

Issuer Free Writing Prospectus  
Filed Pursuant to Rule 433  
Registration No. 333-186003  
May 2, 2013



May 2013

ALCOBRA PHARMA

# Forward-Looking Statements



This presentation includes statements that are, or may be deemed, “forward-looking statements.” In some cases, these forward-looking statements can be identified by the use of forward-looking terminology, including the terms “believes,” “estimates,” “anticipates,” “expects,” “plans,” “intends,” “may,” “could,” “might,” “will,” “should,” “approximately,” “potential” or, in each case, their negative or other variations thereon or comparable terminology, although not all forward-looking statements contain these words. They appear in a number of places throughout this presentation and include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, the ADHD patient market size and market adoption of MG01CI by physicians and patients, the timing and cost of Phase III trials for MG01CI or whether such trials will be conducted at all, completion and receiving favorable results of Phase III trials for MG01CI, the development and approval of the use of MG01CI for additional indications or in combination therapy, the use of the proceeds from this offering, FDA approval of, or other regulatory action with respect to, MG01CI, the timing, cost or other aspects of the commercial launch of MG01CI and the commercial launch and future sales of MG01CI or any other future products or product candidates.

By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics, and healthcare, regulatory and scientific developments and depend on the economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines than anticipated. Although we believe that we have a reasonable basis for each forward-looking statement contained in this presentation, we caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in this presentation as a result of, among other factors, the factors referenced in the “Risk Factors” section of the prospectus contained in Amendment No. 7 to our Registration Statement on Form F-1 filed with the Securities and Exchange Commission on May 2, 2013 for our proposed initial public offering (the “Registration Statement”). In addition, even if our results of operations, financial condition and liquidity, and the development of the industry in which we operate are consistent with the forward-looking statements contained in this presentation, they may not be predictive of results or developments in future periods. Any forward-looking statements that we make in this presentation speaks only as of the date of such statement, and we undertake no obligation to update such statements to reflect events or circumstances after the date of this presentation.

You should read carefully the factors described in the “Risk Factors” section of the prospectus contained in the Registration Statement to better understand the risks and uncertainties inherent in our business and underlying any forward-looking statements.

# Free Writing Prospectus Statement

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This presentation highlights basic information about us and the offering. Because it is a summary, it does not contain all of the information that you should consider before investing.

We have filed a registration statement (including a prospectus) with the SEC for the offering to which this presentation relates. The registration statement has not yet become effective. Before you invest, you should read the prospectus in the registration statement (including the risk factors described therein) and other documents we have filed with the SEC for more complete information about us and the offering. You may get these documents for free by visiting EDGAR on the SEC Web site at [www.sec.gov](http://www.sec.gov). The preliminary prospectus, dated May 2, 2013, is available on the SEC Web site at <http://www.sec.gov/Archives/edgar/data/1566049/000114420413025841/>. Alternatively, we or any underwriter participating in the offering will arrange to send you the prospectus if you contact Aegis Capital Corp., Prospectus Department, 810 Seventh Avenue, 18th Floor, New York, NY 10019, telephone: 212-813-1010, e-mail: [prospectus@aegiscap.com](mailto:prospectus@aegiscap.com).

# Initial Public Offering Summary



Issuer	Alcobra Ltd.
Exchange/Ticker	NASDAQ Capital Market / ADHD
Shares Offered	2,275,000 (100% Primary)
Over-allotment	15% or 341,250 (100% Primary)
Price Range	\$10.00 - \$12.00 per share
Use of Proceeds	Clinical development of MG01Cl, working capital & general corporate purposes
Sole Book-Runner	Aegis Capital Corp
Co-Manager	Sunrise Securities Corp.

# Introduction to Presenters

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## Yaron Daniely, PhD MBA – Chief Executive Officer

- Joined Alcobra in 2010 as CEO and director
- Previously CEO of NanoCyte Inc, and VP Business Development of Gamida Cell Ltd
- PhD (Biochemistry) from NYU School of Medicine

## Udi Gilboa – CFO & Co-Founder

- Co-founded Alcobra in 2008 and has served as CFO/CAO since its inception
- Founder and managing partner of Top-Notch Capital, a prominent Israeli life sciences investment bank
- BA and MBA from Tel Aviv University

## Lenard Adler, M.D. – Head of Clinical Advisory Board

- NYU Langone Medical Center, Departments of Psychiatry and Child and Adolescent Psychiatry
- Emory University School of Medicine, Medical Education
- NYU Medical Center, Residency Training

