# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION

**Washington, D.C. 20549**

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# FORM 8-K

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

**August 10, 2007**
**Date of Report (Date of earliest event reported)**

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# PRO-PHARMACEUTICALS, INC.

**(Exact Name of Registrant as Specified in Charter)**

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| NEVADA | 000-32877 | 04-3562325 |
|---|---|---|
| **(State or Other Jurisdiction of Incorporation)** | **(Commission File Number)** | **(IRS Employer Identification No.)** |

**7 WELLS AVENUE**
**NEWTON, MASSACHUSETTS**
**02459**
**(Address of Principal Executive Offices) (Zip Code)**

**(617) 559-0033**
**(Registrant's telephone number, including area code)**

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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 (*see* General Instruction A.2. below):

☐ 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))

**Regulation Fair Disclosure**

**Item 7.01. Regulation FD Disclosure.**

The information in this Report, including the slides attached hereto as Exhibit 99.1, is being furnished pursuant to this Item 7.01 and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section, and it shall not be deemed incorporated by reference in any filing under the Securities Act of 1933 or under the Exchange Act, whether made before or after the date hereof, except as expressly set forth by specific reference in such filing to this Report.

By filing this Report and furnishing this information, the Company makes no admission as to the materiality of any information in this Report. The information contained in the slides is summary information that is intended to be considered in the context of the Company's filings with the Securities and Exchange Commission (the "SEC") and other public announcements that the Company makes, by news release or otherwise, from time to time. The Company undertakes no duty or obligation to publicly update or revise the information contained in this Report, although it may do so from time to time as its management believes is appropriate. Any such updating may be made through the filing of other reports or documents with the SEC, through news releases or through other public disclosure.

The Company cautions you that information included in the slides attached hereto as Exhibit 99.1 that are not a description of historical facts are forward-looking statements that involve risks, uncertainties, assumptions and other factors that, if they do not materialize or prove to be accurate, could cause the Company's results to differ materially from historical results or those expressed or implied by such forward-looking statements. Such forward-looking statements are made based on management's current expectations and beliefs and should not be regarded as a statement or representation by the Company that any of its plans, including its anticipated milestones, will be achieved on time or at all. The potential risks and uncertainties that could cause actual results to differ materially include, but are not limited to: the risk that the Company will be unable to raise sufficient capital to fund the projects necessary to meet its anticipated or stated goals and milestones; the potential to attract a strategic partner and the terms of any related transaction; the ability to timely enroll subjects in the Company's current and anticipated clinical trials; the potential for DAVANAT® to receive regulatory approval for one or more indications on a timely basis or at all, and the uncertain process of seeking regulatory approval; other difficulties or delays in developing, testing, manufacturing and marketing of and obtaining regulatory approval for DAVANAT®; the market potential for carbohydrate-based compounds, and the Company's ability to compete in those markets; unexpected adverse side effects or inadequate therapeutic efficacy of DAVANAT® or the Company's other products that could delay or prevent regulatory approval or commercialization, or that could result in recalls or product liability claims; the risk that pre-clinical results are not indicative of the success of subsequent clinical trials and that products will not perform as pre-clinical data suggests or as otherwise anticipated; the potential for regulatory authorities to require additional pre-clinical work or other clinical requirements to support regulatory filings; the scope and validity of patent protection for DAVANAT® and the Company's other product candidates; and other risks and uncertainties more fully described in the Company's news releases and periodic filings with the Securities and Exchange Commission. The Company's public filings with the Securities and Exchange Commission are available at http://www.sec.gov.

You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date when made. All forward-looking statements are qualified in their entirety by this cautionary statement and the Company assumes no obligation to revise or update any forward-looking statement, including any information included in the slides attached hereto as Exhibit 99.1, to reflect events or circumstances arising after the date on which it was made. This caution is made under the safe harbor provisions of Section 21E of the Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section, and it shall not be deemed incorporated by reference in any filing under the Securities Act of 1933 or under the Exchange Act, whether made before or after the date hereof, except as expressly set forth by specific reference in such filing to this Report.

**Item 9.01 Financial Statements and Exhibits.**

**(d) Exhibits.**

The list of exhibits called for by this Item is incorporated by reference to the Index to Exhibits filed with this report.

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**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.

PRO-PHARMACEUTICALS, INC.

By: /s/ Carl L. Lueders

Carl L. Lueders
Chief Financial Officer

Date: August 10, 2007

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EXHIBIT INDEX

| Exhibit Number | Exhibit |
|---|---|
| 99.1 | Pro-Pharmaceuticals Presentation Slides - dated August 10, 2007 |

PRO PHARMACEUTICALS, INC.

ADVANCING DRUGS THROUGH GLYCOSCIENCE®

www.Pro-Pharmaceuticals.com

Amex: PRW

# Forward Looking Statements

Any statements in this presentation about future expectations, plans and prospects for the Company, including statements containing the words "believes," "anticipates," "plans," "expects," and similar expressions, constitute forward looking statements, which are subject to the safe harbor for such statements in the Private Securities Litigation Reform Act of 1995. Future events could cause actual results to differ materially from those indicated by such statements. Reference is made to the factors discussed in the "Management Discussion and Analysis" and "Risk Factors" sections of the Company's most recent quarterly or annual report filed with the Securities and Exchange Commission. The forward-looking statements herein represent the Company's views as of the date of this presentation and should not be relied upon to represent the Company's views as of a subsequent date. While the Company anticipates that subsequent events may cause the Company's views to change, the Company disclaims any obligation to update such forward-looking statements.

# Agenda

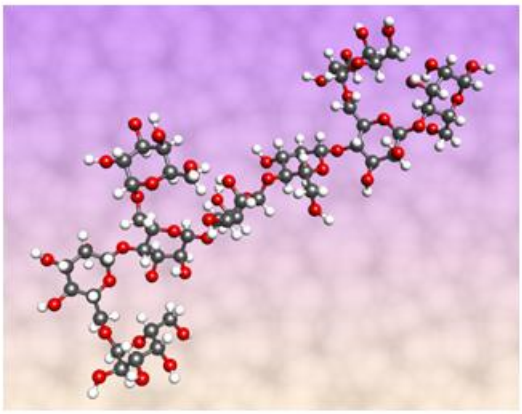
- Highlights
- DAVANAT®
- Milestones To Date
- The Commercial Opportunity
- Clinical Trial Summary
- DAVANAT®/5-FU Side Effects
- Milestones 2H07-1H08
- Product Development Pipeline
- Intellectual Property
- Regulatory Strategy
- Management Team
- Financial Summary
  - Appendices: Carbohydrate Technology – DAVANAT®: Pre-Clinical and Clinical Studies – Other Pro-Pharmaceuticals' Compounds – Regulatory Pathway

# Highlights

- PRW has developed a new class of proprietary carbohydrate compounds, DAVANAT®, which
- Provides a paradigm shift in drug delivery
  - Improves the pharmacokinetics/pharmacodynamics and toxicity profile of current and 'shelved' drugs
  - Creates new intellectual property
  - Implements life cycle management options
- Focuses on major unmet medical needs
  - Initial products will increase the efficacy and reduce toxicity of chemotherapeutics
  - Multi-billion dollar market opportunity
- Utilizes the relatively streamlined 505(b)(2) regulatory process to seek FDA approval
- And, will be brought to market by PRW working in alliance with strategic partners

