INSMED INC
Form FWP
September 28, 2012

Developing Innovative Inhaled Treatments for Serious Lung Infections
August 2012
Free Writing Prospectus
Registration Statement No. 333-182124

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Safe Harbor Statement

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Insmed: Value Proposition
Attractive
Late-Stage
Opportunity
ARIKACE has strong Phase 2 efficacy and safety data in CF
Amikacin is an FDA-approved antibiotic, long recognized as one of the most effective treatments for gram-negative infections

Compelling
Business Model
Two orphan indications with high unmet need and combined global market potential of over $1 billion
Limited commercial infrastructure required
Strong IP and potential for extended exclusivity
Strong Balance
Sheet &
Experienced
Management
As of 6/30/12, company reported ~$75 million in cash, investments & CD
We believe cash is sufficient to take Company through the availability of top-line data for both CF CLEAR-108 trial and TARGET-NTM trial
Management has extensive anti-infective development, regulatory, and commercial experience
ARIKACE
®
* is a highly differentiated product that offers a compelling business opportunity in two orphan diseases
* ARIKACE
®
is a registered trademark of Insmed Incorporated
ARIKACE (liposomal amikacin for inhalation), is in Phase 3 (CLEAR-108) for cystic fibrosis (CF) *Pseudomonas* (*Pa*) lung infections and Phase 2 (TARGET-NTM) for non-TB mycobacteria (NTM) lung infections

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ARIKACE: Amikacin Summary
Amikacin is an FDA-approved antibiotic with proven efficacy in the
treatment of gram-negative infections, including Pseudomonas and NTM
Aminoglycoside antibiotic
Value of the IV use has been limited
by nephro-toxicity and ototoxicity
ARIKACE (liposomal amikacin for inhalation) delivers high, sustained levels of drug to

the lung while reducing systemic exposure to well below established toxicity levels

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ARIKACE: Proprietary Liposomal Formulation Provides Basis
for Important Potential Benefits
Potential Benefit
Lipid Polar Head Groups
(at Both Surfaces)
Lipid Hydrophobic Chains
(Bi-Layer Interior)

Water Core (where Amikacin resides)
ARIKACE delivers the potency of Amikacin at the site of the lung infection;
engineered specifically for improved PK-PD* profile in the lung providing for potential enhanced efficacy, safety and convenience benefits
Greater efficacy by reaching infection site
Greater efficacy by reaching infection site
Greater efficacy and once-a-day dosing
Reduces potential for systemic toxicity
Engineered Specifically for Lung Delivery
Prolonged lung residence time
Biofilm penetration
Preferential uptake into macrophages
Minimal systemic exposure
* Pharmacokinetic-Pharmacodynamic (PK-PD)

5
ARIKACE: Delivery Using Proprietary eFlow
®
Technology
ARIKACE is delivered once daily via the state-of-the-art PARI Optimized,
Investigational eFlow Nebulizer System with Advanced Mesh Technology
Fast
drug delivery with efficient

lung deposition
Small, portable, silent and
cordless
device weighs less than
10 ounces.
eFlow Technology Device
exclusivity
from PARI Pharma for
15 years after first commercial
sale of ARIKACE
* eFlow
®
is a registered trademark of PARI Pharma GmbH

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ARIKACE: Development Plan
Target-NTM
Study in U.S.
ARIKACE vs. placebo in recalcitrant patients who are on a stable ATS/IDSA
guidelines-based
multi-drug
treatment

regimen;
N
100
No
inhaled
antibiotics
approved
for
treating
NTM
lung
infections
and
little
known competitive activity in clinic
Study
initiated
in
May-2012
top-line
results
from
randomized
portion
of
trial projected in 4Q13
CLEAR-109
CF Pseudomonas
Study for U.S.
FDA
removed
the
clinical
hold
for
CF
Pa
Phase
3
study
in
May
Insmed
will
defer
plans
to
initiate
a
Phase