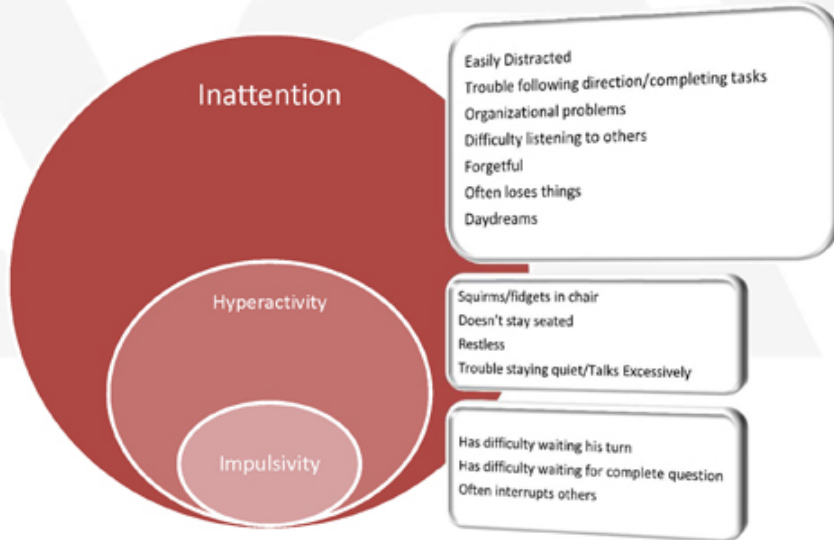
## Key Investment Highlights

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- The market for pharmaceutical treatments of ADHD in 2012 is estimated to be over \$3.8B in the U.S. alone. Europe and Japan are emerging markets.
- The principal current drug regimens are amphetamines with significant side effects.
- We believe MG01CI clinical data confirm a superior safety and efficacy profile with minimal side effects.
  - Robust Phase IIb Proof of Concept study in 120 adult patients meeting primary and secondary endpoints
- US patent allowed March 15, 2013 covering composition of matter (expiration 2028).
- Possibility to leverage unique mechanism of action in other blockbuster indications in cognitive impairment

# Definition of ADHD

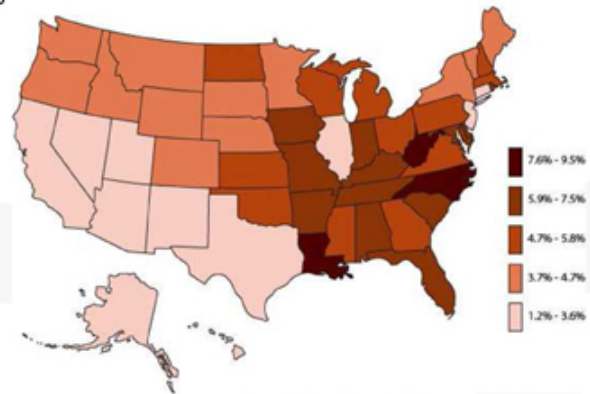
Attention deficit-hyperactivity disorder (*ADHD*) is a neurobehavioral disorder exhibited by difficulty in maintaining attention, as well as hyperactivity and impulsive behavior.



# ADHD – Large & Unpenetrated Primary Care Market



- US market of US\$3.8bn (accounting for 90% of the global ADHD market)
  - Affects 8-10% of school-aged children and about 4-5% of the adult population (fast-growing)
  - US Market forecast to grow at a CAGR of 7.3% per annum and reach US\$6.3 billion by 2018
- European and Japanese ADHD markets to grow at a CAGRs of 4.4% and 18.4% respectively
- Growth is driven by:
  - Increased disease recognition and awareness in the US (using the DSM IV diagnostic criteria), Europe (with entry of new drugs) and ROW
  - Increasing pharmacotherapy adoption rate of 70% in children and adolescents in the US



Percent of all children aged 4-17 years currently taking medication for ADHD by state: United States, 2007<sup>1</sup>



# Impact of Untreated / Undertreated ADHD



## Healthcare System

50% ↑ in bike accidents<sup>(1)</sup>  
33% ↑ in ER visits<sup>(2)</sup>  
2-4x more motor vehicle crashes<sup>(3-5)</sup>

## Patient

↑ Criminal activity  
↑ Incarceration

## Family

3-5x ↑ Parental Divorce or Separation<sup>(11, 12)</sup>  
2-4x ↑ Sibling Fights<sup>(13)</sup>

## School and Occupation

46% Expelled<sup>(6)</sup>  
35% Drop Out<sup>(6)</sup>  
Lower Occupational Status<sup>(7)</sup>

## Society

Substance Use Disorders:  
2x Risk<sup>(8)</sup>  
Earlier Onset<sup>(9)</sup>  
Less Likely to Quit in Adulthood<sup>(10)</sup>