# DAVANAT®

- Proprietary polysaccharide galactomannan polymer consisting of galactose units attached to a mannan backbone
- Derived from seeds of the plant Cyamopsis tetragonoloba
- Affects biology of galectin molecules
- Changes the efficacy, toxicity, pharmacokinetic and distribution properties of chemotherapeutic drugs in animal & human models

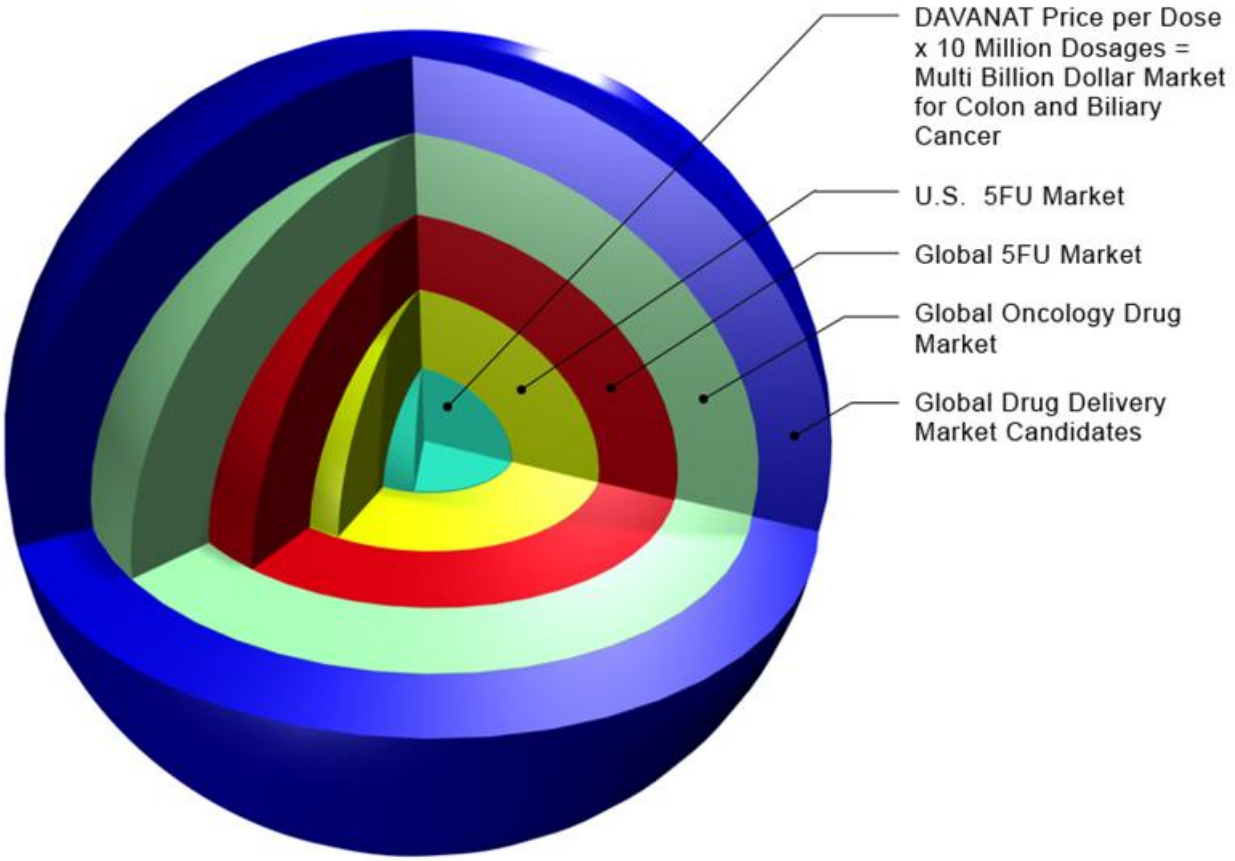


- Galactomannans have GRAS (generally recognized as safe) status

# Key Milestones To Date

- PRW commenced operations in 2001
- Raised $36 million to date
- Built strong team with carbohydrate polymer experience
- 5 patents issued
- Completed Phase I/II cancer trials; 60 patients dosed with DAVANAT®/5-FU
  - Stabilized 43% of end stage patients w/ measurable disease: 2-13 months
  - Stabilized 36% of end stage colorectal cancer patients vs. 19% for Avastin®
- Results from ongoing Phase II biliary/colorectal trials promising
- Hired a major regulatory consulting firm to advise on regulatory filings
- Qualified a manufacturing source with a major biopharmaceutical partner
- Completed research agreements with two bio-pharmaceutical companies
- Active discussions ongoing with potential commercial partners

# DAVANAT®/5-FU Commercial Opportunity



# Clinical Trial Summary

- 60 cancer patients dosed with DAVANAT®/5-FU in completed Phase I/II
- Stabilized 43% of end stage patients with measurable disease: 2-13 months
- Stabilized 36% of end stage colorectal cancer patients vs. 19% for Avastin®
- Maximum Tolerated Dose/Dose Limiting Toxicity not reached
- DAVANAT® increased 5-FU exposure with no toxicity increase
- Dosing biliary and colorectal cancer patients in Phase II front line trials:
  - Biliary (8 patients dosed) – 1 PR; 5 stabilized more than 5 cycles
  - Colorectal (8 patients dosed) – 2 PR; 5 stabilized more than 7 cycles

# DAVANAT®/5FU Major Side Effects

- No Mucositis
- No Drug Related Diarrhea
- No Drug Related Abdominal Cramping
- No Drug Related Leukopenia

"For as long as I have been in practice, 5-FU/LV has been the standard of care for patients with localized colon cancer. Side effects included mucositis, frequent diarrhea, abdominal cramping and leukopenia"

Source: Dr. George R. Bowers MD/Cooley Dickinson Hospital. CDH Oncology, November 2004, Volume 8: No 11.

