

INFINITY PHARMACEUTICALS INC  
Form 425  
September 11, 2006

Filed by Discovery Partners International, Inc. Pursuant to Rule 425

Under the Securities Act of 1933

and Deemed Filed Pursuant to Rule 14a-12

Under the Securities Exchange Act of 1934

Subject Company: Infinity Pharmaceuticals, Inc.

Commission File No. 333-134438

**Additional Information about the DPI-Infinity Merger and Where to Find It**

In connection with the proposed merger between Discovery Partners International, Inc. (DPI) and Infinity, on August 7, 2006, DPI filed an amended registration statement on Form S-4 that contains a proxy statement/prospectus, which registration statement has been declared effective by the SEC. Investors and security holders of DPI and Infinity are urged to read the proxy statement/prospectus (including any amendments or supplements to the proxy statement/prospectus) regarding the proposed merger because it contains important information about DPI, Infinity and the proposed merger. Security holders will be able to obtain a copy of the proxy statement/prospectus, as well as other filings containing information about DPI and Infinity, without charge, at the SEC's Internet site (<http://www.sec.gov>). Copies of the proxy statement/prospectus can also be obtained, without charge, by directing a request to Discovery Partners International, Inc., 9640 Towne Centre Drive, San Diego, CA 92121, Attention: Investor Relations, Telephone: (858) 455-8600.

**Participants in the solicitation**

DPI and its directors and executive officers and Infinity and its directors and executive officers may be deemed to be participants in the solicitation of proxies from the stockholders of DPI in connection with the proposed merger of DPI with Infinity. Information regarding the special interests of these directors and executive officers in the merger transaction is included in the proxy statement/prospectus referred to above. Additional information regarding the directors and executive officers of DPI is also included in DPI's proxy statement for its 2006 Annual Meeting of Stockholders, which was filed with the SEC on April 6, 2006. This document is available free of charge at the SEC's web site ([www.sec.gov](http://www.sec.gov)) and from Investor Relations at DPI at the address described above.

Infinity gave the following presentation on September 8, 2006.

Introduction to Infinity  
September 8, 2006

## Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995 that involve risks and uncertainties that could cause actual results to be materially different from historical results or from any future results expressed or implied by such forward-looking statements. You are urged to consider statements that include the words

may,  
will,  
would,  
could,  
should,  
believes,  
estimates,  
projects,  
potential,  
expects,  
plans,  
anticipates,  
intends,  
continues,  
forecast,  
designed,  
goal,

or the negative of those words or other comparable words to be uncertain and forward-looking. Such forward-looking statements include statements regarding the expected benefits of the merger of Infinity and DPI for stockholders of the combined company, the expectation that the merger will enable the combined company to be well positioned to drive forward its pipeline of anti-cancer agents and create substantial value for patients and stockholders, and the expectation that the combined company will have cash to support its current operating plan through at least December 31, 2009. Such statements are subject to numerous factors, risks and uncertainties that may cause actual events or results to differ materially from the combined company's current expectations. For example, there can be no guarantee that any product candidate the combined company is developing will successfully complete necessary preclinical and clinical development phases, be approved for sale in any market or that, if approved, revenues from sales of such product will reach any specific level. In particular, management's expectations could be affected by risks and uncertainties relating to: results of clinical trials and preclinical studies, including subsequent analysis of existing data and new data received from ongoing and future studies; the combined company's dependence on its collaborations with MedImmune and Novartis; the combined company's ability to obtain additional funding required to conduct its research, development and commercialization activities; unplanned cash requirements and expenditures; and the company's ability to obtain, maintain and enforce patent and other intellectual property protection for any products it is developing. These and other risks which may impact management's expectations are described in greater detail under the caption "Risk Factors" in DPI's

registration statement on Form S-4, as amended, as filed with the Securities and Exchange Commission and DPI s other SEC reports.