3
study
of
ARIKACE
in
the
U.S.
for
CF patients until the Company reviews top-line results from CLEAR-108
Insmed is focusing on CLEAR-108 (CF Pa Phase 3 Study) and TARGET-NTM
(NTM Phase 2 Study)
CLEAR-108
CF Pseudomonas
Study for
EU/Canada
ARIKACE
vs.
Tobi
®
(inhaled
tobramycin
solution);
N
300
Builds off of strong Phase 2 efficacy and safety data
Broad population with preferred trial design
Trial
initiated
in
April
2012
top-line
results
projected
in
mid-2013
Eligible
patients
roll-over
into
open-label
ARIKACE®
long
term
safety
and
tolerability study, CLEAR-110
* Tobi
®
is a Registered Trademark of Novartis Pharmaceuticals Corporation

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Arikace Cystic Fibrosis
Epidemiology and Disease Description
Cystic fibrosis is a life-threatening disease with significant unmet needs
Affects about 70,000 children
and adults worldwide (30,000 in
U.S. and Europe, each)
Inherited disease that causes

thick, sticky mucus to build up
in the lungs
Despite expanded use of current
products, lung function often
continues to decline
High treatment burden
major compliance issue
Source: Adapted from Cystic Fibrosis Foundation, Patient Registry
Annual Data Reports 2010
Mean = 51.2%
Pseudomonas Lung Infections Increase with Patient Age
Age (Years)
0.0
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
<2
2 to 5
6 to 10
11 to 17
18 to 24
25 to 34
35 to 44
45+

8
ARIKACE: Cystic Fibrosis
Need for New Inhaled Antibiotics
Current inhaled antibiotics produce modest efficacy in a limited patient
population providing an opportunity for ARIKACE to become first-line treatment
Current inhaled antibiotics are not indicated for a significant segment of the

CF population --
patients with FEV-1 % predicted of greater than 75%
Improvement in lung function with current inhaled antibiotics is
not sustained
in the off-treatment period, and appears to decline over multiple cycles
Lung function continues to decline at an average rate of 1% to 3% per year
with some patients experiencing much greater declines

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Cayston
®
vs. Tobi
®
CF Phase 3 Trial Results: Pulmonary Function
Lung Function
Adjusted

Mean
Relative
Change
in
FEV
1
%
Predicted
Source: 2010 North American CF Conference Poster 305 and Slide Presentation, 10/10.
* Cayston
®
(aztreonam
for
inhalation
solution)
is
a
registered
trademark
of
Gilead
Sciences.
** Tobi
®
(Tobramycin Inhalation Solution) is a registered trademark of Novartis.
*** AZLI = Cayston; TIS = Tobi
Lung function returned to baseline or lower during each off treatment
period and at the end of 24 weeks, both treatment groups showed a
decline in lung function from baseline
Week:
2
AZLI
TIS
+ 7.8
P
= 0.0001
95% CI (3.86, 11.73)
-6
-4
-2
0
2
4
6
8
10
12
0
4
8

12
16
20
24
AZLI/
TIS
28 Days
AZLI/
TIS
28 Days
AZLI/
TIS
28 Days

10
Off-Treatment
Period
P = 0.033
P = 0.003
(36/36)
(36/35)
(33/36)

(32/35)
(34/35)
(34/34)
(N=ARIKACE/Placebo)
ARIKACE: Cystic Fibrosis
Phase 2 Pooled Results (560mg QD): Pulmonary Function
(N)
Mean (SE)
ARIKACE demonstrated statistically significant and clinically meaningful improvement in pulmonary function throughout the 28-day treatment period that was sustained through the off-treatment period
-6%
-3%
0%
3%
6%
9%
12%
15%
18%
0
7
14
21
28
56
Visit Day
% Change in FEV
1
(ml) vs. Baseline
Arikace
560mg
Placebo

11
Visit Days
ARIKACE: Cystic Fibrosis
Open Label Extension (TR02-105): Durability of Response
Treatment
Period
* Significance at end of treatment over 6 cycles
** Significance 56 days off-treatment over 6 cycles