# Upcoming Milestones 2H07 – 1H08

- Submit 505(b)(2) application to FDA with DAVANAT® as a functional excipient to 5-FU
- Submit DAVANAT®/5-FU/Leucovorin under 505(b)(2)
- Submit DAVANAT®/5-FU/Leucovorin/Irinotecan under 505(b)(2)
- Submit DAVANAT®/5-FU/Leucovorin/Avastin®* under 505(b)(2)
- Report additional results from ongoing Phase II biliary and colorectal cancer trials; both represent potential orphan drug status
- Scale-up production of DAVANAT®
- Actively pursue corporate partnerships for commercialization
- Continue to complete research agreements with biopharma companies for drugs with potential 505(b)(2) submissions

** Avastin® is a registered trademark of Genentech, Inc.*

# Product Development Pipeline: August 2007

| PRODUCT | INDICATION | DEVELOP | PRE-CLINICAL | PHASE 1 | PHASE 2 | PHASE 3 |
|---|---|---|---|---|---|---|
| DAVANAT®/5-FU | All Solid Tumors Completed | | | → | | |
| DAVANAT®/5-FU | Colorectal Cancer Completed | | | → | → | |
| DAVANAT®/5-FU | Biliary Cancer Ongoing | | | → | → | |
| DAVANAT®/5-FU/LV/ AVASTIN® | Colorectal Cancer Ongoing | | | → | → | |
| PRO-GR 300 | Liver Disease | | | → | | |
| PRO-NAC 050 | Microbial Disease | | | → | | |

# Strong IP Position in Carbohydrate Polymers

- 5 issued patents, 13 pending U.S. applications
- Composition of matter and field of use patents
- Subset of key patents
  - U.S. Pat 6,642,205 (11/04/03) – Methods and Compositions for Reducing side effects in Chemotherapeutic Treatments
  - U.S. Pat 6,645,946 (11/11/03) – Delivery of a Therapeutic Agent in a Formulation for Reduced Toxicity
  - U.S. Pat 6,914,055 (07/05/06) – Delivery of a Therapeutic Agent in a Formulation for Reduced Toxicity
  - U.S. Pat 6,982,255 (01/03/06) – Delivery of a Therapeutic Agent in a Formulation for Reduced Toxicity
  - U.S. Pat 7,012,068 (03/14/06) – Co-administration of a Polysaccharide with a Chemotherapeutic agent for the Treatment of Cancer
- Patents pending for a variety of non-oncology indications

# Regulatory Strategy

- Submit data to allow a 505(b)(2) designation for DAVANAT® as a functional excipient to be co-administered w/5-FU for intravenous application to treat cancer
- Retained Camargo Pharmaceutical to provide regulatory support
  - 24 successful 505(b)(2) programs
  - 150 FDA approvals, NDA, ANDA, 505(b)(1), 505(b)(2)
- Submit additional 505(b)(2) applications
  - DAVANAT®/5-FU/Leucovorin (LV)
  - DAVANAT®/5-FU/LV/Irinotecan
  - DAVANAT®/5-FU/LV/Avastin®*
  - DAVANAT®/5-FU/LV/Cisplatin
  - DAVANAT®/5-FU/LV/Oxaliplatin

**Avastin® is a registered trademark of Genentech, Inc.*

# DAVANAT® – 505(b)(2) Submissions

| Compound | Submission Type | Date | Treatment Regimen(s) | | |
|---|---|---|---|---|---|
| DAVANAT® | 505(b)(2) | 4Q07/1Q08 | 5-FU | | |
| | | | 5-FU | Leucovorin | |
| | | | 5-FU | Irinotecan | Leucovorin |
| | | 2Q08/3Q08 | 5-FU | Avastin®* | Leucovorin |
| | | | 5-FU | Oxaliplatin | Leucovorin |
| | | | 5-FU | Cisplatin | Leucovorin |

**Avastin® is a registered trademark of Genentech, Inc.*

# Management Team

- David Platt, Ph.D., Chairman & Chief Executive Officer
  - Co-founder, co-developer of Glycoscience technology. Founder: SafeScience; developed anti-angiogenesis drug. U of Michigan, Weizmann Institute, Hebrew U
- Anatole Klyosov, Ph.D., D.Sc., Chief Scientist
  - Co-founder, co-developer of Glycoscience technology. National Prize in Science & Technology (Russia); Visiting Biochemistry Prof at Harvard. Moscow State U
- Carl Lueders, MBA, CPA, Chief Financial Officer
  - 20+ years in finance & strategic planning at Polaroid
- Maureen Foley, Chief Operating Officer
  - 25+ years in biotech, high-tech in operations management
- Eliezer Zomer, Ph.D., Exec. V.P., Clinical Development & Mfg
  - Former Research Associate at Harvard Medical
- Anthony Squeglia, MBA, V.P., Investor Relations
  - 20+ years in IR/PR
- David Donabedian, Ph.D., MBA, Business Development (Consultant)
  - 12+ years in life sciences industry; VP, Bus Dev, Surface Logix; Accenture; Dow Chemical
- Bruce Silver, M.D., Medical Director (Consultant)
  - 20+ years in oncology

# Financial Summary

- Founded: July 2000
- Capital raised: $36 million (cumulative)
- Cash: $2.4 million (06/30/07)
- Burn rate: $1.2 million per quarter
- Shares outstanding: 40.4 million (06/30/07)
- Fully diluted: 52.1 million (06/30/07)
- Debenture converted (except for $280K as of 08/09/07)

# Appendices

# Carbohydrate Technology

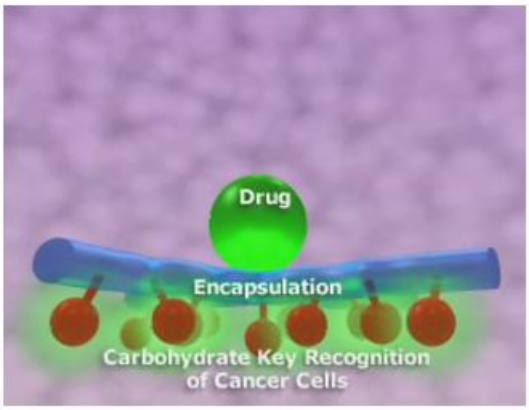
# Carbohydrates as Therapeutics

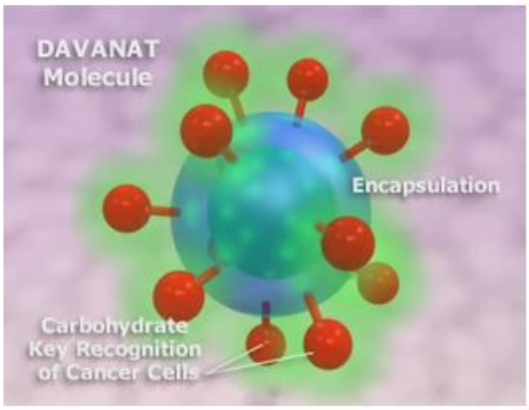
- A novel class – only now beginning to be explored for therapeutic potential
- Structurally heterogeneous – linear and branched, small and large molecules
- Diverse biological forms – as glycoproteins, glycolipids, sugars, and complex carbohydrates in plants, animals, fungi, and bacteria
- Diverse biological roles – structure, energy, signaling, adhesion, protection
- Natural biological sources
- Interact with lectins – carbohydrate-specific proteins involved in cell-cell and cell-matrix interactions

# DAVANAT®: Proposed Mechanism of Action

- DAVANAT® targets galectins on cancer cells. Galectins affect cell development and angiogenesis
- DAVANAT® "escorts" chemotherapy into cancer cells via galectin receptors in a more efficient manner
- DAVANAT® encapsulates chemotherapy drugs in a CARBOSOME™ formation; improves pharmacokinetics