## Employer

↑ Parental Absenteeism<sup>(14)</sup>  
And Lower Productivity<sup>(15)</sup>

(1) DiScala et al., 1998

(2) Cuffe et al., 2009

(3) NHTSA, 1997

(4) Cox et al., 2006

(5) Kieling et al., 2011

(6) Loe & Feldman, 2007

(7) Galera et al., 2012

(8) Molina et al., 2012

(9) Joss et al., 2012

(10) Wilens et al., 1995

(11) Schermerhorn et al., 2012

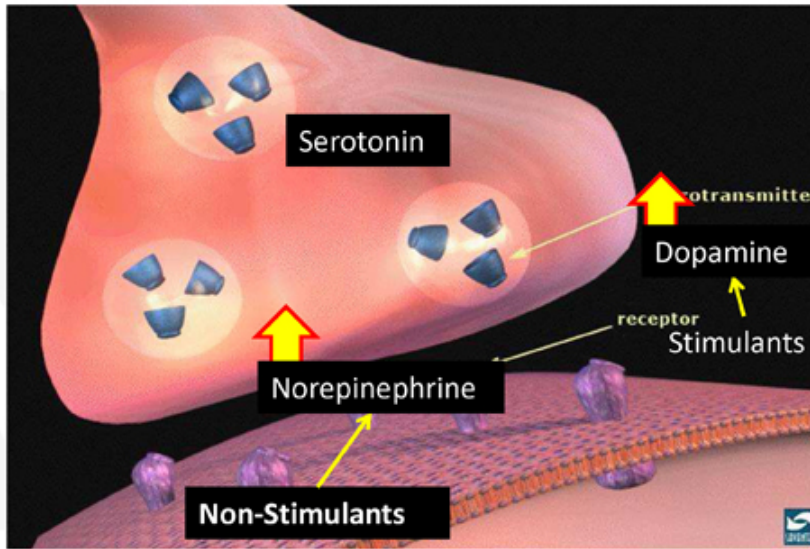
(12) Wymbs, 2008

(13) Mash & Johnston, 1983

(14) Kupper et al., 2012

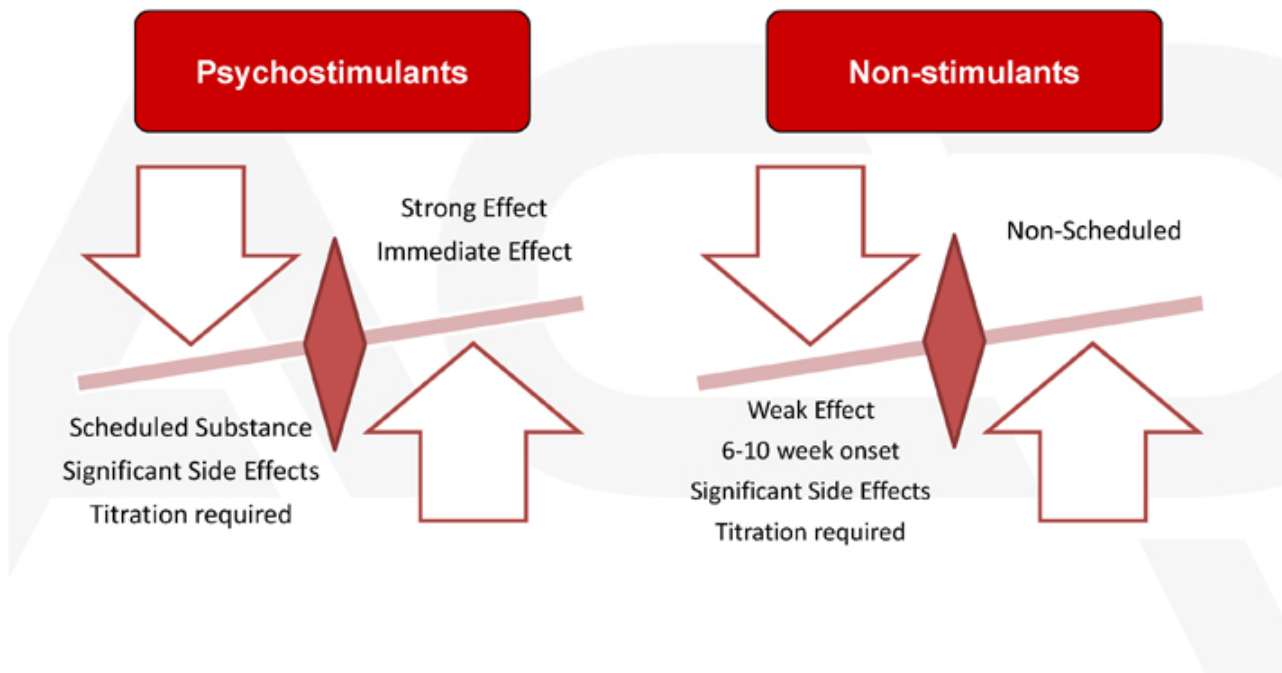
(15) Kleinman et al., 2009

# ADHD – Underlying Pharmacology



In the ADHD brain, low neurotransmitters levels are modulated by either stimulants or non stimulants

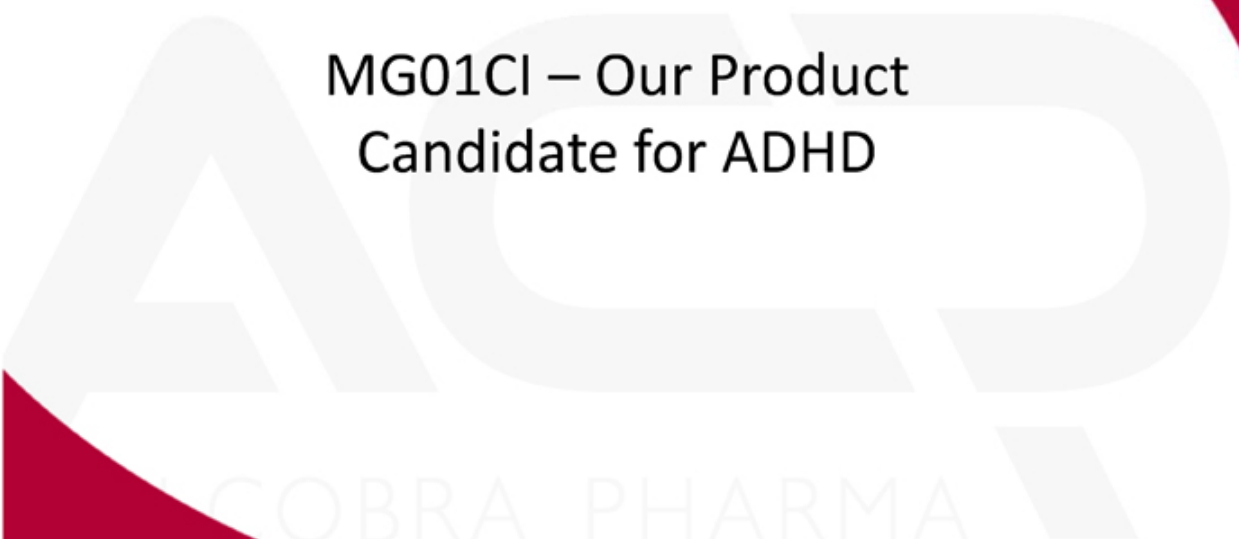
# Types of ADHD Treatments



## ADHD – Principal Medications



Brand (launch)	Generic Name	Owner	Class	Peak Sales US\$m
Vyvanse (2008)	Lisdexamfetamine	Shire (\$2.6B acquisition of New River Pharma in 2007)	Stimulant	1,635 (2016E)
Concerta (2000)	Methylphenidate	J&J	Stimulant	1,326 (2009)
Adderall XR (2001)	Amphetamine	Shire	Stimulant	1,102 (2008)
Strattera (2002)	Atomoxetine	Eli Lilly	Non-Stimulant	667 (2004)



