UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): **April 14, 2016**

SYNTA PHARMACEUTICALS CORP.

(Exact name of registrant as specified in its charter)

Delaware	**001-33277**	**04-3508648**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

45 Hartwell Avenue **Lexington, MA**	**02421**
(Address of principal executive offices)	(Zip Code)

(781) 274-8200
Registrant's telephone number, including area code

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☒ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Item 8.01 Other Events.

On Thursday, April 14, 2016, Synta Pharmaceuticals Corp. ("***Synta***" or the "***Company***") held an investor conference call regarding the previously announced proposed transaction pursuant to the Agreement and Plan of Merger and Reorganization (the "***Merger Agreement***"), dated April 13, 2016, by and among the Company, Saffron Merger Sub, Inc., a Delaware corporation and a wholly owned subsidiary of Synta, Madrigal Pharmaceuticals, Inc., a Delaware corporation ("Madrigal"), a company focused on the development of novel small-molecule drugs addressing unmet needs in cardiovascular and metabolic diseases, pursuant to which the Merger Sub will be merged with and into Madrigal (the "Merger"), with Madrigal surviving the Merger as a wholly-owned subsidiary of the Company.

A copy of the internal script for the conference call and the corporate presentation referred to on the conference call are attached hereto as Exhibit 99.1 and Exhibit 99.2, respectively, and incorporated herein by reference in their entirety. The Company expects to file the full transcript generated after the occurrence of the conference call as soon as it is available.

Additional Information about the Merger and Where to Find It

This Form 8-K does not constitute an offer to sell or the solicitation of an offer to buy any securities or a solicitation of any vote or approval. A definitive proxy statement and a proxy card will be filed with the SEC and will be mailed to Synta's stockholders seeking any required stockholder approvals in connection with the proposed transactions. The proxy statement will contain important information about Synta, Madrigal, the transaction and related matters. BEFORE MAKING ANY VOTING OR INVESTMENT DECISION, INVESTORS AND STOCKHOLDERS ARE URGED TO READ THE PROXY STATEMENT (INCLUDING ANY AMENDMENTS OR SUPPLEMENTS THERETO) AND ANY OTHER RELEVANT DOCUMENTS THAT SYNTA MAY FILE WITH THE SEC WHEN THEY BECOME AVAILABLE BECAUSE THEY WILL CONTAIN IMPORTANT INFORMATION ABOUT THE PROPOSED TRANSACTIONS. Stockholders may obtain, free of charge, copies of the definitive proxy statement and any other documents filed by Synta with the SEC in connection with the proposed transactions at the SEC's website (http://www.sec.gov), at Synta's website under the heading "Investors / SEC Filings", or by directing a written request to: Synta Pharmaceuticals Corp., 45 Hartwell Avenue, Lexington, MA 02421, Attention: Wendy Rieder, Esq.

Synta and its directors and executive officers and Madrigal and its directors and executive officers may be deemed to be participants in the solicitation of proxies from the stockholders of Synta in connection with the proposed transaction. Information regarding the special interests of these directors and executive officers in the merger will be included in the proxy statement referred to above. Additional information regarding the directors and executive officers of Synta is also included in Synta's Definitive Proxy Statement on Schedule 14A relating to the 2015 Annual Meeting of Stockholders, which was filed with the SEC on April 30, 2015. This document is available free of charge at the SEC web site (www.sec.gov), at Synta's website under the heading "Investors / SEC Filings", or by directing a written request to Synta as described above.

Cautionary Statement Regarding Forward-Looking Statements

Any statements made herein relating to future financial or business performance, conditions, plans, prospects, trends, or strategies and other financial and business matters, including without limitation, the potential closing date of the transaction, the amount of Synta's net cash at closing, the prospects for commercializing or selling any drug candidates, are forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. In addition, when or if used in this press release, the words "may," "could," "should," "anticipate," "believe," "estimate," "expect," "intend," "plan," "predict" and similar expressions and their variants, as they relate to Synta, Madrigal or the management of either company, before or after the aforementioned merger, may identify forward-looking statements. Synta cautions that these forward-looking statements are subject to numerous assumptions, risks, and uncertainties, which change over time. Important factors that may cause actual results to differ materially from the results discussed in the forward-looking statements or historical experience include risks and uncertainties, including (i) the timing and completion of the Company's merger with Madrigal, including its ability to satisfy the closing conditions of the Merger Agreement with Madrigal, including the closing condition that Synta have a minimum net cash amount of $28.5 million, (ii) the Company's continued listing on NASDAQ, (iii) the failure by Synta or Madrigal to secure and maintain relationships with collaborators; (iv) risks relating to clinical trials; (v) risks relating to the commercialization, if any, of Synta's or Madrigal's proposed product candidates (such as marketing, regulatory, product liability, supply, competition, and other risks); (vi) dependence on the efforts of third parties; (vii) dependence on intellectual property; and (viii) risks that Synta or Madrigal may lack the financial resources and access to capital to fund proposed operations. Further information on the factors and risks that could affect Synta's business, financial conditions and results of operations are contained in Synta's filings with the U.S. Securities and Exchange Commission, which are available at www.sec.gov. The forward-looking statements represent Synta's and Madrigal's estimate as of the date hereof only, and Synta and Madrigal specifically disclaim any duty or obligation to update forward-looking statements.