Any forward-looking statements contained in this presentation speak only as of the date hereof and Infinity expressly disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

Mission

To develop targeted therapies for the treatment of cancer and related conditions discovered through the use of our innovative small molecule drug technologies

Lead product candidate: IPI-504, a novel Hsp90 inhibitor

Two ongoing Phase I cancer studies in GIST and multiple myeloma

Phase II expected 2007

Pipeline of preclinical cancer drug candidates

Internally discovered and developed, chemistry platform

5 Pharma/Biotech corporate alliances

MedImmune, Novartis  
(2), Amgen, and J & J

Proven biotech leadership team

Significant cash position after MEDI alliance and DPI merger

Funds sufficient for projected operating expenses through end of  
2009

Infinity Snapshot

Strategy

Drugs

Internally discovered, novel small molecules

Targets

Well-credentialed, but not well-trodden

Products

Opportunity for first-in class or fast follower best-in-class

## Overview

Founded in late 2001 (~5 years old)

## Team

Recognized biotechnology investor, business and R&D leaders

~115 employees (~55 PhD / MDs)

## Alliance and Financing Strategy

Hsp90 and Hedgehog pathway product alliance with MedImmune



Bcl  
family product alliance with Novartis

Small molecule technology access alliances with Amgen, J&J and Novartis

Public financing via Reverse Merger with Discovery Partners

IPI-504  
lead proprietary oncology drug candidate (Hsp90)

Phase I in GIST and multiple myeloma commenced 2005

Phase II anticipated in 2007

Hedgehog pathway  
preclinical oncology candidate

Our Team: ~115 full-time employees

Infinity headcount

Biology/Clinical/Regulatory

36

Chemistry

50

Management & other

12

(~55 MD or PhDs)

R&D Total

98

Total

115

G&A

17

Well-balanced

Moderate near-term growth

anticipated

Primarily in downstream  
disciplines (i.e. clinical,  
regulatory, CMC/ADME/tox)

Leadership

Mr. Steven Holtzman, CEO

Millennium, DNX

Dr. Julian Adams, President & CSO

Millennium, ProScript

Boehringer

Ingelheim, Merck

Ms. Adelene Perkins, CBO

Transform, Genetics Institute,

Bain, GE

Dr. David Grayzel, VP Clinical

Development & Medical Affairs

Dyax, Mass General Hospital

Dr. Vito Palombella, VP Discovery Biology

Syntonix, Millennium, ProScript

Dr. Jeffrey Tong, VP Corp & Prod Dev

McKinsey & Co, Harvard Center for

Genomics Research

Dr. Jim Wright, VP Pharm

Dev

Millennium, Alkermes, Boehringer

Ingelheim, Syntex, U. of Wisconsin

SAB  
Oncology & Chemistry

Co-chair: Stuart Schreiber, PhD -  
Co-Director Broad Institute, Prof. of Chemistry and  
Chemical Biology Harvard University

Co-chair: Rick Klausner, MD  
Column Group, former Head of the NCI

Arnie  
Levine, PhD -  
Institute for Advanced Study

Eric Lander, PhD -  
Co-Director Broad Institute, Whitehead, MIT, Harvard

Todd Golub, MD -  
DFCI, Broad Institute, Harvard, MIT

David Livingston, MD  
Professor of Medicine, Harvard Medical School, DFCI

Ken Anderson, MD -  
Robert Kraft Prof. of Medicine Harvard Medical School, DFCI

Matthew Shair, PhD  
Professor of Chemistry, Harvard University

Vicki Sato, PhD  
former President Vertex Pharmaceuticals

Phil Needleman, PhD -  
former Head of R&D Searle, Pharmacia

Investors  
Venture Capitalists

Prospect Venture Partners

Venrock Associates

Advent Venture Partners

HBM BioVentures

Vulcan Ventures

Novartis BioVentures

Wellcome  
Trust

POSCO BioVentures

Tallwood

Alexandria Equities

Lotus BioScience  
Pharmaceutical Companies

Amgen

Novartis

J&J

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## IPI-504

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Phase II anticipated in 2007