MG01Cl – Our Product  
Candidate for ADHD

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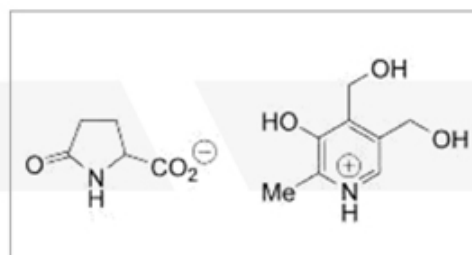
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# Overview – MG01CI

## About MG01CI

MG01CI contains Pyridoxine Pyroglutamate salt (Metadoxine)

MG01CI is a proprietary dual-release formulation of Metadoxine



## Metadoxine Safety

Metadoxine is available (since the 1980's) in immediate release forms for acute treatment of Alcohol Intoxication and chronic treatment of Alcoholic Liver Disease (ALD) in a few countries (Italy, Portugal, Hungary, Russia, India, China, Mexico and Thailand)

In 30 years of product availability no published safety/tolerability issues to our knowledge

Papers reporting on treatment with Metadoxine at ~1500mg levels demonstrate safety and tolerability<sup>(1)</sup>

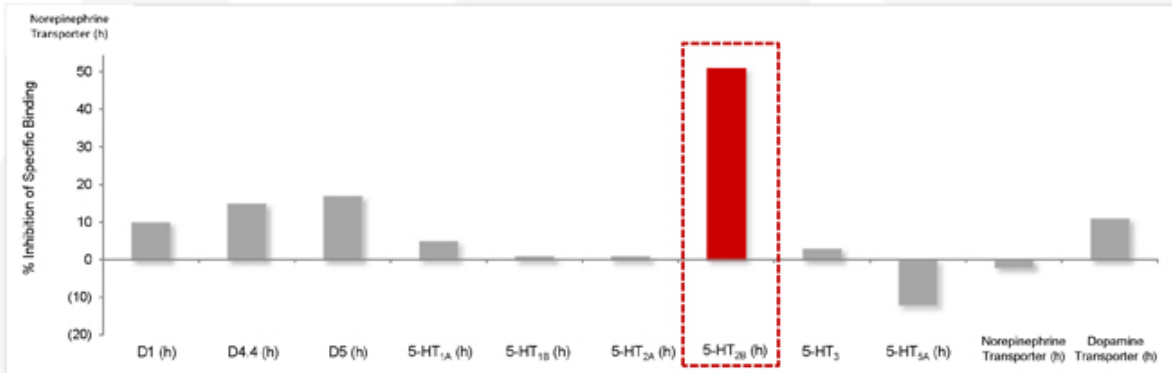
(1) Caballeria et al (J Hep, 1998) – n=69, 3 months, 1500mg  
Cacciatore et al (Clin Trial J, 1988) – n=30, 300mg IM twice daily for 30 days, then 500mg tablet 3 times a day for 5 months (6 months – 1500mg)  
Bono et al (Int J Clin Pharm Res, 1991) – n=20, 900mg IV twice daily (10 days - 1800mg)

# Metadoxine Proposed MOA

Over 80 CNS receptors tested in vitro (Cerep, France)

Muscarinic, Dopaminergic, Serotonergic, Gabaergic, Noradrenergic, Opioid, Cannabinoid

→ Complete and specific binding by Metadoxine to the 5-HT<sub>2B</sub> Serotonin Receptor.

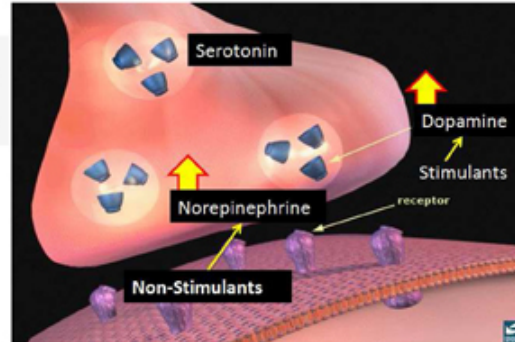


- Displays selectivity over other 5-HT receptor subtypes and a variety of other receptors
- Shown to be a receptor antagonist using the rat stomach fundus bioassay

# Metadoxine Proposed MOA

## Serotonin and ADHD

- Gainetdinov et al. (Science v283, 15 JAN 1999, p397) implicate serotonin pathway in MOA of amphetamines
- Some Serotonin-based medications show some clinical effects in treatment of ADHD
- Some Serotonin-related alleles identified as potential targets



## Serotonin Receptor 5-HT2B and ADHD

- Markowitz et al. (J CHILD AND ADOL PSYCHOPHARM, v16, n6, 2006, pp687–698) report measurable stereo-selective binding of d-MPH observed for the 5-HT2B receptor sites.
- Auclair et al. (J NEUROCHEM, v16, n114, 2010, pp1323–1332) demonstrate that 5-HT2BRs exert a tonic facilitatory control on basal DA outflow in the NAc, and modulate exocytotic and non-exocytotic DA outflow under activated conditions.