An open label extension study demonstrated the sustained efficacy
of ARIKACE during and between multiple cycles of therapy
Patients Receiving 560 mg ARIKACE Once Daily for 28 Days and Off-Treatment for 56 Days
p=0.0001**
p<0.0001*
Cycle
1
Cycle
2
Cycle
3
Cycle
4
Cycle
5
Cycle
6
0
5
10
15
20
14
28
56
70
85
98
112
140
154
169
182
196
224
238
253
266
280
308
322
337
350
364
392
406
421
434
448
476

490
504

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ARIKACE: Cystic Fibrosis
Phase 3 Program Has Been Initiated in Europe and Canada
Insmed has reached agreement with EMA and Health Canada on pivotal study
requirements for CF patients with Pseudomonas lung infections
* Patients who complete CLEAR-108 are eligible to participate in CLEAR-110, which is a long term
open-label extension study in which patients receive ARIKACE every other month for up to 2 years
CLEAR-108: Phase 3 Primary Efficacy Study (vs. Tobi

®
, N
300)*
Primary End-Point: Relative Change in FEV-1 at week 24
Key Secondary End-Point: Time to First Pulmonary Exacerbation
Patient
Population:
Patients
ages
6
and
above
with
FEV-1
%
Predicted
25%
Approximately 260 patients required to demonstrate non-inferiority at agreed upon
Top-Line results projected in mid-2013
margin with 80% power

13
ARIKACE: Non-TB Mycobacteria
Disease Description and High Unmet Need
NTM
are
intracellular
organisms
that

invade
and
multiply
chiefly
within
macrophages
in
the lung and are characteristically resistant to most antibiotics
NTM lung infections occurs commonly in patients with structural lung disease (e.g.
COPD, bronchiectasis and CF), patients taking immunosuppressive medications, and in
postmenopausal women without clear risk factors
NTM lung infections are often debilitating and progressive
Virtually all patients experience chronic or recurring cough
Other frequent symptoms including sputum production, fatigue, malaise, dyspnea,
fever, hemoptysis, chest pain and weight loss
Non-TB mycobacteria (NTM) are intracellular pathogens that can cause
severe, chronic pulmonary disease with limited effective treatment options
ATS -
American Thoracic Society;
IDSA -
Infectious Disease Society of America
Current
treatment
for
NTM
lung
disease
requires
lengthy
multi-drug
regimens
that
can
be
poorly
tolerated
and
have
limited
efficacy,
especially
in
patients
with
severe
disease
or
in
those
who

have failed prior treatment attempts David E. Griffith, M.D., Lead author of the ATS/IDSA's diagnosis and treatment guidelines for NTM, and Professor of Medicine at the University of Texas Health Science Center at Tyler;(Insmed Press Release, 6/27/12)

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ARIKACE: Non-TB Mycobacteria
Market Opportunity
The prevalence of this debilitating chronic disease continues to
grow, and
the current NTM treatment paradigm lacks acceptable treatment options *
Sources: 1. Clarity Pharma Research, Patient Chart Study, 2012.
2.

Adjemian et al. Prevalence of Pulmonary Nontuberculous Mycobacterial Disease among Medicare Beneficiaries, USA, 1997-2007, American Journal of Respiratory and Critical Care Medicine. Apr 2012.
3. SDI Healthcare Database, July 2009.
Mycobacterium avium Complex; M. abscessus
Mycobacterium abscessus
U.S. Patients Diagnosed with NTM Lung Infections in 2011
50K
40K
21K
Diagnosis
growing
at~
8%
annually
2
MAC and M. abscessus* account for
75%-85% of NTM lung disease in U.S.
Mean age is ~ 57 years with 53%
treated
with
antibiotics
1
Treated patients use an average of 7.6
antibiotic
courses
per
year
3
Average length of inpatient hospital
stay
is
10.2
days
3
Patients over the age of 65 years were
40% more likely to die than those
without
NTM
from
1997
to
2007
2
* Mark Rolfe, M.D. FCCP, President of New Lung Associates P.A., Medical Director of the Lung Transplant and Adult Cystic Fibrosis Programs at Tampa General Hospital; Insmed press release, June 27, 2012
0
10,000
20,000
30,000
40,000