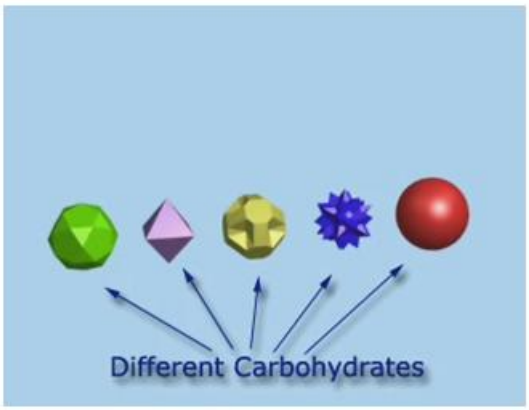
# Hypothesis: CARBOSOME™

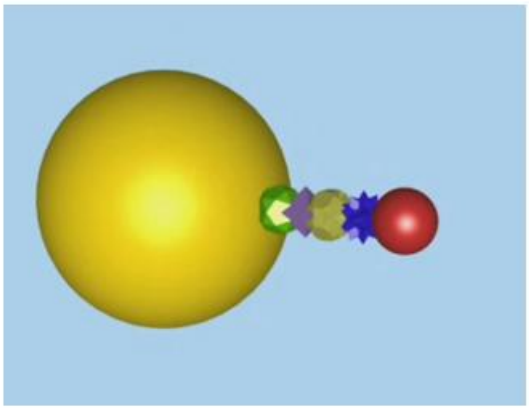



- DAVANAT® polymer exists as a "3D" structure in solution with lectin targeting units protruding from the mannan backbone

# Other Technology Platforms: UCLT™



- Enhances delivery to the target by covalently binding a carbohydrate to the inactive side of the molecule

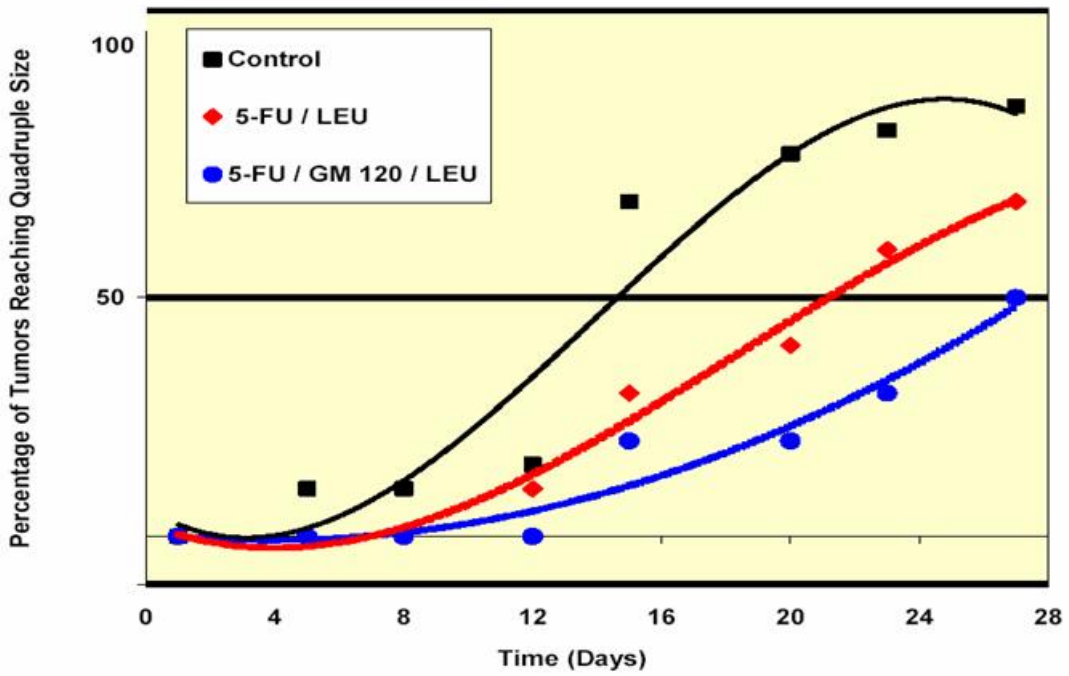
# DAVANAT®: Pre-Clinical and Clinical Studies

# Pre-Clinical Results

## Response of HT-29, Human Colon Tumor Xenografts to DAVANAT® in Combination with 5-FU and Leucovorin

Charles River Labs
(Dose: I.V., Q4D x 4, of 5-FU: 48 mg/kg; DAVANAT®: 120mg/kg;
Oral, Leucovorin 25 mg/kg)

DAVANAT®/5-FU/LV improved tumor inhibition
vs. 5-FU/LV (21 to 27 days)

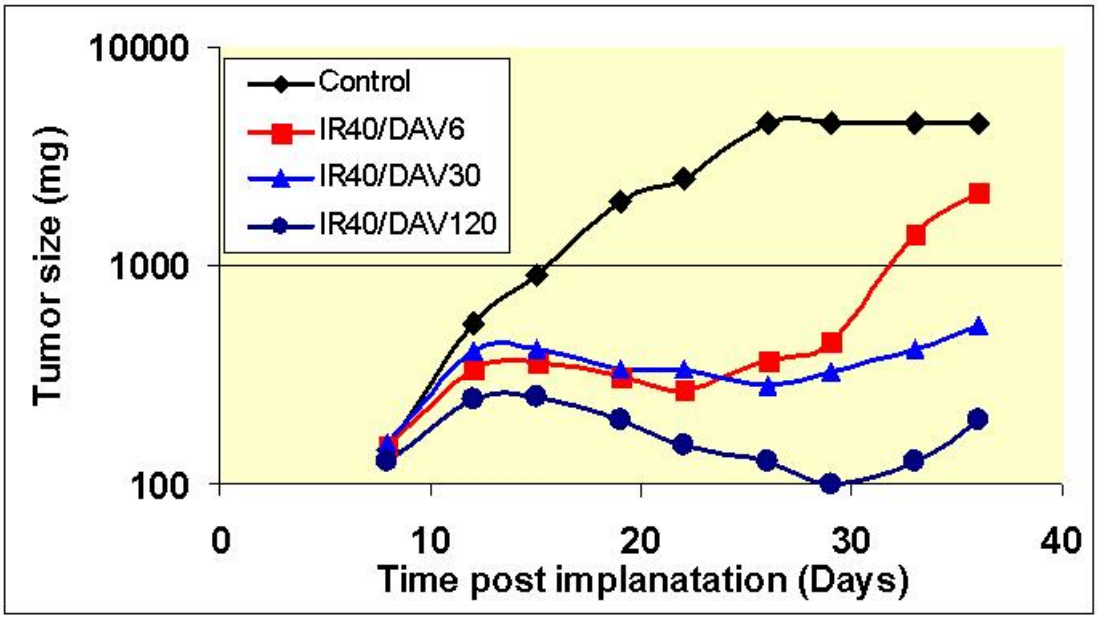


# Pre-Clinical Results

## Response of SC ZR75-1,Human Mammary Tumor Xenografts, to dose escalation DAVANAT® in Combination with Irinotecan

Southern Research Institute
(Dose I.V., Q4D x 4, of
IR 40 mg/kg; DAVANAT®:
6, 30 & 120 mg/kg)

DAVANAT®/Irinotecan improved tumor inhibition by delaying tumor growth vs. control