Item 9.01 Financial statements and Exhibits

(d) The following exhibits are furnished with this report:

Exhibit Number	Description
99.1	Internal Script of Conference Call, dated April 14, 2016.
99.2	Corporate Presentation, dated April 14, 2016.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

SYNTA PHARMACEUTICALS CORP.

Date: April 14, 2016

/s/ Marc Schneebaum
Marc Schneebaum
Senior Vice President and Chief Financial Officer

EXHIBIT INDEX

Exhibit Number	Description
99.1	Internal Script of Conference Call, dated April 14, 2016.
99.2	Corporate Presentation, dated April 14, 2016.

Exhibit 99.1

Synta Pharmaceuticals/Madrigal Pharmaceuticals Merger Announcement

Date: April 14, 2016 – 8:30 AM ET
Participant Call in numbers:
(855) 451-4851 (US) or (503) 343-6064 (International)
Participant Passcode**:** 91034442

Speakers:

Chen Schor, President and Chief Executive Officer of Synta
Marc R. Schneebaum, Senior Vice President, Chief Financial Officer of Synta
Dr. Paul Friedman, Chairman and Chief Executive Officer of NewCo.
Dr. Rebecca Taub, Founder and Chief Executive Officer of Madrigal

Conference ID number: 91034442
Speaker dial in: (855) 601-0052 (US) or (503) 343-6697 (international)
Becky: We have secured a toll-free dial-in for you to access from Barcelona. The dial-in numbers are:
09 349 23253 or 09 349 23260
Speaker Passcode: 91034442

OPERATOR:

SLIDE 1

Good day, and welcome to the Synta/Madrigal conference call. Today's conference call is being recorded and webcast.

At this time, for opening remarks, I will turn the call over to Marc Schneebaum, Synta's Senior Vice President, Chief Financial Officer. Please go ahead.

Marc Schneebaum

Good morning to everyone and thank you for joining our call today. Today, we plan to discuss the merger agreement, announced this morning, between Synta Pharmaceuticals and Madrigal Pharmaceuticals. Today's call is accompanied by a webcast slide presentation, which is available at syntapharma.com.

With me on today's call are Chen Schor, President and Chief Executive Officer of Synta, Dr. Paul Friedman, who will become Chairman and Chief Executive Officer of the combined company following the anticipated close of the merger, and Dr. Becky Taub, Founder and Chief Executive Officer of Madrigal, and the designated Chief Medical Officer, Executive Vice President, Research & Development, of the

combined company. Our plan today is to provide you with a brief overview of Madrigal. This is a new story to many of you and a new direction for Synta, one we're very excited to be embarking on. Following our remarks, we will open the call for a question and answer period.

SLIDE 2

Before we begin, I would like to point out that we will be making forward-looking statements based on our current intents, beliefs and expectations, which are subject to certain risks and uncertainties.

Forward-looking statements include statements herein with respect to financial projections and estimates and their underlying assumptions, including, without limitation, whether and when our recently announced merger with Madrigal will close; the ability of the combined company to raise needed capital; the success of our merger with Madrigal, if consummated; the estimated size of the market for product candidates, the timing and success of the combined company's development and commercialization of its anticipated product candidates; and the availability of alternative therapies for the combined company's target market.

The Company's actual results could differ materially from those anticipated in these forward-looking statements as a result of various

factors. Additional information regarding factors that could cause results to differ are available in the Risk Factors section of the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 15, 2016 and in the Company's other periodic filings with the SEC.

SLIDE 3

I also note that in connection with the merger, Synta will be filing a Proxy Statement with the SEC. We encourage you to read it and the other relevant materials filed by Synta with the SEC, because these documents have or will have important information about the proposed transaction.

I will now turn the call over to Chen.

Chen Schor

SLIDE 4

Thank you Marc. And thank you all, for taking the time to join us today. As Marc noted, this morning, we issued a press release to announce that Synta has entered into a definitive merger agreement with privately-held Madrigal Pharmaceuticals. This all-stock transaction is one which the Board and management team of Synta are very excited about, for reasons we'll outline in a moment.

Under the terms of the merger agreement, Synta will acquire all outstanding shares of Madrigal Pharmaceutical in exchange for approximately 253.9 million newly issued shares of Synta common stock. Upon completion of the proposed acquisition, existing Synta shareholders will own 36.0% of the combined company and Madrigal shareholders will own 64.0% of the combined company. The transaction has been approved by the boards of directors of both companies and by Madrigal's shareholders, and is expected to close by the end of the third quarter of 2016, subject to customary closing conditions, including approval of the merger by the stockholders of Synta. Upon the close of the transaction, the combined company will be known as Madrigal Pharmaceuticals.

An investor syndicate that includes Bay City Capital, Dr. Fred Craves, Founder of Bay City, and SQN LLC, a corporation held by Drs. Friedman and Taub, has committed to invest up to $9 million in Madrigal prior to the closing of the Merger. The combined company intends to use these proceeds, in addition to Synta's cash balance at closing to fund the development of Madrigal's lead development compound, MGL-3196, through the completion of Phase 2 clinical studies in non-alcoholic steatohepatitis, or NASH, and familial hypercholesterolemia.