Hedgehog pathway  
preclinical oncology candidate



DOS Small Molecule Technology: Discovery and Alliance Engine

Innovative small molecule platform, diversity oriented synthesis (DOS), enables the creation of novel, natural product-like synthetic drug candidates

Potential  
to  
access  
previously  
undruggable  
drug  
targets

Unique asset for:

Internal drug discovery

Value-accretive technology access alliances

Diversity Oriented Synthesis (DOS)

2004

2006: > \$60 million upfront/committed cash

Additional milestone and royalty potential

No license of proprietary Infinity product rights

Small Molecule Technology Access Alliances

Total payments >\$400M  
Early product pipeline: Bcl  
family alliance with Novartis

Joint discovery of novel Bcl  
family (Bcl-2, Bcl-xL) targeted  
cancer drugs

Infinity participation in clinical  
development (at NVS expense)  
COLLABORATION

Infinity participation in US sales  
effort (at NVS expense)  
\$30M

Upfront &  
committed funds  
FINANCIALS

Royalties on WW sales

Clinical and  
commercial  
milestones

Lead products: Hsp90 and Hedgehog alliance with MedImmune

Infinity leads early translational  
development through proof of concept

MedImmune  
leads later clinical  
development, worldwide registration and  
sales and marketing, with Infinity  
participation

COLLABORATION

Infinity has right to provide up to 35% of  
US promotional activity (cost shared by  
alliance)  
\$70M

Upfront funds  
FINANCIALS

50% R&D cost sharing  
\$430M

50% worldwide profit split

Discovery  
Preclinical  
Start Clinical  
Trials  
Hsp90  
(IPI-504)  
Bcl-2/Bcl-xL  
2005  
2007/2008  
50% WW profit  
share with MEDI  
50% WW profit  
share with MEDI  
Royalty from  
Novartis  
Non-exclusive

Amgen

Novartis

J&J

Small molecule drug technologies

Alliance and financing strategy: value retention

Hedgehog

Pathway

(IPI-609)

2007



Reverse Merger  
with  
Discovery Partners International, Inc.  
(NASDAQ: DPII)

\*  
\*  
\*  
\*  
\*  
\*

DPI reverse merger opportunity

Discovery Partners International

Publicly traded company on NASDAQ (DPII)

Cash position 1/1/06: > \$83M

Board mandate (Q1, 2006):

Shut down existing business

Seek alternative, high-value biotech investment opportunity

DPI undertakes extensive evaluation of merger candidates

DPI selects Infinity as preferred partner

A  
financing  
event  
only

NO  
programs,  
employees,  
partnerships,  
or  
obligations of DPI transferred to Infinity

DPI invests  
cash and divests operating units

7/7/06: Sale of all DPI operating assets to Galapagos

If DPI cash between \$70M and \$75M, ownership:

DPII stockholders = 31%

Infinity stockholders = 69%

If cash above \$75M or below \$70M, adjustment applied

4:1 reverse stock split approved by DPI board to lower share  
number and bring share price >\$10

The reverse merger: a creative financing and access to  
public markets

Lead clinical product in two ongoing Phase I cancer studies

Phase II expected 2007

Pipeline of preclinical cancer drug candidates

Internally discovered and developed, chemistry platform

5 Pharma/Biotech corporate alliances

MedImmune, Novartis  
(2), Amgen, and J & J

Proven biotech leadership team

Significant cash position

Projected cash runway through end of 2009

Enough cash to reach key value-driving events before any additional  
alliances or financing

Snapshot of Post-Merger Infinity (NASDAQ: INFI)

Status of Reverse Merger

Announce merger

File Initial S4

S-4 is Declared Effective

S-4 mailed to DPI and IPI Stockholders

Stockholder meeting/vote scheduled

Deal Closes, INFI publicly traded

April 12, 2006

July 11, 2006

August 7, 2006

August 9-10, 2006

September 12, 2006

Following successful vote

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## IPI-504

lead proprietary oncology drug candidate (Hsp90)