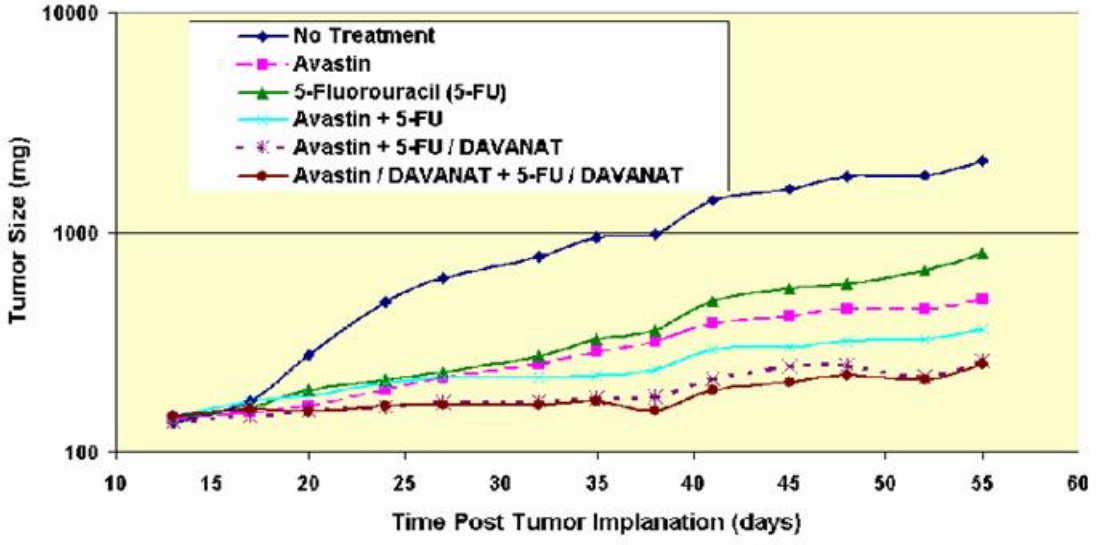


# Pre-Clinical Results

## Response of COLO 205, Human Colon Tumor Xenografts, to DAVANAT® in Combination with 5-FU & Bevacizumab

Southern Research Institute (Dose: I.V., Q4D x 4, of 5-FU 50 mg/kg; DAVANAT®: 120 mg/kg; AVASTIN: 20-80 mg/kg)

DAVANAT® enhances effectiveness of AVASTIN® & 5-FU



# Clinical Trial Summary

- 60 cancer patients dosed with DAVANAT®/5-FU in completed Phase I/II
- Stabilized 43% of end stage patients with measurable disease: 2-13 months
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- DAVANAT® increased 5-FU exposure with no toxicity increase
- Dosing biliary and colorectal cancer patients in Phase II front line trials:
  - Biliary (8 patients dosed) – 1 PR; 5 stabilized more than 5 cycles
  - Colorectal (8 patients dosed) – 2 PR; 5 stabilized more than 7 cycles

# DAVANAT® vs. AVASTIN®*

- **Response rate – stable disease in end-stage colorectal cancer patients**

| 5-FU/LV (Historical) | AVASTIN®/5-FU/LV** (Genentech/Literature) | DAVANAT®/5-FU*** (Pro-Pharmaceuticals) |
|---|---|---|
| Median progression free survival 5.2 months | Stable disease rate 19%<br>100 Patients | Stable disease rate 36%<br>25 Patients |

- **Stable disease rate of DAVANAT®/5-FU at 36% vs. 19% for Avastin®/5-FU/LV in end stage colorectal cancer patients**

** No head-to-head studies conducted.*

*** Data obtained from AVASTIN® drug insert/ASCO Abstract. Avastin® is a registered trademark of Genentech, Inc.*

**** Data compiled from PRW Phase I and Phase II colorectal cancer patients.*

# Phase I Clinical Trial – All Solid Tumors (End Stage)

**Indication:**
All solid tumors.
End stage patients;
minimum 12 weeks to live

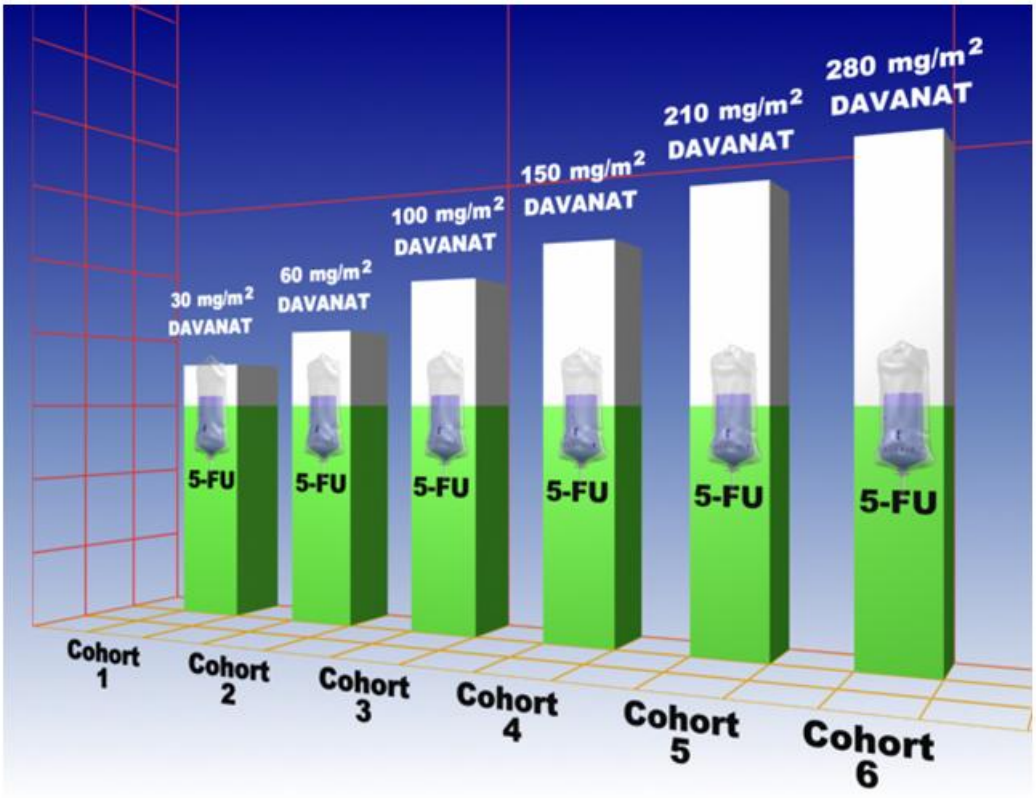
**Objectives:**
Primary – Safety
Secondary – Tumor progression; PK profile of 5-FU

**Design:**
Multi-center (4 sites), open label study.
Two cycles; six cohorts.
Cycle 1 – DAVANAT® alone
Cycle 2- DAVANAT®/5-FU

**Regimen:**
DAVANAT® escalating dose level (30-280 mg/m$^2$); 5-FU constant at 500 mg/m$^2$; dose for 4 consecutive days, observe for 24 days