SLIDE 5

The decision to pursue this agreement follows an extensive review of strategic alternatives by the Board and senior management team here at Sytna. We believe that this agreement offers shareholders a very compelling opportunity for long-term value creation, which Paul will outline for you in a moment. At the heart of this transaction is MGL-3196, a drug candidate with a unique lipid lowering profile that has been validated through early clinical and preclinical studies. The combination of Synta and Madrigal offers its shareholders a company that is well capitalized with a lead program that has both a substantial potential commercial opportunity in NASH, and a fast-to-market strategy in genetic lipid disorders.

We believe the combined company has the potential to achieve multiple value creating events over the next 18 months.

Also, Synta's historical assets also offer the potential opportunity for monetization.

SLIDE 6

The future Madrigal Pharmaceuticals benefits from the leadership of two very accomplished physicians and drug developers in Drs. Friedman and Taub.

Paul, who is likely well known to many of you, is the former Chief Executive Officer and a current Director of Incyte Corporation, as well as the former President of DuPont Pharmaceuticals Research and Associate Professor of Medicine and Pharmacology at Harvard Medical School.

Becky, who is a recognized expert in liver regeneration and in diseases of the liver, led teams that discovered Eliquis and MGL-3196, Madrigal's lead compound. She is CEO of Madrigal and will become Chief Medical Officer, Executive Vice President, Research & Development. And Marc, whom you heard from a moment ago, will remain as chief financial officer.

The combined company's board of directors will be comprised of seven representatives, one from Synta, five from Madrigal, and one will be designated by mutual agreement. The combined company will be based in the Philadelphia area.

SLIDE 7

With that, I will turn the call over to Dr. Friedman to walk you through the Madrigal value proposition. Afterwards, Dr. Taub will discuss

MGL-3196, Madrigal's lead development compound, in greater detail. Paul?

Paul Friedman

[See Corporate Presentation Slides]
I would now like to turn the call over to Dr. Becky Taub.

Becky Friedman

[See Corporate Presentation Slides]
I would like to turn the call back over to Paul.

Paul Friedman

I know this story is very new to you, but we wanted to provide the opportunity to take your questions, so, with that, I will open the call up, operator?

Q&A

Closing Statement – Paul Friedman

Thank you all for listening in. We look forward to seeing many of you in the weeks ahead and to addressing your questions as you get to know the Madrigal story in greater detail.

Exhibit 99.2


SYNTA
PHARMACEUTICALS®
Synta Pharmaceuticals and Madrigal Pharmaceuticals Merger Agreement
NASDAQ: SNTA | April 14, 2016
Madrigal
Pharmaceuticals

Forward-Looking Statements

Any statements made in this press release relating to future financial or business performance, conditions, plans, prospects, trends, or strategies and other financial and business matters, including without limitation, whether and when our recently announced merger with Madrigal will close; the ability of the combined company to raise needed capital; the success of our merger with Madrigal, if consummated; the estimated size of the market for product candidates, the timing and success of the combined company's development and commercialization of its anticipated product candidates; and the availability of alternative therapies for the combined company's target market, are forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. In addition, when or if used in this press release, the words "may," "could," "should," "anticipate," "believe," "estimate," "expect," "intend," "plan," "predict" and similar expressions and their variants, as they relate to Madrigal, Synta or the management of either company, before or after the aforementioned merger, may identify forward-looking statements. Madrigal and Synta caution that these forward-looking statements are subject to numerous assumptions, risks, and uncertainties, which change over time. Important factors that may cause actual results to differ materially from the results discussed in the forward-looking statements or historical experience include risks and uncertainties, including the timing and completion of the merger, including the parties' ability to satisfy the closing conditions of the Merger Agreement with Madrigal, including the closing condition that Synta have a minimum net cash amount of $28.5 million, Synta's continued listing on NASDAQ, the failure by Madrigal or Synta to secure and maintain relationships with collaborators, risks relating to clinical trials; risks relating to the commercialization, if any, of Madrigal or Synta proposed product candidates (such as marketing, regulatory, product liability, supply, competition, and other risks); dependence on the efforts of third parties; dependence on intellectual property; and risks that Madrigal or Synta may lack the financial resources and access to capital to fund proposed operations. Further information on the factors and risks that could affect Synta's business, financial conditions and results of operations are contained in Synta's filings with the U.S. Securities and Exchange Commission, which are available at www.sec.gov. The forward-looking statements represent the estimate of Madrigal and Synta as of the date hereof only, and Madrigal and Synta specifically disclaim any duty or obligation to update forward-looking statements.

Additional Information about the Merger and Where to Find It

This presentation does not constitute an offer to sell or the solicitation of an offer to buy any securities or a solicitation of any vote or approval. A definitive proxy statement and a proxy card will be filed with the SEC and will be mailed to Synta's stockholders seeking any required stockholder approvals in connection with the proposed transactions. The proxy statement will contain important information about Synta, Madrigal, the transaction and related matters. BEFORE MAKING ANY VOTING OR INVESTMENT DECISION, INVESTORS AND STOCKHOLDERS ARE URGED TO READ THE PROXY STATEMENT (INCLUDING ANY AMENDMENTS OR SUPPLEMENTS THERETO) AND ANY OTHER RELEVANT DOCUMENTS THAT SYNTA MAY FILE WITH THE SEC WHEN THEY BECOME AVAILABLE BECAUSE THEY WILL CONTAIN IMPORTANT INFORMATION ABOUT THE PROPOSED TRANSACTIONS. Stockholders may obtain, free of charge, copies of the definitive proxy statement and any other documents filed by Synta with the SEC in connection with the proposed transactions at the SEC's website (http://www.sec.gov), at Synta's website under the heading "Investors / SEC Filings", or by directing a written request to: Synta Pharmaceuticals Corp., 45 Hartwell Avenue, Lexington, MA 02421, Attention: Wendy Rieder, Esq.