# MG01CI Phase IIb – Study Design



- Adult, Israeli study (Geha MHC & Rambam MC)
- n = 120
- Design: 6 week randomized, double-blinded parallel comparison 1400mg MG01CI vs. Placebo

## Primary Endpoint

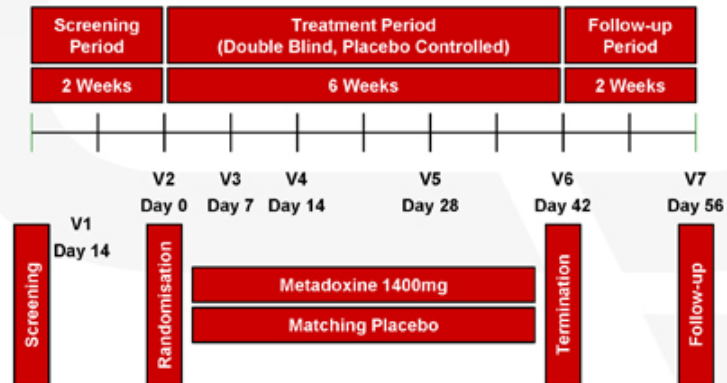
- Prompted CAARS

## Secondary Endpoints:

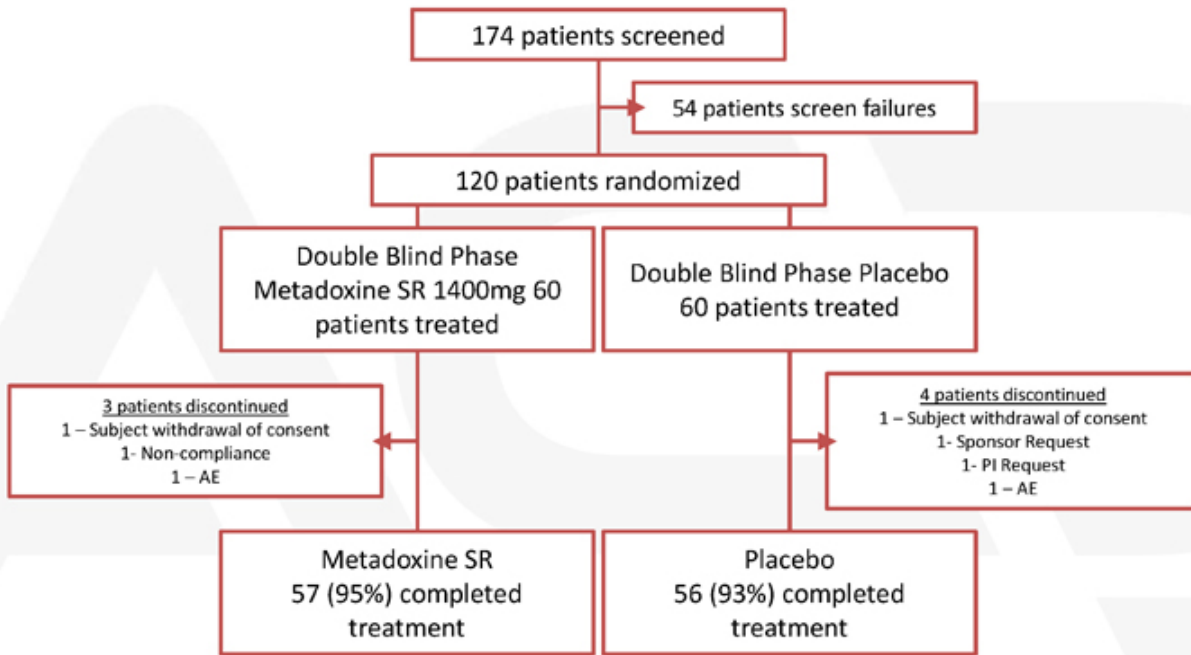
- Adult ADHD QoL (AAQoL)
- TOVA

## Exploratory Endpoints:

- Rate of AE's
- Dropout Rates



# MG01CI Phase IIb – Study Flow



# MG01CI Phase IIb – Patient Demographics



Baseline Scores	MG01CI (n=58)				Placebo (n=59)				
	CAARS Score	CGI-S	AAQoL	TOVA ADHD Score	CAARS Score	CGI-S	AAQoL	TOVA ADHD Score	
Visit 1 (Screening)	Mean	37.1	5.1	58.4	-6.6	37.1	4.9	56.3	-7.3
	Std	8.4	0.8	14.7	8.5	8.5	0.6	13.3	7.2
	Min	23.0	4.0	21.6	-38.1	21.0	4.0	34.5	-27.4
	Median	37.0	5.0	59.9	-4.9	37.0	5.0	54.7	-6.4
	Max	52.0	7.0	93.1	3.2	54.0	6.0	87.1	4.5