**Patients:**
40; 3-10 per cohort

**Completed:**
March 2005



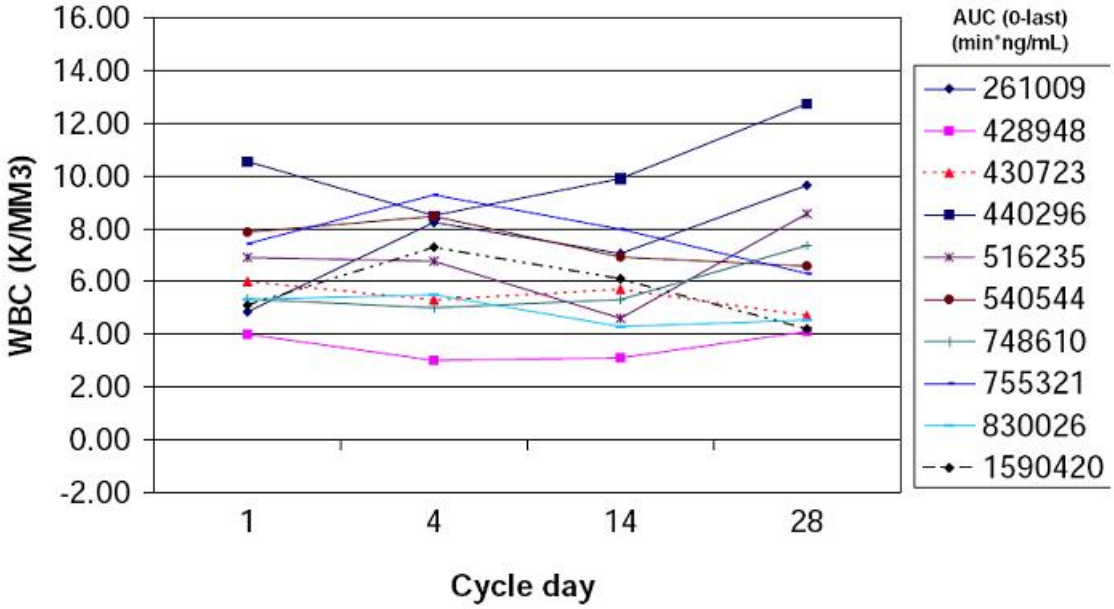
# Phase I Patient Summary: Stabilized 70% at Highest Dose Level

| | |
|---|---|
| SD | Stable Disease |
| PD | Progressive Disease |
| NM | Non-Measurable Disease |
| | Cycles Completed |

| Patient Number | Dose, cycle 2 /m2 | Tumor Type | Outcome, end of cycle 2 (RECIST) | CYCLES 1+2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|---|---|
| 1001 | 30 mg | Colorectal | PD | ■ | | | | | |
| 1002 | | | SD | ■ | ■ | | | | |
| 2001 | | Hepatocellular | PD | ■ | | | | | |
| 2002 | 60 mg | Hepatocellular | SD | ■ | | | | | |
| 3001 | | Colorectal | PD | ■ | | | | | |
| 3002 | | | SD | ■ | | | | | |
| 3004 | | | PD | ■ | ■ | | | | |
| 3003 | | | PD | ■ | | | | | |
| 5001 | | | SD | ■ | ■ | | | | |
| 2004 | 100 mg | Colorectal | SD | ■ | ■ | ■ | | | |
| 3005 | | | PD | ■ | ■ | | | | |
| 4001 | | | PD | ■ | | | | | |
| 4002 | 150 mg | Colorectal | PD | ■ | | | | | |
| 3006 | | Prostate | NM | ■ | | | | | |
| 2005 | | Colorectal | SD | ■ | ■ | ■ | | | |
| 5003 | 210 mg | Colorectal (appendix) | NM | ■ | | | | | |
| 5004 | | Colorectal | SD | ■ | | | | | |
| 4003 | | | PD | ■ | | | | | |
| 2007 | 280 mg | Spindle Cell | PD | ■ | | | | | |
| 5005 | | Pancreatic | SD | ■ | | | | | |
| 2008 | | Colorectal | SD | ■ | ■ | ■ | ■ | ■ | ■ |
| 2009 | | Colorectal | SD | ■ | ■ | ■ | ■ | ■ | |
| 5006 | | Billiary | SD | ■ | ■ | | | | |
| 2010 | | Colorectal (cecal) | SD | ■ | | | | | |
| 2014 | | Breast | SD | ■ | | | | | |
| 2016 | | Hepatic | PD | ■ | | | | | |
| 2018 | | Cholangiocarcinoma | SD | ■ | ■ | ■ | ■ | ■ | ■ |
| 5008 | | Pancreatic | PD | ■ | | | | | |

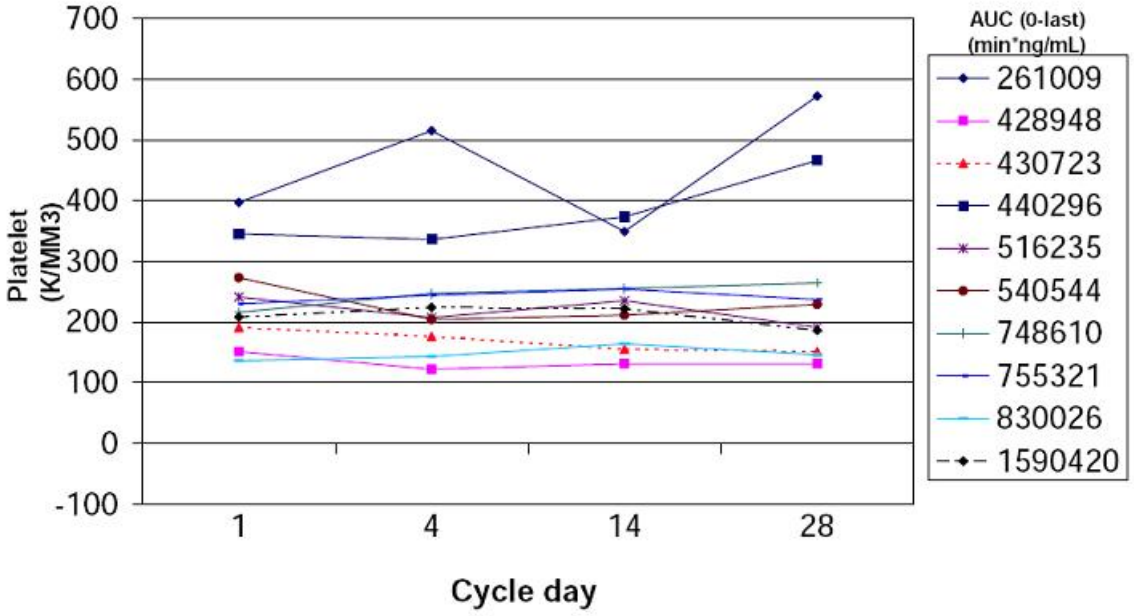
# Phase I Results

## White Blood Cell Counts Fluctuations vs. Cycle day in 10 Subjects (Cohort 6) Dosed with DAVANAT® (280 mg/m²) plus 5-FU (500mg/m²)



# Phase I Results

## Blood Platelet Count Fluctuations vs. AUCDay 1 in 10 Subjects (Cohort 6) Dosed with DAVANAT® (280 mg/m²) plus 5-FU (500mg/m²)