Phase I in GIST and multiple myeloma commenced 2005

Phase II anticipated in 2007

## Hedgehog pathway

preclinical oncology candidate

Novel Hsp90 inhibitor

Currently in 2 phase I clinical trials:

GIST

Multiple myeloma

Ready for Phase II in 2007

Both IV (water-soluble) and oral  
formulations

CI

-

Infinity's lead clinical product: IPI-504 (Hsp90 inhibitor)

IPI-504

OH

N

H

N  
OH  
O  
OH  
Me  
O  
O  
O  
O  
NH  
2  
H  
H  
+



Heat Shock Protein 90 (Hsp90) is an emerging cancer target

Hsp90 in cancer cells differs from

Hsp90 in normal cells

Function of Hsp90 in cancer cells

General chaperone function

essential for protein homeostasis

Specific chaperone function

stabilization of oncogenic proteins in key cell signaling pathways

Preferential targeting to cancer

Dependence  
on Hsp90  
Apoptosis  
Tyrosine kinase  
inhibitor  
(e.g  
Gleevec, Tarceva)  
Oncogene  
Cancer cell  
survival &  
proliferation  
Resistance  
mutations  
Hsp90  
inhibitor  
Targeting specific oncogenic Hsp90 client proteins  
Hsp90  
inhibitor

Velcade  
Gleevec / dasatinib  
Investigational  
Gleevec / Sutent  
Herceptin  
Tarceva  
/ Erbitux  
Sorafenib  
/ Sutent  
Sorafenib  
Investigational  
Targeted therapy  
The emerging world of targeted cancer therapies  
Indication  
Myeloma  
CML  
AML  
GIST

Breast (HER2+)  
NSCLC  
Renal cell  
Melanoma  
Prostate (PTEN -/-)  
NF-  
B  
Bcr-Abl  
Flt3  
c-Kit  
HER2  
EGFR  
VEGFR / HIF-1a  
b-Raf  
p-Akt  
Molecular Target

The emerging world of targeted cancer therapies

NF-

B

Bcr-Abl

Flt3

c-Kit

HER2

EGFR

VEGFR / HIF-1a

b-Raf

p-Akt

Molecular Target

All are clients of Hsp90

Inhibiting Hsp90 affects the  
stability of these targets

Attractive alternative to  
chasing tumor-specific  
resistance mutations

History of Geldanamycin  
analogs

17-AAG is a semi-synthetic natural  
product, derived from Geldanamycin

17-AAG activity:

Potent & selective inhibitor of  
Hsp90

Well-tolerated in humans (>400  
patients tested in multiple  
Phase I trials)

Removed chemical reactivity of

geldanamycin

Problems:

Highly insoluble

Sub-optimal DMSO-and  
Cremophor  
based formulations

Off-patent

O

N

H

H

N

O

Me

O

OH

Me

Me

O

Me

O

O

O

N

H

Me

Me

17-AAG

\*Reference: Kamal  
et al, Nature,  
2003, 425,.407-410



Novel chemical entity

Patient-friendly formulations

IV in two Phase 1 trials

Oral under development

Broad therapeutic potential

Large therapeutic window  
consistent with targeted therapies

Activity in resistant settings

Strong intellectual property position

Ready for Phase 2 in 2007

CI

-

Infinity's lead clinical product: IPI-504 (HSP90 inhibitor)

IPI-504

OH

N

H

N

OH

O

OH

Me

O

O

O

O

NH

2

H

H

+

IPI-504

IPI-504 competitive landscape for IV formulation

POTENCY

NCE

PATENT?