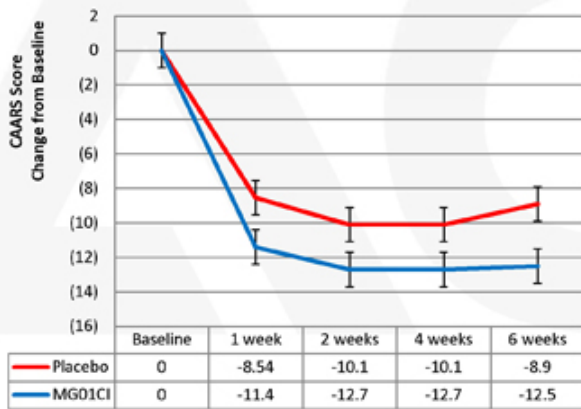
	MG01CI	Placebo	p-value
Number of Patients (n)	60	60	
Age, years (mean±SD)	32.3±7.4	31.2±7.0	0.4140
Gender, n(%)			
Female	26 (43.3)	21 (35)	0.3497
Male	34 (56.7)	39 (65)	
Height, cm (mean±SD)	171.0±10.3	171.7±9.4	0.6986
Weight, kg (mean±SD)	74.8±16.4	73.8±15.8	0.7379
DSM-IV ADHD subtype, n(%)			
Combined	36 (60)	33 (55)	
Hyperactive/Impulsive	1 (1.7)	1 (1.7)	0.8547
Inattentive	23 (38.3)	26 (43.3)	
Educational Background, n(%)			
9-12 years	10 (16.7)	12 (20)	0.6370
12+ years	50 (83.3)	48 (80)	

# MG01CI Phase IIb - Efficacy



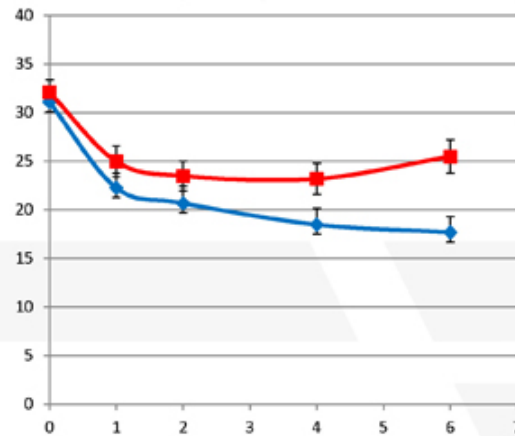
- Statistically Significant Differences Between MG01CI and Placebo Starting Week 2: Primary Endpoint Analysis

CAARS TOTAL SCORE (n=113)



Wilcoxon rank test analysis:  $p < 0.016$   
 Median difference at 6 weeks: 4.0  
**Effect Size: 0.4**

CAARS TOTAL SCORE (n=48) – INATTENTION Only

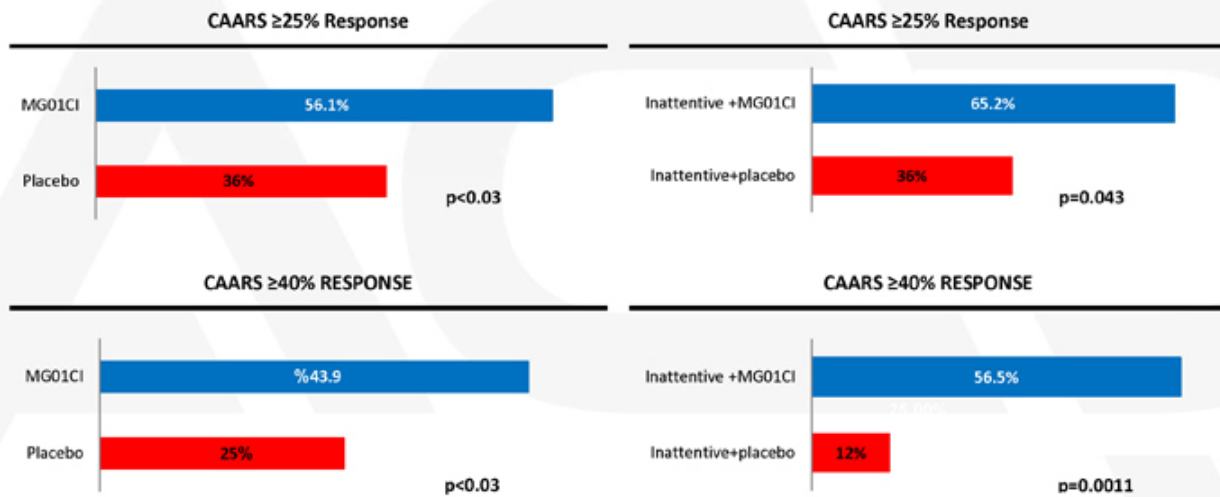


Wilcoxon rank test analysis:  $p < 0.05$   
 Median difference at 6 weeks: 10.0  
**Effect Size: 0.9**

# MG01CI Phase IIb - Efficacy



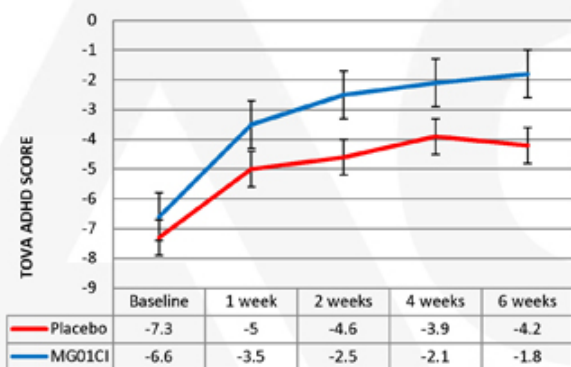
- Predominantly-Inattentive ADHD subtype shows superior effect size: Response Rate Analysis