# Phase I SAEs by Patient, Cycle, and Relationship to Study Drug

| DAVANAT ($mg/m^2$) | Patient No. | Cycle | SAE (MEDRA preferred Term) | Relationship to Study Drug |
|---|---|---|---|---|
| 30 | 01003 | 1 | Colon cancer metastatic | Not related |
| | | | Death | Not related |
| 100 | 02004 | 3 | Rectal hemorrhage | Not related |
| | | | Anemia | Not related |
| | | | Hemorrhoids | Not related |
| | | | Hemorrhoidal hemorrhage | Not related |
| | 05002 | 1 | Perirectal abscess | Not related |
| 150 | 03006 | 1 | Prostate cancer metastatic | Not related |
| | | | Death | Not related |
| 210 | 03007 | 1 | Ovarian epithelial cancer stage IV | Not related |
| | | | Death | Not related |
| | 04003 | 2 | Atrial flutter | Not related |

# Phase I SAEs by Patient, Cycle, and Relationship to Study Drug (cont.)

| DAVANAT® (mg/m²) | Patient No. | Cycle | SAE (MEDRA preferred Term) | Relationship to Study Drug |
|---|---|---|---|---|
| 280 | 02006 | 1 | Pulmonary embolism<br>Hypoglycemia<br>Syncope | Not related<br>Not related<br>Not related |
| | 02007 | 1 | Hepatic hemorrhage | Not related |
| | 02010 | 2 | Dyspnea | Possibly related |
| | 02012 | 1 | Dehydration<br>Acute renal Failure | Possibly related<br>Not related |
| | 02013 | 1 | Abdominal Pain | Not related |
| | 02014 | 2 | Pneumonia<br>Arthritis | Not related<br>Not related |
| | 02015 | 1 | Asthenia | Not related |
| | 02017 | 1 | Nausea<br>Vomiting<br>Diarrhea | Not related<br>Not related<br>Not related |
| | 03008 | 1 | Leukocytosis (grade 4)<br>Thrombocytopenia (grade 3)<br>Abdominal Pain<br>Oedema peripheral | Probably related<br>Probably related<br>Not related<br>Not related |
| | 05007 | 1 | Hyperbilirubinemia (grade 3) | Not related |

# Phase I Clinical (End Stage) Trial Summary

- DAVANAT® was well tolerated in end-stage patients
- Maximum Tolerated Dose and Dose Limiting Toxicity of DAVANAT® not reached
  - DAVANAT® 280 mg/m$^2$ recommended for Phase II dose
- Pharmacokinetics
  - Half life of 5-FU alone is 6-22 minutes
  - Half life of 5-FU with DAVANAT® is 28-137 minutes
  - No increase in 5-FU toxicity w/ increased exposure
- Stable disease in 14 of 26 evaluable patients
  - 7 of 10 patients stabilized at the highest DAVANAT® dose level

# Phase II Colorectal Cancer Trial (End Stage)

**Indication:**
Colorectal cancer;
End stage patients.

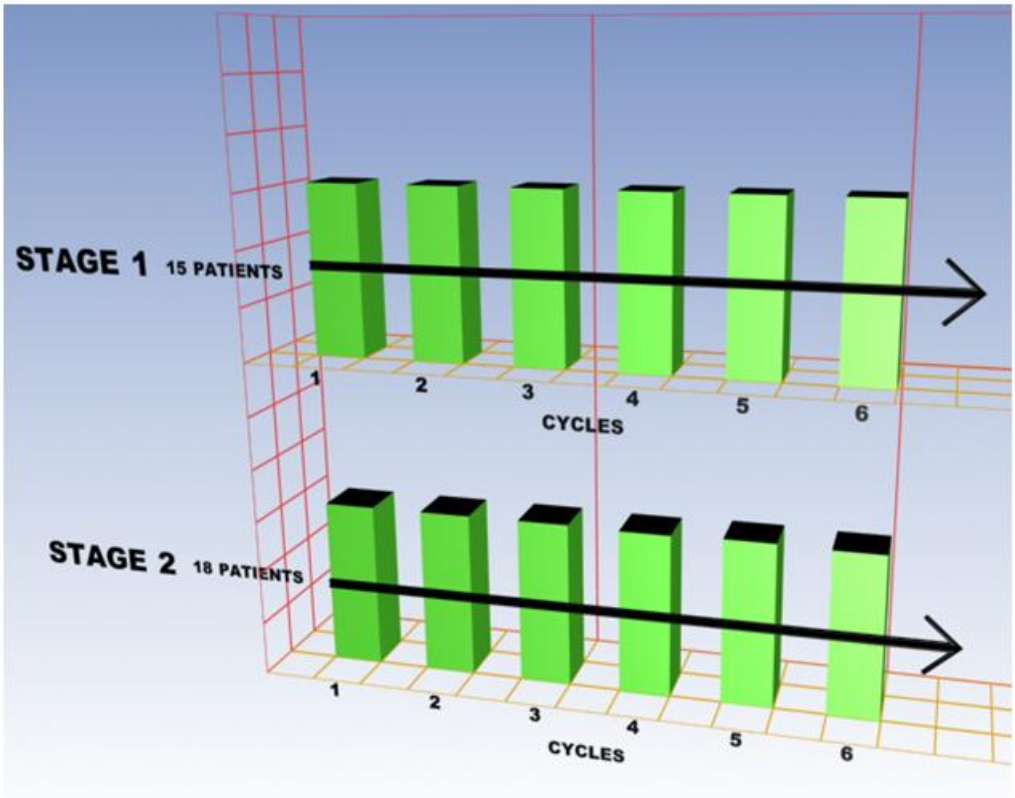
**Objectives:**
Complete/ partial tumor response (RECIST); stable disease.

**Design:**
Multi-center (6 sites), open label study.
Evaluate at least two cycles (up to six) or to disease progression.

**Regimen:**
DAVANAT® 280 mg/m$^2$;
5-FU 500 mg/m$^2$;
dose for 4 consecutive days, observe for 24 days.

**Patients:**
Began dosing in May 2005. Six sites.
Study finalized in August 2006.

**Results (un-audited):**
20 patients:
1 Partial Response (RECIST)
6 Stable Disease.



# Phase II Colorectal (End Stage) Trial Summary

- DAVANAT® was well tolerated in end-stage, refractory patients
- Anti-tumor activity was seen with DAVANAT® /5-FU
  - 1 patient experienced Partial Response
  - 6 of 20 patients stabilized for 2-8 months
- No increase in 5-FU toxicity with increased exposure