Synta and its directors and executive officers and Madrigal and its directors and executive officers may be deemed to be participants in the solicitation of proxies from the stockholders of Synta in connection with the proposed transaction. Information regarding the special interests of these directors and executive officers in the merger will be included in the proxy statement referred to above. Additional information regarding the directors and executive officers of Synta is also included in Synta's Definitive Proxy Statement on Schedule 14A relating to the 2015 Annual Meeting of Stockholders, which was filed with the SEC on April 30, 2015. This document is available free of charge at the SEC web site (www.sec.gov), at Synta's website under the heading "Investors / SEC Filings", or by directing a written request to Synta as described above.

Synta-Madrigal Terms

- All-stock transaction: Synta to acquire all outstanding shares of Madrigal in exchange for approximately 253.9 million newly issued shares of Synta common stock
- Upon completion of the proposed acquisition, existing Synta shareholders will own 36.0% of the combined company and Madrigal shareholders will own 64.0% of the combined company
- Upon closing of the transaction, the combined company will be known as Madrigal Pharmaceuticals
- Investor syndicate committed to invest up to $9 million in Madrigal prior to the closing of the Merger
  - Combined anticipated Synta cash balance and private placement provides sufficient cash to fund several clinical readouts
- The transaction has been approved by the boards of directors of both companies and Madrigal shareholders
- Expected to close by the end of 3Q 2016, subject to the approval of the stockholders of Synta as well as other customary closing conditions, including satisfaction of Synta having at least $28.5 million in net cash at closing

Synta-Madrigal Merger Agreement

- Follows Synta's extensive review of strategic alternatives
- Combined company will be focused on the development of novel small-molecule drugs addressing major unmet needs in cardiovascular-metabolic diseases and NASH
- Lead compound, MGL-3196, is a first-in-class, Phase 2-ready, once-daily, oral, liver-directed selective thyroid hormone receptor-ß (THR-ß) agonist
- Initial indications are NASH and familial hypercholesterolemia; possibility to expand indications
- Combined company is a potentially attractive therapeutic, commercial and investment opportunity
- Possibly multiple value creating events over the next 18 months
- Historical Synta assets offer potential opportunity for monetization

Synta-Madrigal Leadership

- Combined company will be led by an experienced management team with multiple successful NDA/EMAs and marketed products
  - **Paul Friedman, M.D. - Chairman and CEO**
    - Former CEO of Incyte Pharmaceuticals; former President of DuPont Pharmaceuticals Research
  - **Rebecca Taub, M.D. - Chief Medical Officer, Executive Vice President, R&D**
    - Led teams that discovered Eliquis and MGL-3196, Madrigal's lead compound
    - Recognized expert in liver regeneration and diseases of the liver
  - **Marc Scheenbaum - Chief Financial Officer**
    - SVP, CFO of Synta since 2014
- Board comprised of seven directors: five from Madrigal, one from Synta, and one mutually agreed upon designee
- Corporate headquarters will be located in the Philadelphia area

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Madrigal Pharmaceuticals

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Paul A. Friedman, M.D.

Madrigal Pharmaceuticals

Building a Platform in Lipid and Liver Disorders with MGL-3196, a First-in-Class Thyroid Hormone-β (THR-β) Agonist

First-in-Class Approach	Lead compound, MGL-3196, a Phase 2-ready liver-directed thyroid hormone receptor-β (THR-β) agonist • Once-daily oral dosing • Favorable safety and efficacy profile • World-wide patent exclusivity
Significant Opportunity in NASH	Directly targets lipotoxicity and metabolic defects in NASH • Strong disease link: THR-β receptor deficiency in NASH livers • Supported by preclinical and clinical data • Differentiation: CV benefit, MGL-3196 LDL cholesterol lowering up to 30% in humans
Streamlined Clinical Development Plan in Genetic Lipid Disorder	Heterozygous and homozygous familial hypercholesterolemia (HeFH, HoFH) • Affect up to 1:200 and 1:250,000 patients world-wide • MGL-3196 demonstrated robust efficacy in LDL lowering • Clinically validated, multiple complementary lipid pathways • Potentially fast to market, early Phase 2 favorable safety and efficacy profile

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Madrigal Pharmaceuticals

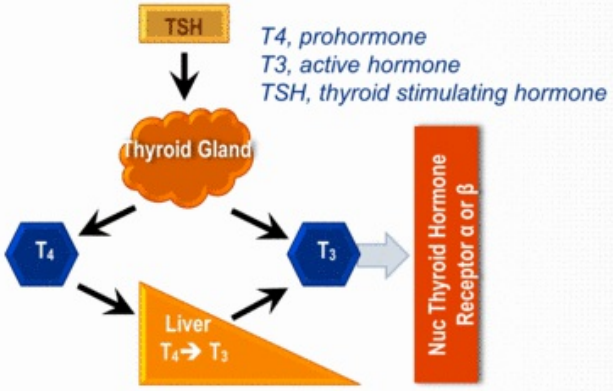
SYNTA PHARMACEUTICALS®

Rebecca Taub, M.D.