DELIVERY

CHEMICAL

PROPERTIES

MTD

COMPOUND

COMPANY

17-DMAG

KOS-1022

~25-50 nM

Yes

IV 60 120

min

Chemically

reactive

alkylating

agent

<24 mg/m<sup>2</sup>

Kosan

17-AAG

KOS-953

~25-50 nM

No

IV 60-120 min

in Cremophor

Special tubing

Steroid

pretreatment

Emulsion

changes

distribution

and PK

Dose escalation

ongoing;

>

340 mg/m<sup>2</sup>

Kosan

Emulsion

changes

distribution

and PK

17-AAG

CNF-1010

~25-50 nM

No

IV 60 min

in lipid

emulsion

175 mg/m<sup>2</sup>

Biogen/

Conforma

Emulsion

changes

distribution

and PK

17-AAG

~25-50 nM

No

IV 60 min in

DMSO/Egg  
220 mg/m<sup>2</sup>  
Kosan  
IPI-504  
~25-50 nM  
IV 30 min  
Diffusion  
controlled  
distribution  
Dose escalation  
ongoing at  
400 mg/m<sup>2</sup>  
Yes  
Infinity

IPI-504 competitive landscape for PO formulations

IPI-504 (same  
molecule as IV)

17-DMAG

CNF-2024

Small Molecule

Small Molecule

Small Molecule

Compound

Company

Phase of Development

Infinity

Kosan

Biogen

Idec

Serenex

Novartis /

Vernalis

Synta

Pre-clinical

Phase I

Phase I

Preclinical

Preclinical

Preclinical

No competitive oral product is significantly more advanced

Novel small

molecules not

derived from

geldanamycin



Intellectual property protection for IPI-504

Composition of matter

Formulations (IV and PO)

Methods of making

Methods of using

Infinity has broad patent applications pending for IPI-504

IPI-504 Preclinical Data

\*  
\*  
\*  
\*  
\*  
\*  
\*  
\*

Highly  
responsive to  
Hsp90 inhibition  
T315I  
T790M  
T670I  
Preclinical evidence of potential as salvage therapy  
BCR-ABL  
EGFR  
KIT  
Hsp90 Client  
Disease  
Drug  
CML  
NSCLC  
GIST  
Gleevec,  
Dasatinib  
Tarceva,  
Iressa  
Gleevec,

Sutant  
Kinase  
Inhibitor  
Resistance  
Mutation

CML / Bcr-Abl  
Wild-type protein  
Bcr  
Abl  
Non-cancer related  
Protein status  
Entity  
Function  
Hsp90-  
dependent  
Gain-of-function  
mutant  
Bcr-Abl  
fusion  
Constitutively  
activated signaling  
Drug-resistant  
mutant  
Bcr-Abl  
(T315I)

TKI-resistant  
kinase

Gleevec-refractory primary CML cells sensitive to IPI-504

0

10

20

30

40

50

60

70

Pt 1

Pt 2 (T315I)

Pt 3

Control

0.5 uM IPI-504

2.0 uM IPI-504

Collaboration:

Kapil Bhalla, Moffitt Cancer Center

Placebo  
Gleevec  
IPI-504  
Collaboration:  
Shauguang  
Li, Jackson Labs  
0.0%  
20.0%  
40.0%  
60.0%  
80.0%  
100.0%  
15  
17  
19  
21  
23



25

27

29

31

33

Days

Oral IPI-504: survival benefit in Gleevec-resistant T315I

CML transplantation model

Placebo  
Gleevec  
IPI-504  
0.0%  
20.0%  
40.0%  
60.0%  
80.0%  
100.0%  
15  
17  
19  
21  
23  
25  
27  
29

31

33

Days

Oral IPI-504: survival benefit in Gleevec-resistant T315I

CML transplantation model

Collaboration:

Shauguang

Li, Jackson Labs

Placebo  
Gleevec  
IPI-504  
0.0%  
20.0%  
40.0%  
60.0%  
80.0%  
100.0%  
15  
17  
19  
21  
23  
25  
27  
29

31

33

Days

Oral IPI-504: survival benefit in Gleevec-resistant T315I

CML transplantation model

Collaboration:

Shauguang

Li, Jackson Labs

NSCLC / EGFR  
Wild-type protein  
EGFR  
Ligand-dependent  
RTK  
Protein status  
Entity  
Function  
Hsp90-  
dependent  
Gain-of-function  
mutant  
EGFR  
(  
exon19 or  
L858R)  
Ligand-  
hypersensitive RTK  
Drug-resistant  
mutant

EGFR  
(  
exon19 or  
L858R + T790M)  
TKI-resistant,  
ligand  
hypersensitive RTK

0  
500  
1000  
1500  
2000  
2500  
3000  
3500  
4000  
12  
15  
19  
22  
26  
27  
32



Days Post-Implant  
IPI-504 Vehicle, IP  
Gefitinib Vehicle, PO  
100mpk Gefitinib, PO  
100mpk IPI-504, IP

100mpk  
IPI-504  
2X  
weekly  
IP;  
100mpk  
Gefitinib  
daily  
PO  
for  
3  
weeks

21%  
difference  
in  
tumor  
volumes  
between  
vehicle  
and  
Gefitinib  
treated  
groups  
( $p=0.54$ )

69% difference in tumor volumes between vehicle and IPI-504 treated groups ( $p=0.009$ )

69%  
Non small cell lung cancer xenograft with T790M EGFR  
Tarceva/Iressa-resistance mutation

GIST / Kit  
Wild-type protein  
Kit  
Ligand-dependent  
RTK  
Protein status  
Entity  
Function  
Hsp90-  
dependent  
Gain-of-function  
mutant  
c-Kit  
Ligand-independent  
RTK  
Drug-resistant  
mutant  
c-Kit (T670I)  
TKI-resistant,  
ligand-independent

RTK

GIST: Gleevec-resistant cells more sensitive to IPI-504

GIST 882\*

Gleevec-Sensitive

(primary: exon

13, K642E)

10

100

1000

10

20

30

40

50

10000

60

70

Compounds concentrations (nM)

10

100

1000

10

20

30

40

50

10000

10000

60

70

Compounds concentrations (nM)

IPI-504 : EC50 = 121 +/-

21 nM

IM : EC50 = 147 +/-

42 nM

Gleevec-

Resistant

(primary: exon

11, V560D +

Gleevec resistance: exon

17, D820A)

10

100

1000

5

15

25

35

45

55

65

75

85

Compounds concentrations (nM)

IPI-504

Imatinib

GIST 48\*

IPI-504 : EC50 = 54 +/-

7 nM

IM : 25% inhibition @ 10uM

Collaboration:

Fletcher, Demetri, DFCI

IPI-504 Clinical Development Strategy

\*  
\*  
\*  
\*  
\*  
\*  
\*  
\*  
\*

Development and registration of IPI-504 in hematologic malignancies and solid tumors

Preclinical support for broad role of Hsp90

Early human proof-of-concept with most rapid path to registration

Strong scientific rationale

Trials targeted to homogenous patient population (disease-focused)

Surrogate marker

Rapid patient accrual

Single-agent activity in refractory setting (potential for expedited approval)

In parallel, initiate broader development for larger indications (additional diseases, combination therapy, front-line therapy)  
IPI-504 Clinical Development Strategy

Principal Investigator:

Dr. George Demetri, DFCI

Objectives:

Safety, PK, dose-ranging

Establish Phase II dose

Surrogate marker of response:

PET scans

Solid Tumor

Gastrointestinal Stromal Tumors

(Gleevec-resistant)



Schedule / status:

Days 1, 4, 8, 11 of 21 day

Continuing dose escalation

Current ongoing phase I clinical trials

Principal Investigator:

Dr. Paul Richardson, DFCI

Dr. Sundar Jagannath, SVCCC

Dr. David Siegel, HUMED

Objectives:

Safety, PK, dose-ranging

Establish Phase II dose

Surrogate marker of response:

M protein levels

Hematologic

Multiple Myeloma

(relapsed, refractory)

Schedule / status:

Days 1, 4, 8, 11 of 21 day

Continuing dose escalation

Phase I dose escalation for IPI-504 (GIST)

