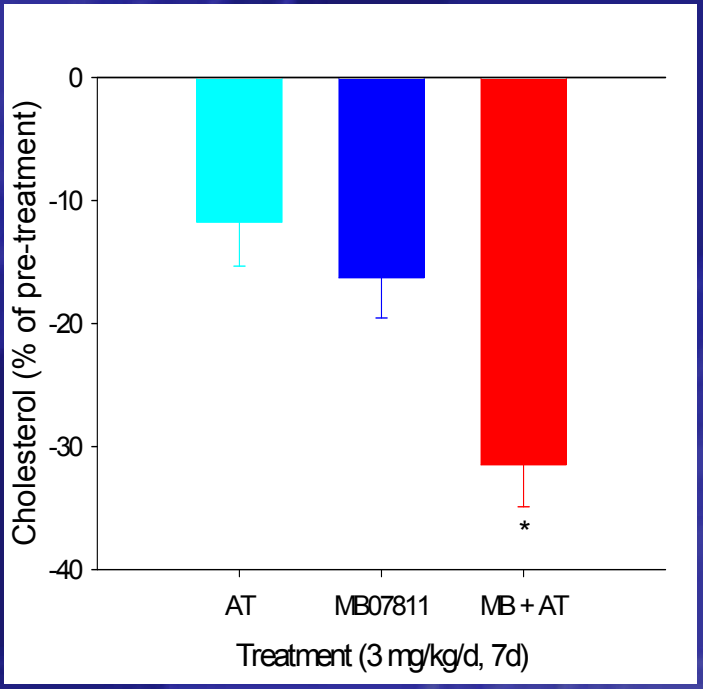
Potential for Use with Statins

- Excellent efficacy demonstrated in animals
  - Shown to be additive to statins in key models, monkeys (shown below) and rabbits





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MB07811 - Development Status and Plans

- 14-day, multiple-dose Phase 1b clinical trial underway
  - Enrolling individuals with modestly elevated LDL-cholesterol
  - Evaluating safety and tolerance
    - Carefully monitoring for signs of non-hepatic T3 receptor activation
  - Preliminary results positive
    - Safe and well tolerated after four dose escalations
    - Preliminary evidence for efficacy
      - Reduced LDL cholesterol and triglycerides
  - Continuing to dose escalate, 5th cohort completed and 6th is underway
- Moving to initiate Phase 2a POC trial, 12 weeks of dosing
  - Data expected in 1st quarter 2009
- Also plan to conduct an important DDI study with a statin in 2008

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Future Metabolic Disease Opportunities

- All product candidates in the clinic were discovered internally
- Potential to recommend additional compounds for clinical development
  - Glucagon antagonist for diabetes
  - Next generation liver-targeted TRβ agonist for hyperlipidemia
  - AMPK activators of diabetes/hyperlipidemia
    - Collaboration with Merck
- Represent current or future partnering opportunities

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Glucagon Antagonist Project Rationale

- T2DM is characterized by relative insulin deficiency and glucagon excess
- Targeting glucagon
  - Increases glucose production by liver
  - Inhibits glucose metabolism in liver
  - Decreases glucose uptake by liver
- Concept validation
  - Glucagon receptor knockout mice have lower fed and fasting blood glucose & lean phenotype
  - Byetta and Januvia work in part by reducing glucagon secretion
- Approaching a recommendation for development
- Strong partnering interest from Pharma

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Non-Core Liver Disease Pipeline

- MB07133 – Liver-targeted Oncolytic for Treating Primary Liver Cancer
- Pradefovir – Liver-targeted Anti-viral for Treating Hepatitis B Infection
- Liver-targeted Approaches for Targeting Hepatitis C

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MB07133 – A Novel Treatment for Primary Liver Cancer

- Intravenously administered, clinical stage drug candidate designed to prolong the life of patients suffering with primary liver cancer (HCC)
- Liver-targeted approach for using a proven anti-cancer agent called cytarabine
- Phase 1/2 clinical trial completed with promising results reported
  - Safe and well-tolerated
  - Promising evidence for anti-tumor activity
- Metabasis is currently preparing for next trial
  - Potential for use in combination with sorafenib
    - Combination of a cytostatic agent (sorafenib) and a cytotoxic agent like MB07133 appears promising
- Plan to seek a licensee to complete development

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Pradefovir for the Treatment of Hepatitis B

- Orally-active, clinical stage drug candidate
- Liver-targeted prodrug of a proven anti-viral agent (adefovir)
- Phase 2b clinical trial successfully completed
- Metabasis recently regained control of product and is reviewing options
  - Expect to seek a licensee to complete development

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Strategic Plan

- Focusing on development of core metabolic disease assets
  - Potential blockbuster products approaching POC milestones
    - MB07803 for type 2 diabetes
    - MB07811 for hyperlipidemia
  - Establish collaborations at appropriate time to share risk and accelerate development
  - Adding new metabolic disease candidates to development pipeline for independent development or with partners

- Plan to license non-core assets
  - MB07133 for HCC
  - Pradefovir for HBV

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Strategic Plan

- Short term goal is to operate through key value driving milestones with minimal reliance on the equity markets
  - Controlling expenses and growth
  - Venture loan and other sources
  - Collaborative partnerships
- Have equity offerings available
  - Have a shelf filing and access to a $50M CEFF

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Financial Snapshot

Results of Operations

(in thousands)	YE 2006	YE 2007
Revenues	$ 4,386	$ 9,019
Operating Expenses	41,195	53,357
Loss from Operations	(36,809)	(44,338)
Interest Income, net	3,541	2,539
Net Loss	(33,268)	(41,799)
Net Loss per Share	$ (1.15)	$ (1.37)
Cash & ST Invest.	$ 77,923	$ 42,438

2008 Guidance

Net cash usage* — Between $40M and $45M

* 2008 cash usage includes the proceeds from a $5M venture loan executed in Q1 08

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Upcoming Milestones

MB07803 Diabetes	*MB07811 Hyperlipidemia*	*Pradefovir Hepatitis B*	*MB07133 HCC*	*Discovery*
• Complete 28-day Proof of Concept trial • Report top-line POC data • Complete metformin DDI study				

Multiple Paths to Value!

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