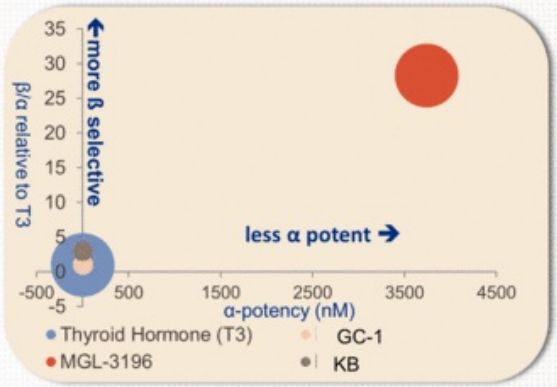
Madrigal Pharmaceuticals

MGL-3196, a First-in-Class Liver-Directed THR- β Agonist

- We believe MGL-3196 is the first bona fide THR-β selective molecule
  - Discovery of MGL-3196 and backups at Roche utilized a novel functional assay that went beyond what previous companies had done (simple receptor binding assay)
  - Earlier compounds purported to be THR-β selective show no functional selectivity and, like thyroid hormone, activate the THR-α receptor equally well as the β receptor
    - β-selectivity and liver targeting are key to beneficial metabolic actions and avoiding safety issues
  - MGL-3196: excellent safety; unlike prior analogue, no cartilage findings in chronic toxicology or ALT increases in human studies



Thyroid Hormone Pathway



J Med Chem. 2014;57(10):3912-3923

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Madrigal Pharmaceuticals

Madrigal Pipeline

Compound/Target	Disease State	Pre-Clinical	Phase 1	Phase 2	Phase 3
MGL-3196 Thyroid Hormone Receptor-β (THR-β) Agonist	NASH	→	→	→	
	FH	→	→	→	
MGL-3745 Thyroid Hormone – Receptor-β (THR-β) Agonist (Backup)	(Same as 3196)	→			

- Thyroid analogue platform (MGL-3196, backup, new molecules)
  - Biliary disorders (progressive familial intrahepatic cholestasis-PFIC)
  - Subclinical hypothyroidism
  - Genetic dyslipidemias
  - Orphan thyroid diseases, RTH, MCT8 deficiency: new molecule, brain penetrant

Nature Rev. Endocrinol. 10, 164, 2014

Differentiated NASH Opportunity

Large & Growing Unserved Market

- WW NASH market estimated at $35bn-$40bn
  - While epidemiology data varies, ~2-3% of the US population is thought to have NASH, and expected to grow given the high rate of growth of obesity and diabetes
  - No FDA approved treatment options

Unique & Differentiated Approach

- MGL-3196 is a novel differentiated cardio-protective therapy
  - Strong disease link: THR-β receptor activity is deficient in NASH livers
    - Supported by preclinical and clinical data
  - Differentiation: CV benefit, MGL-3196 LDL cholesterol lowering up to 30% in humans
  - Critical differentiation in NASH, a disease more likely to lead to death by cardiovascular disease than liver disease

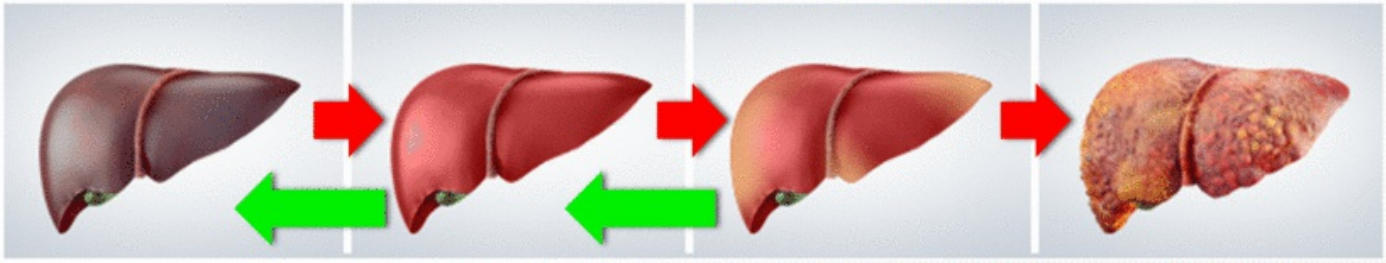
Defined, Regulatory Path

- Treating NASH, rather than fibrosis, is key to addressing the disease
  - Recent FDA guidance indicates that resolution of NASH, without reducing fibrosis, is an approvable endpoint
    - Recognition that liver fibrosis will decrease with time after NASH resolves (similar to reduction of fibrosis as the liver regenerates after cure of HCV)

Note: Market size statistics sourced from various Wall Street equity research.