50,000
60,000
NTM Patients Diagnosed
NTM Patients Diagnosed with MAC or M. Abscessus
MAC & M. abscessus
Patients Treated with Anitbiotics
1

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ARIKACE: Non-TB Mycobacteria
Rationale for ARIKACE
NTM lung infections are difficult to treat since NTM are taken up and multiply inside lung macrophages and most antibiotics have poor macrophage penetration
Amikacin IV is a recommended treatment for MAC and M. abscessus in the ATS/IDSA's NTM diagnosis and treatment

guidelines
1
but
use
is
limited
due
to
nephro-
and
oto-toxicity
The proprietary liposomal formulation enables ARIKACE to be
preferentially
taken
up
and
concentrated
in
the
lung
macrophages
while
potentially
decreasing systemic exposure and related toxicities
ARIKACE
was
shown
to
have
superior
in
vitro
activity
against
MAC
and
M.
abscessus
vs.
free
amikacin
2
ARIKACE
is
well
positioned
to
become
the
first

drug
approved
for
NTM
lung
infections
ARIKACE opportunity: achieve superior efficacy in NTM treatment by
better penetrating lung macrophages where NTM bacteria reside while
limiting systemic drug exposure
Sources: 1. Griffith et al. ATS/IDSA Statement: Diagnosis, Treatment, and Prevention of NTM
Diseases, American Journal of Respiratory and Critical Care Medicine, 2007.
2.
Study conducted by L. E. Bermudez at Oregon State University. (Data on File)

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ARIKACE: Non-TB Mycobacteria
TARGET-NTM Clinical Study Initiated in Mid-2012
Trial Design and Patient Population (N
100):

Randomized, double-blind, placebo controlled Phase 2 study in patients with recalcitrant/persistent NTM lung infections who are on a stable ATS/IDSA

guidelines-based multi-drug treatment regimen

Patients receive ARIKACE or placebo daily for 84 days; then all patients can receive ARIKACE 560 mg in an open-label manner for an additional 84 days

Study population: patients ages 18 to 75
Key Inclusion Criteria: History of chronic infection with either Mycobacterium avium complex (MAC) or Mycobacterium abscessus or mixed infection with both species
Primary endpoint: Change in mycobacterial culture results from baseline to end of treatment [Time Frame: 84 days]
Insmed appears to be the only company with an NTM clinical program; top-line Phase 2 data projected in 4Q 2013
There have been very few clinical trials to support current NTM treatment recommendations, and no new drugs have been assessed in randomized trials for NTM lung disease in many years. (Insmed Press Release, June 27, 2012) according to Kenneth N. Olivier, M.D., M.P.H., Principal Investigator of the study and staff pulmonologist at the NIAID, part of NIH

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Projected
Cash at year
end 2012
(including cash,
investments & CD
)
Approximately $60 to $64 million currently forecast

We believe cash is sufficient to take Company through the availability of top-line data for both CLEAR-108 and TARGET-NTM top-line results

Current Overview: Capital Structure and Key Financials

Balance Sheet

Cash of ~$75 million as of June 30, 2012 consisting of cash, investments & CD

Present Capital Structure (INSM)

26.5 million fully diluted shares:

24.9 million Common Shares

1.6 million options, restricted stock units, and warrants

Insmed has a strong cash position

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Appendix
Addressing the Potential for Cross-Resistance of ARIKACE

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Summary: Addressing Potential for Cross-Resistance in
ARIKACE
While resistance to TOBI (tobramycin) has been documented, we believe there is no cross-resistance in ARIKACE (amikacin) for the following reasons.
Well-characterized clinical isolates of Pseudomonas aeruginosa (Pa) from Dr. Burns
collection have been tested against amikacin
and