1 cycle = 21 days

4 doses (days 1, 4, 8, 11 followed by 10 days off)

Phase I schedule

25%

500

6

33%

400

5

33%

300

4

50%

225  
3  
66%  
150  
2  
100%  
90  
1  
Escalation over  
previous dose  
Dose (mg/m<sup>2</sup>)  
Group

Near-term sequence of additional clinical indications  
(2006/2007)

Resistance

Mutation

Disease

PI

T. Lynch

T. Kipp, CLL  
consortium

Matsui, Smith /

Bhalla

NSCLC

CLL

CML

Tarceva-R

(T790M )

Zap-70

T315I

Focused trials would determine IPI-504 activity in patients with known resistance to targeted therapy

If positive, trials provide opportunity to rapidly advance to market

Additional indications to follow

Site

MGH

UCSD

JHU, Moffitt

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## IPI-504

lead proprietary oncology drug candidate (Hsp90)

Phase I in GIST and multiple myeloma commenced 2005

Phase II anticipated in 2007

## Hedgehog pathway

preclinical oncology candidate

Potential for first-in-class systemic hedgehog inhibitor

Proprietary NCE s

Systemic (sub-cu and oral) products

Lead molecule (IPI-609) in advanced preclinical development

First in man expected in 2007

Broad anti-cancer potential

Strong data supporting pancreatic, metastatic prostate, SCLC, others

Single agent activity

Potential for synergy with standards of care  
Infinity s Hedgehog program

History of cyclophosphamide  
chemical discovery  
1950 s

Lambs born in Idaho with cyclopic  
features (defect in development of  
left-right asymmetry)

USDA determines that pregnant  
ewes grazed on the plant *Veratrum*  
*californicum*

Cyclophosphamide  
identified as the  
teratogenic substance in *V.*  
*californicum*



Purified cyclopamine given to  
animals recapitulates cyclopic  
features and other birth defects  
*V. californicum*  
cyclopamine

History of hedgehog  
genetics  
40 years later (1980 s to today)

Genes are discovered that control  
embryonic development and pattern  
formation

One such gene is called hedgehog

Hedgehog mutations in the Drosophila  
fruit fly result in cyclopia

Hedgehog function in humans related  
to development of the pancreas, gut,

and other elements of GI tract

Cyclopamine chemistry meets hedgehog genetics

Chemistry

The chemical cyclopamine  
results in cyclopic animals

Genetics

Mutation of hedgehog pathway  
results in cyclopic animals

Might the chemical cyclopamine interact  
with genes in the hedgehog pathway?

YES

Cyclopamine is a smoothed antagonist

\*Chen et al., 2002 **G&D**

16:2743

Cyclopamine

Normal

Cancer

Cancers have hijacked components of the hedgehog pathway

#

ON = active repressor of Smo

\* Mutation in Patched

1

Hahn *et al.*, 1996, **Cell**

85: 841

2

Bale & Yu, 2001, **Human Molec. Genetic.** 10: 757 (review)

3

Berman *et al.*, 2002 **Science**

297: 1559

4

Berman *et al.*, 2003 **Nature**

425: 846

5

Kayed *et al.*, 2004 **Int. J. Cancer**

110: 668

6

Thayer *et al.*, 2003 **Nature**

425: 851

7

Karhadkar *et al.*, 2004 **Nature**, 431: 707

8

Fan *et al.*, 2004 **Endocrinology**

145: 3961

9

Watkins *et al.*, 2003, **Nature**

422: 313

10

Sicklick 2005 **ASCO**; Mohini, 2005 **AACR**

11

Kubo *et al.*, 2004 **Cancer Res.** 64

:6071

State

Normal

Basal cell carcinoma\*

1,2

Medulloblastoma\*<sup>3</sup>

Pancreatic cancer

4,5,6

Prostate cancer

7,8

Small cell lung cancer

9

Hepatocellular cancer

10

Breast Cancer

11

Smoothened

OFF

ON

ON

ON

ON

ON

ON

ON

Patched

#

ON

Mutant -

OFF

Mutant -

OFF

OFF

OFF

OFF

OFF

OFF

Hedgehog

OFF

OFF

OFF

Turned ON

Turned ON

Turned ON

Turned ON

Turned ON

Frequency

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95%

30-40%

100%

100%

50%

n/a

100%



Cyclopamine validates Hedgehog as a cancer target

Cyclopamine is a plant natural product produced by *Veratrum californicum*

Cyclopamine activity:

Potent inhibitor of Smoothed

Highly active in pancreatic, prostate, small cell lung cancer animal models

Drawbacks:

Insoluble

Caustic formulations

Off-patent

HO

O

HN

H

H

H

H

H

Infinity's lead Hedgehog pathway inhibitors

Novel candidates based on cyclopamine

On mechanism

Superior to cyclopamine:

More chemically stable

More potent

More soluble

Most advanced candidate (IPI-609) in late-preclinical development

First in man 2007

i.v., s.c., or oral formulations

Better oral bioavailability

Better tumor PK

IPI-609 competitive landscape

CUR-61414

Curis and Genentech Hedgehog antagonist

Highly insoluble: not suitable for systemic administration

Topical formulation failed in Phase 1 Basal Cell Carcinoma trial; failure attributed to formulation, not pathway

Curis and Genentech have expressed continued interest in the Hedgehog pathway for systemic agents

Intellectual property protection for IPI-609

Novel scaffold for IPI-609 and analogs with patent applications pending

We believe there are no patents preventing us from marketing IPI-609 or its analogs

0  
200  
400  
600  
800  
1000  
1200  
1400  
1600  
31  
36  
41  
46  
51  
56  
61

Days

Vehicle

IPI-609 10 mpk/day

IPI-609 efficacious in PC-3 prostate xenograft

IPI-609 slows tumor growth rates

0  
200  
400  
600  
800  
1000  
1200  
30  
35  
40  
45  
50  
55  
60

Day

Linear Fit

Bivariate Fit of P 10 By Day



200  
400  
600  
800  
1000  
1200  
30  
35  
40  
45  
50  
55  
60  
Day  
Linear Fit  
Bivariate Fit of VP 6 By Day  
Median vehicle-treated  
animals  
Median IPI-609 treated  
animals

Clinical development strategy of hedgehog pathway inhibitors

Strong scientific rationale supports targeting of cancers dependent on the Hedgehog pathway

Pancreatic

Small cell lung

Metastatic prostate

Metastatic breast

Ovarian

Others (medulloblastoma, glioma, basal cell carcinoma, etc.)

Identify a rapid path to registration

Potential for sole agent activity or

Combination with a single Standard of Care

Key Principal Investigator relationships established

Pancreatic cancer

Manuel Hidalgo, MD Johns Hopkins

(PCRT

Dan Van Hoff, MD)

Small cell lung cancer

Charles Rudin, MD Johns Hopkins

Prostate cancer

Phil Kantoff, MD DFCI

Howard Scher, MD MSKCC

Chris Logothetis, MD MD Anderson

Prostate Consortium

Breast

Max Wicha, MD U of Michigan

Heme malignancies

Doug Smith, MD Johns Hopkins

Bill Matsui, MD Johns Hopkins  
Kapil Bhalla, MD Moffitt Cancer Ctr

Infinity Pharmaceuticals  
Summary

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\*  
\*  
\*  
\*  
\*

Product Pipeline

IPI-504: Complete Phase I trials

Publish First Clinical Data

IPI-504: Expect to initiate Phase II in 2007

Hedgehog Pathway: Expect to initiate  
Phase I in 2007

Successful alliance execution

At least one new corporate alliance

Financing event

Year-end cash runway:

12-24 months

2006/Early 2007 Goals, Achievements and Anticipated News Flow

Pending

DPII merger

AMGN

extension

Expected

at EORTC

11/7/06

NVS (Bcl)

MEDI (Hsp90, HH)