THR-β Benefits Across the Spectrum of Early to Advanced NASH

Evidence from human and animal data from Madrigal and multiple published studies



Effects of MGL-3196:

METABOLIC BENEFITS
- ↓liver fat & lipotoxicity
- ↑insulin sensitivity
- ↓LDL cholesterol
- ↓atherosclerosis

ANTI-INFLAMMATORY ANTI-FIBROTIC
- ↓apoptosis,
- ↓liver enzymes
- ↑regeneration
- ↓fibrosis & inflammation

REDUCED NASH COMPLICATIONS
- ↓CV disease
- ↓HCC

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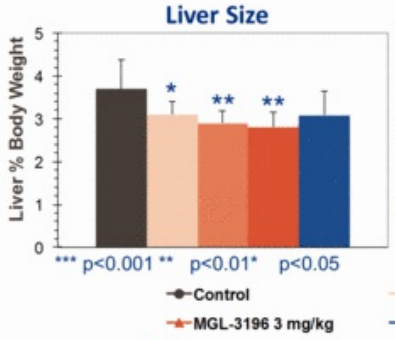
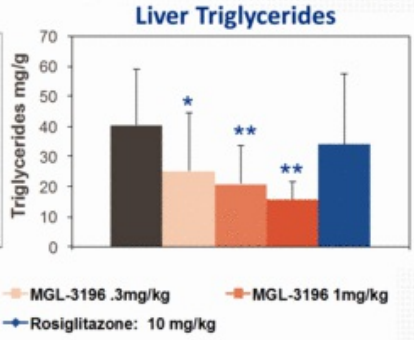
Hepatology. 2009;49(2):407-417; FASEB J. 2008;22(8):2981-2989; Taub et al,, So et al, unpub; Trends Endocrinol Metab. 2014;25(10):538-545PLoS One. 2010;5(1):e8710 Toxicol Pathol. 2003;31(1):113-120; J Lipid Res. 2014;55(11):2408-2415 ; Endocrinology. 2014;155(11):4591-4601; PLoS One. 2013;8(12):e78534

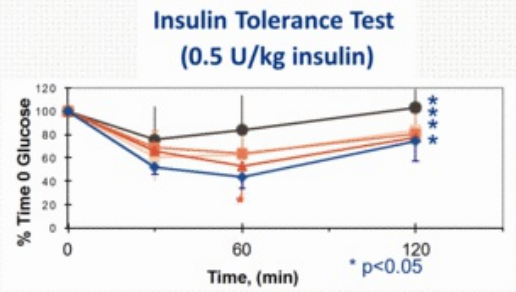
Madrigal Pharmaceuticals

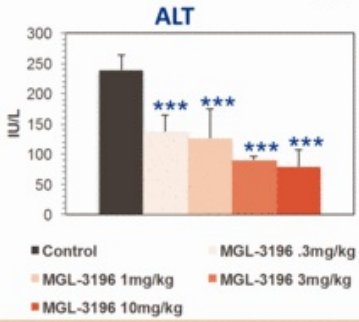
MGL-3196: Marked and Rapid Improvement in Liver Health

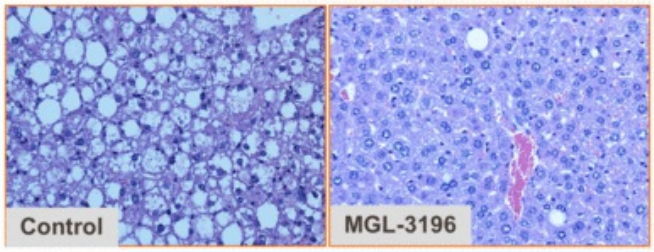
Upper panels: 24d study in 17 wk old DIO mice (po, qd) on high fat diet (HFD) 13 wks; lower panels: 24d study in 40 wk old DIO mice on HFD 35 wks











MGL-3196

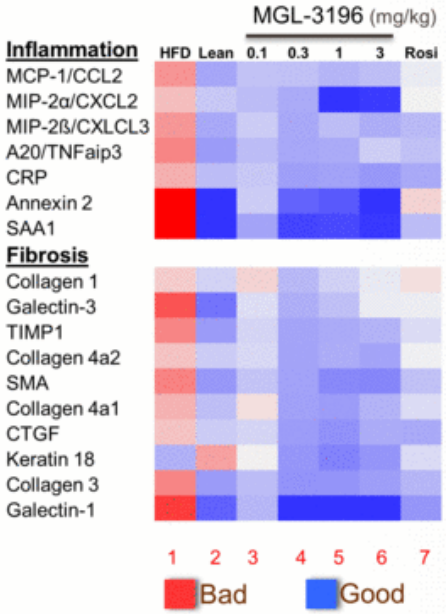
- Reduced hepatic triglycerides (>50%), normalized liver size
- Insulin sensitivity improved at all doses
- Reduced liver enzymes (ALT, AST)
- Improved liver histology, reduced NASH score

SYNTA PHARMACEUTICALS®

Madrigal Pharmaceuticals

MGL-3196: Reduction of Key NASH, Fibrosis Pathway Genes at Human Comparable Drug Levels

25 week study in DIO, lean control mice and HFD mice treated with 0.1 to 3 mg/kg MGL-3196 or Rosiglitazone (3mg/kg)



"HFD", lane 1 mean HFD gene expression normalized to mean Lean; Lanes (2-7) mean gene expression normalized to mean of DIO; "Rosi" (rosiglitazone, 3 mg/kg, 24 wks)
Red, higher expression; blue decreased expression

HFD mouse model

- Up-regulation of NASH and fibrosis related transcripts in HFD as compared with lean mice controls

Effects of MGL-3196 in 25 week HFD mouse model

- Downregulation of key NASH, inflammation and fibrosis pathway genes
  - Reduced to lean mouse level
  - Highly statistically significant
- Reduction of ALT
- More improvement than rosiglitazone
  - Rosiglitazone has been shown to be modestly efficacious in human NASH (HEPATOLOGY 2011;54:1631-1639)
- Drug exposures at .3-1 mg/kg in HFD mice are similar to human dose where maximum lipid lowering is observed
  - Maximum efficacy ~ .3-1 mg/kg in 25 week study