ARIKACE.
ARIKACE
has
shown
activity
against
aminoglycoside-resistant
and
multi-drug
resistant
isolates.
Dr.
Burns
felt
ARIKACE performed a bit better than free amikacin. (Report on file.)
Overall, amikacin has lower potential for inducing resistance as
compared to tobramycin (literature).
Additionally,
aminoglycoside-inactivating enzymes elaborated by Pa are different for these two aminoglycosides. Thus, we there is no complete cross resistance. The issue of emerging tobramycin resistance secondary to TOBI (inhaled antibiotic) use is not
completely
quantified.
However,
it
is
primarily
due
to
poor
compliance
with
the
prescribed
regimen
of
TOBI.
Patients
do
not take
the drug twice a day consistently. This leads to drug levels much below the MICs of most phenotypes of Pa for prolonged perio
and thus increased potential for emergence of resistance.
Additionally, there is non-specific binding of cationic tobramycin to
sputum and further low levels available to microbes. Typically, levels >10x of the MICs are needed for entire dosing interval.
Thus, compliance with dosing regimen is critical as is penetration of antibiotics into biofilms.
Features of ARIKACE that overcome some of the issues responsible
for resistance include: charge neutral liposomes shield
amikacin, providing penetration into biofilm, and high Cmax and AUC, enabling once a day dosing and improved compliance.
unique features of ARIKACE will reduce potential for emergence of amikacin resistance vs. free aminoglycoside for inhalation
Most importantly, the sustained clinical benefit of Arikace in the off month
and convenience of once a day will shape the use of

inhalation antibiotics in CF patients.

Use of ciprofloxacin is known to contribute to emergence of Pa isolates with antimicrobial resistance. Tobramycin is also used IV for treatment of exacerbations and for tune-ups. This may also be contributing to emergence of resistance as low levels of drug reach the lung after IV use.

Our phase 2 data have shown that 65% of isolates were resistant to aminoglycosides and ~90% were mucoid variant. However were able to demonstrate reduction in bacterial density and improvement in lung function and pros. Thus, we expect to have significant treatment effect in phase 3 studies even if isolates are resistant. We have also done in vitro work against mdr isolates and shown ARIKACE to be effective.

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21
Percent Change in FEV
1
ITT
Visit Day
Arikace 560 *
15.4% (16.5)
18.4% (21.3)

13.2% (15.3)
13.2% (16.2)
11.5% (16.4)
13.2% (24.3)
Arikace 280 *
10.9% (10.6)
9.4% (12.6)
9.6% (12.5)
10.1% (12.8)
1.7% (9.0)
2.0% (8.6)
Placebo *
0.6% (11.7)
-3.2% (12.2)
1.8% (10.9)
2.2% (11.9)
-0.3% (12.0)
-4.4% (13.0)
* Mean (SD)
Arikace 280
Placebo
Arikace 560
p=0.016
p=0.005
p=0.07
p=0.04

22
Change in FEV
1
(% predicted) ITT
Visit Day
Arikace 560 *
12.9% (17.2)
15.8% (22.5)

10.5% (15.6)
11.0% (16.4)
8.6% (17.7)
13.8% (26.2)
Arikace 280 *
10.8% (10.8)
9.2% (13.1)
9.4% (12.9)
9.6% (13.7)
1.6% (9.6)
1.8% (8.8)
Placebo *
-0.9% (10.7)
-4.4% (11.3)
0.3% (9.9)
0.5% (10.5)
0.7% (9.6)
-3.8% (13.5)
Arikace 280
Placebo
Arikace 560
P=0.009
P=0.019
P=0.124
P=0.021
* Mean (SD)

23
ARIKACE TR02-05
PFT: Prior Use of Inhalation Antibiotic
Arikace
(N = 8)
Placebo
(N = 4)
Day 28

10 %
-5 %
Day 56
5 %
-1 %
Relative Change FEV
1
(ml)