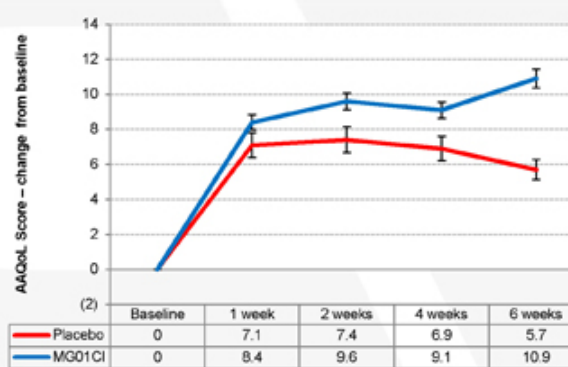
# MG01CI Phase IIb - Efficacy



- Statistically Significant Differences Between MG01CI and Placebo Starting Week 1: Secondary Endpoint Analyses – TOVA And AAQOL (n=113)



ANOVA T-Test (with adjustments for gender, site, age and baseline scores): **p<0.02 (Week 2+)**



ANOVA T-Test (with adjustments for gender, site and age scores): **p<0.01 (Week 6)**

# MG01CI Phase IIb - Efficacy



- Visit 7 (Follow-up) Analysis

Group MG01CI n=58	CAARS			AAQoL			TOVA		
	n	Mean	Std	n	Mean	Std	n	Mean	Std
Visit 1 (Screening)	58	37.10	8.38	58	58.35	14.66	58	-6.59	8.54
Visit 6 (Termination)	57	25.02	11.21	57	69.57	14.32	57	-1.77	4.93
Visit 7 (follow-up)	40	27.89	8.31	40	65.89	14.06	40	-4.50	6.67
Δ between Visit 6 and 7 <sup>(1)</sup>	40	2.87	6.57	40	-3.66	7.14	40	-2.41	5.83
Δ from Visit 7 to Screening <sup>(2)</sup>	40	-8.73	6.10	40	8.41	11.59	40	1.96	5.98

- Statistically significant deterioration in MG01CI group after treatment completion<sup>1</sup>
- No statistically significant difference between MG01CI and Placebo groups at follow-up<sup>2</sup>

## MG01CI Phase IIb – Safety Outcomes

- No SAE's related to Study Drug
- No significant change from Placebo in AE profile, with possible exception of Nausea (17%) and Initial Insomnia (5%)
- No stat. sig. changes in cardiac function (HR, BP)
- No effect on appetite, mood
- No other changes (ECGs, C-SSRS, CBC, Chem, Urinalysis)

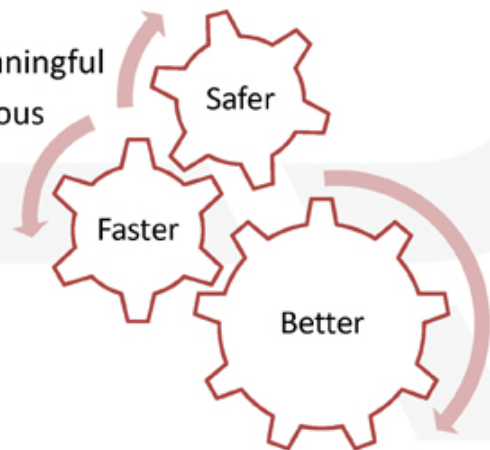
Brand	Generic Name	Class	Common Side Effects
Vyvanse	Lisdexamfetamine	Stimulant	Appetite Suppression; Growth Retardation; Mood Disorders; Ticks; Cardiovascular Dysfunction; Sexual Dysfunction
Concerta	Methylphenidate	Stimulant	
Adderall XR	Amphetamine	Stimulant	
Strattera	Atomoxetine	Non-Stimulant	All of the above <b>plus</b> suicidality; liver toxicities

Less than 20% of prescriptions are re-filled after 1 month!



## Overall findings:

- Significant effect size; particularly large on Inattentive patients
- Response rate higher than other non-stimulants
- Response is more rapid than available non-stimulants
- Tolerability appears superior to all approved drugs
- The absence of cardiovascular effects (seen with existing ADHD drugs) is highly meaningful
- Lack of a need for dose titration is advantageous



## MG01CI Next Steps

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- Continue discussions with the U.S. FDA to seek approval, via an IND Application submission
  - Conduct a Phase II/III clinical trial in the United States for the use of MGO1CI to treat ADHD in adults (~200 participants).
  - Conduct one additional Phase III clinical trial (~250 patients) in order to submit an NDA to the FDA for adult use.
  - Each adult ADHD clinical trial is expected to cost \$6mm to complete.
- If successful in completing ADHD trial in adults, the Company will look to conduct clinical trials with children and adolescents (only one Phase III trial in each population required for approval).
- Similar plans to seek marketing approval in the European Union and later in Japan.