TIMP1 tissue inhibitor metalloproteinase
CTGF connective tissue growth factor
SMA smooth muscle actin
SAA serum amyloid A
CRP C-reactive protein

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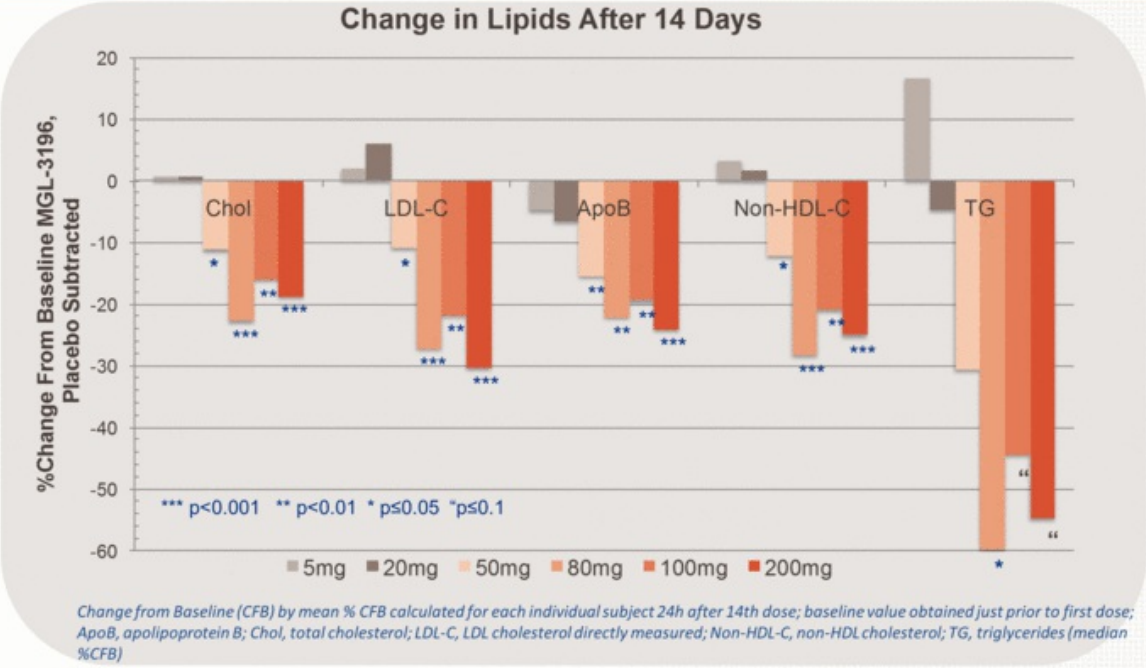
MGL-3196: Robust LDL and Triglyceride Lowering in 14 Day Multiple Dose Phase 1 Study



Change from Baseline (CFB) by mean % CFB calculated for each individual subject 24h after 14th dose; baseline value obtained just prior to first dose; ApoB, apolipoprotein B; Chol, total cholesterol; LDL-C, LDL cholesterol directly measured; Non-HDL-C, non-HDL cholesterol; TG, triglycerides (median %CFB)

Once daily oral treatment led to highly significant and dose-dependent up to ~30% reduction of apolipoprotein B (ApoB), total, LDL, non-HDL cholesterol; Strong trends in triglyceride reduction up to 60%; Near maximal effect at 80mg dose

Strong Positioning in NASH Landscape

Compound	Phase	NAS Score	Fibrosis Score	Liver Lipids	NASH Prevention	Insulin Sensitivity	LDL	TGs	CV Risk	Side Effects
MGL-3196	1	✓	✓	✓	✓	✓	↓	↓	CV Benefit	Well-tolerated

✓Benefit ✓Small benefit ↓Decrease Green = Good

- Pleiotropic and cardio-beneficial actions position MGL-3196 as potential best-in-class NASH therapeutic
  - Metabolic regulator, reduces lipotoxicity, the driver of NASH and fibrosis
  - Cardiovascular disease is the number one killer of NASH patients
    - MGL-3196 potently reduces LDL-C and TGs
- Opportunities for differentiation from other NASH agents
  - Intercept's OCA elevates LDL-C, potentially raising the regulatory bar for approval and limiting the market opportunity
  - Elafibrinor demonstrates modest reduction in LDL-C
  - Anti-fibrotics do not address underlying cause of NASH
- Efficacy on NASH and cardiovascular endpoints position MGL-3196 as an ideal NASH drug to be used in combination with anti-fibrotic and/or anti-inflammatory agents

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Lancet 385:956-65; 2015
Gastroenterology Feb 11 2016; pii:S0016-5085(10)00140-2

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Unmet Needs in FH, a Severe Genetic Dyslipidemia

Severe Debilitating Dyslipidemia	• HeFH and HoFH caused primarily by inactivating mutations in LDL receptor • Early onset cardiovascular disease, HoFH < age 20
Prevalence	• 1/200-1/500 HeFH; 1/250,000-1/1,000,000 HoFH • Higher frequency in certain genetically homogeneous populations
Novel Therapeutic Approaches Needed	• Despite current and newer therapies (i.e. PCSK9 ab), HoFH and many HeFH (severe HeFH) not achieving treatment goals • Significant commercial opportunity for MGL-3196 in HoFH, refractory HeFH