24
Tobramycin
FEV
1
(L) Absolute

25
ARIKACE TR02-05
By Prior Tobramycin Use
Patients With Prior
Tobramycin Use
Patients Without Prior
Tobramycin Use
Arikace

N=5
Placebo
N=3
Arikace
N=16
Placebo
N=8
Day 28
0.326 (0.290)
5
-0.083 (0.123)
3
0.126 (0.203)
16
-0.016 (0.144)
8
Day 56
0.152 (0.186)
5
-0.040 (0.284)
3
0.001 (0.161)
15
-0.120 (0.168)
8
*
Absolute
Change
from
Baseline
-
FEV
1
(L)
Cohort I
280 mg

ARIKACE TR02-05
By Prior Tobramycin Use
26
* Mean (SD)
280mg Cohort
Patients without Tobramycin
280mg Cohort
Patients with Tobramycin

Arikace
Placebo
Arikace
Placebo
Visit Day
Visit Day
Arikace *
326 (290)
152 (186)
Placebo *
-83 (123)
-40 (284)
Arikace *
126 (203)
1 (161)
Placebo *
-16 (144)
-120 (168)
RUN12AUG2008
26

27
Tobramycin
FEV
1
(L) Relative

28
ARIKACE TR02-05
By Prior Tobramycin Use
Patients With Prior
Tobramycin Use
Patients Without Prior
Tobramycin Use
Arikace

N=5
Placebo
N=3
Arikace
N=16
Placebo
N=8
Day 28
0.136 (0.088)
5
-0.052 (0.075)
3
0.091 (0.138)
16
-0.002 (0.067)
8
Day 56
0.051 (0.093)
5
-0.010 (0.148)
3
0.009 (0.084)
15
-0.053 (0.083)
8
* Mean (SD)
*
Relative
Change
from
Baseline
-
FEV
1
(L)
RUN12AUG2008
Cohort I
280 mg

29
ARIKACE TR02-05
By Prior Tobramycin Use
* Mean (SD)
RUN12AUG2008
280mg Cohort
Patients without Tobramycin
280mg Cohort

Patients with Tobramycin
Arikace
Placebo
Arikace
Placebo
Visit Day
Visit Day
Arikace *
13.6% (8.8)
5.1% (9.3)
Placebo *
-5.2% (7.5)
-1.0% (14.8)
Arikace *
9.1% (13.8)
0.9% (8.4)
Placebo *
-0.2% (6.7)
-5.3% (8.3)

30
Arikace
-
Efficacy in Patients with Prior Tobramycin Use:
TR02-106
Mean
Change in Log
10

CFU
Subjects with 5-6 Cycles of TOBI in prior 12 months
Change in FEV_1 (ml)
Subjects with 5-6 Cycles of TOBI in prior 12 months
Placebo
Visit Day
Visit Day
Arikace 560
90 (220)
90 (30)
230 (60)
90 (90)
Placebo
-140 (210)
-110 (350)
-200 (20)
-290 (10)
Arikace 560
Arikace 560
-1.99
(0.70)
-1.26
(0.86)
-0.93
(1.19)
-1.43
(0.89)
-0.27
(0.44)
Placebo
0.15
0.03
-0.55
-0.29
0.08
Placebo
Arikace 560
Mean
-3
-2
-1
0
1
2
3
0
7

14
21
28
35
-300
-250
-200
-150
-100
-50
0
50
100
150
200
250
0
28
56
70
84

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Insmed has filed a registration statement (including a prospectus) with the Securities and Exchange Commission (the SEC) for the offering to which this communication relates. Before you invest, you should read the prospectus in that registration statement and other documents Insmed has filed with the SEC for more complete information about Insmed and this offering. You may get these documents for free by visiting EDGAR on the SEC web site at
www.sec.gov.

Alternatively, Insmed will arrange to send you a copy of the prospectus if you request it by calling Insmed s corporate secretary at: (732) 997-4600.