# MG01CI Next Steps



Therapy	Indication	Preclinical	Phase 1/2a	Phase 2b	Phase III	Timeline
MG01CI for ADHD	USA Adults					Trial to launch 2013
	USA Pediatric/Adolescents					Trial to launch 2014
	EU Adults & Pediatric				★	Trial to launch 2014
	Japan Adults & Pediatric				★	Trial to launch 2015

★ Phase III Study to follow after completion of one US study

## MG01CI – Significant Upside



- Possibility of MG01CI to be tested in additional indications with cognitive deficits such as:
  - Cognitive impairment in schizophrenia
  - Mild Cognitive Impairment (MCI) in Alzheimer’s disease
  - Tourette’s cognitive impairment/executive dysfunction
  - Cognitive impairment in Mood Disorders (Bipolar)
  - Autism
  - Jet-Lag/Shift Work Disorders

Therapy	Indication	Preclinical	Phase 1/2a	Phase 2b	Phase III	Timeline
MG01CI for other Disorders	Executive Dysfunction/Sluggish Cognitive Tempo					Trial to launch 2013
	Mood Disorders					Trial to launch 2014

## IPO – Use of Proceeds

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- Completing two Phase III clinical trials of MG01CI for adult ADHD, estimated at \$6.0mm each
- Complete a Phase I/II clinical trial of MG01CI for pediatric ADHD, estimated at \$1.0mm to \$2.0mm
- Preparing for our proposed studies in adults and children for MG01CI, including engaging the FDA in discussions related to protocols for the trials, estimated at \$1.0mm to \$3.0mm
- Evaluating MG01CI in Phase II trials for additional disorders of cognitive function, estimated at \$1.0mm to \$2.0mm
- The remainder will be used for working capital and general corporate purposes.

### **Alcobra's submitted patents may provide multiple layers of protection:**

- Protection of all Extended Release formulations of Metadoxine – ***PATENT ALLOWED IN USA MARCH 2013***
- Protection of use of Metadoxine for cognitive disorders and impairments (Important for possible extended indications of Metadoxine)
- Protection of new Metadoxine derivatives
- Protection of combination therapies containing Metadoxine
- Protection of Metadoxine manufacturing process

# Management



## Yaron Daniely, PhD MBA – Chief Executive Officer

- Joined Alcobra in 2010 as CEO and director
- Previously CEO of NanoCyte Inc, and VP Business Development of Gamida Cell Ltd
- PhD (Biochemistry) from NYU School of Medicine

## Udi Gilboa – CFO & Co-Founder

- Co-founded Alcobra in 2008 and has served as CFO/CAO since its inception
- Founder and managing partner of Top-Notch Capital, a prominent Israeli life sciences investment bank
- BA and MBA from Tel Aviv University

## Dalia Megiddo, MD – Co-Founder

- Co-founded the Company in 2008
- Previously managed InnoMed Ventures, as well as 7 Health Ventures, two Israeli venture capital funds
- MD from Hebrew University Hadassah Medical School

## Hanna Ron, MSc – Director of Non-Clinical Development

- Joined Alcobra in 2011 as manager, Non-Clinical Development
- Over 26 years of experience in the pharmaceutical industry as an expert in chemistry, manufacturing and controls
- Previously VP Chemistry, Manufacturing and Controls at Bioline Innovations Ltd

### Board of Directors

**Aharon Schwartz, PhD**  
Chairman  
VP Innovative Ventures,  
TEVA (former)

**Howard B. Rosen**  
VP Commercial Strategy,  
Gilead (former)

**Daniel Geffken**  
CFO, Transkaryotic  
Therapies (Former)

**Dalia Megiddo, MD**

**Udi Gilboa**

**Yaron Daniely, PhD MBA**

# Advisory Board

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- **Lenard A Adler, MD**, Professor of Psychiatry and Child and Adolescent Psychiatry, New York University Langone Medical Center – **Chair**
- **Stephen V Faraone, PhD**, Professor of Psychiatry and Behavioral Sciences, State University of New York Upstate
- **Thomas J Spencer, MD**, Associate Professor of Psychiatry, Assistant Director, Pediatric Psychopharmacology Unit, Mass General Hospital
- **Jeffrey Newcorn, MD**, Professor of Psychiatry, Mount Sinai Hospital
- **Mark A Stein, PhD, MD**, Professor, Dept of Psychiatry and Pediatrics, University of Illinois at Chicago
- **Betsy Busch, MD**, Associate Clinical Professor of Pediatrics at the Tufts University School of Medicine
- **Anthony L Rostain, MD**, Professor of Psychiatry and Pediatrics, University of Pennsylvania School of Medicine
- **Phillip Asherson, MB,BS, MRCPsych, PhD**, Professor of Molecular Psychiatry at the MRC Social, Genetic and Developmental Psychiatry centre at the Institute of Psychiatry, King's College London
- **Iris Manor, MD**, Associate Professor of Psychiatry, Director of the ADHD Unit, Geha Mental Health Center
  
- **Paul Leber, MD**, former director, Div of Neuro-Pharmacological Drug Products at FDA



# Capitalization Structure



Capitalization	Shares Outstanding	% Outstanding
Common Stock	7,794,256	90.45%
Stock Options	764,444	8.87%
Warrants	<u>58,700</u>	<u>0.68%</u>
Fully-diluted Shares Outstanding	8,617,400	100%

\*Excludes (assuming an offering price of \$11 per share which is the midpoint of the price range set forth in the prospectus) (i) 7,009 shares reserved for future grants under equity incentive plan; and (ii) 89,044 shares resulting from the mandatory conversion upon closing of offering of our outstanding convertible notes, and (iii) 97,214 shares issued upon the closing of the offering consequent to cashless exercise of 129,257 warrants with an average exercise price of \$2.73

## Investment Summary

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- MG01CI addresses significant market opportunities in the ADHD market
  - An immediately effective, non-stimulant with a differentiated mechanism of action that is neither dopaminergic nor noradrenergic
  - Possibility to leverage unique mechanism of action in other blockbuster indications in cognitive impairment
- Positive Phase IIb clinical data confirm superior safety and efficacy profile
- Ready to move forward with advanced clinical studies for ADHD
- Raising approximately \$25mm, which will be used to fund the company and its advanced clinical trials for MG01CI