European Heart Journal
doi:10.1093/eurheartj/ehu274; 2014

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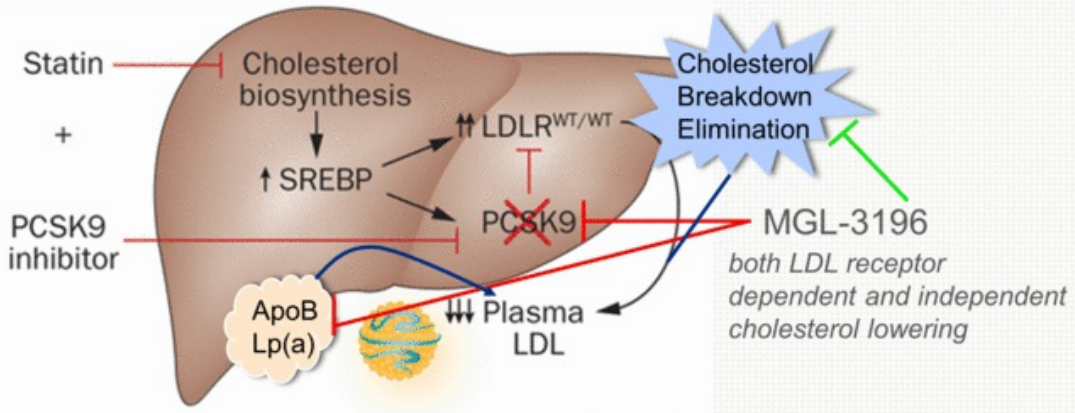
MGL-3196: Unique and Complementary Lipid Lowering Profile



- Thyroid pathway clinically validated and differentiated in FH
  - MGL-3196 lowers LDL in concert with statins in clinical, preclinical studies
  - In Phase 3 trials in HeFH, earlier THR agonist lowered LDL cholesterol and Lp(a)*
  - Thyroid agonists lower cholesterol in LDL receptor knockout mice
  - MGL-3196 is one of the only mechanisms that lowers Lp(a)
    - Lp(a) is a severely atherogenic particle that is elevated in FH and not well-treated by existing therapeutics

*Endocrinology 2012 Nov;153(11):5143-9

*Lancet Diabetes Endocrinol2014; 2: 455–63

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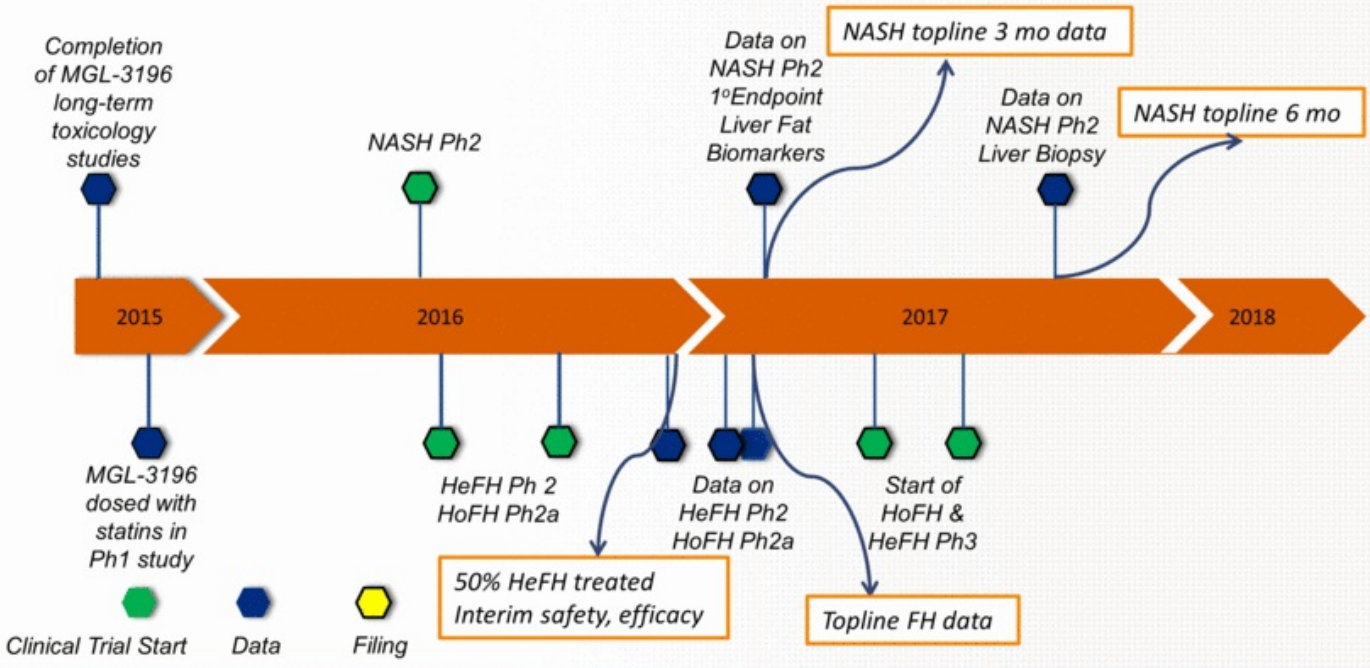
Potential Near and Long-term Value Drivers

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21