# Phase II Colorectal Trial – First Line (Ongoing)

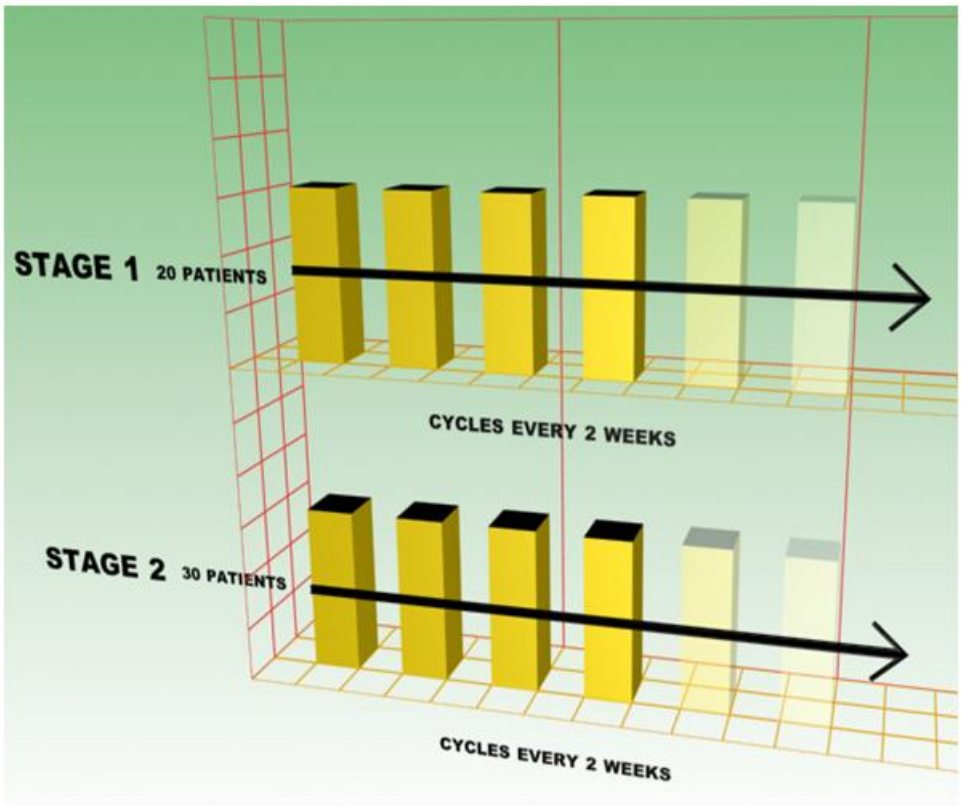
**Indication:**
First line treatment of patients with metastatic, unresectable colorectal cancer who are unable to tolerate irinotecan or oxaliplatin.

**Objectives:**
Complete/partial tumor response (RECIST); 14 of 41 responders (34%). Progression Free Survival at 6 and 12 months.

**Design:**
Multi-center, open label study. Evaluate for six months or to disease progression or toxicity.

**Regimen:**
Leucovorin, DAVANAT®/5-FU, AVASTIN®. IV Dose for 3 consecutive days. Repeat cycles disease progression or unacceptable toxicity.

**Patients:**
Up to 50. 8 patients dosed: 2 partial response; 5 stabilized.



# Phase II Biliary Trial – First Line (Ongoing)

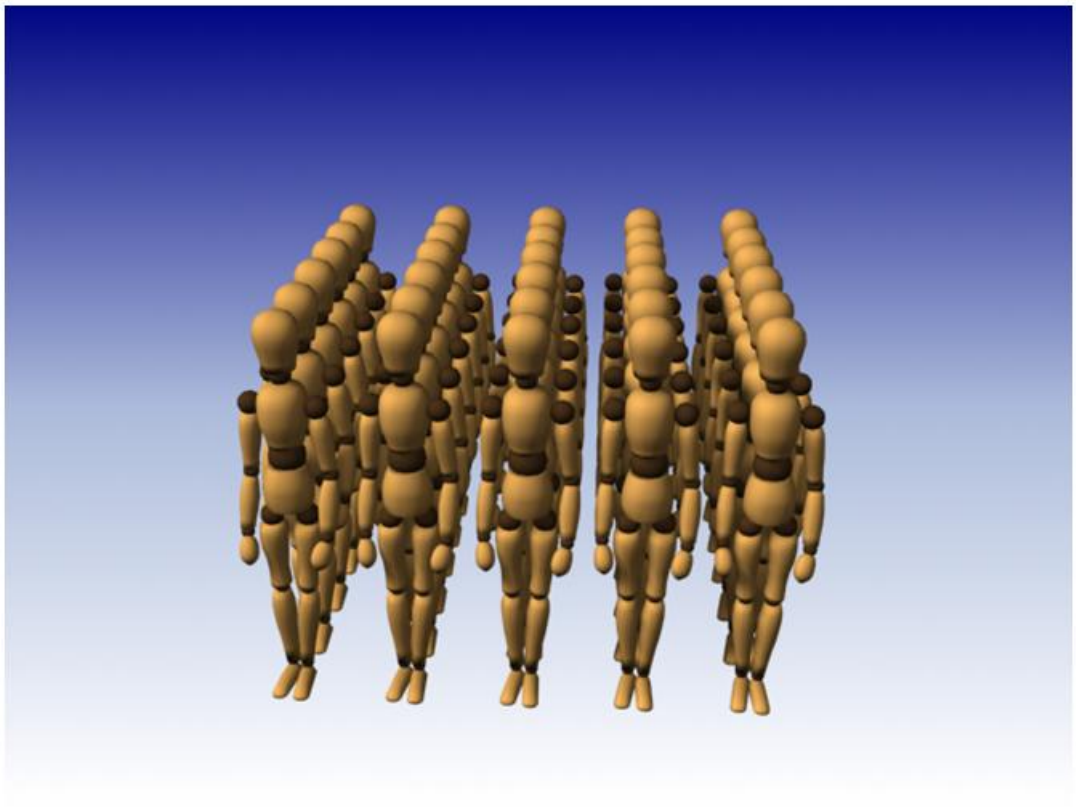
**Indication:**
First line treatment of patients with biliary cancer.

**Objectives:**
Complete/ partial tumor response (RECIST);
7 of 35 responders (20%).
Progression free survival.

**Design:**
Multi-center, open-label study.

**Regimen:**
DAVANAT® with 5-FU. Evaluate for 2 cycles or to disease progression. Repeat cycles until disease progression.

**Patients:**
Up to 42. 8 patients dosed:
1 partial response;
5 stabilized.



# Other Plans for DAVANAT®

- **Pre-clinical**
  - **Stability & compatibility studies of DAVANAT® & chemotherapeutics in solution**
  - **Investigate dose-toxicity response curve**
  - **Investigate covalent linkers of therapeutics to DAVANAT®**
  - **Animal toxicity studies in combination therapies**

- **Clinical**
  - **Escalating doses of 5-FU: Identify Max Tolerated Dose**
  - **Test other chemotherapeutics in Phase I trials with DAVANAT®**

# Other Pro-Pharmaceuticals Compounds

# Other Pro-Pharmaceuticals Compounds

- Fibrosis
  - No available treatment for fibrosis
  - Fibrosis (scarring) is the reason patients develop liver failure & may need a transplant
  - 25 million Americans have liver/biliary disease
  - More than 4 million Americans with Hepatitis C virus; many will develop severe fibrosis and liver failure
- PRO-GR 300, first in class, carbohydrate compound in combination with other drugs to treat fibrosis
  - Research collaboration w Dr. Scott Freidman, Division Director of Liver Diseases of Mt. Sinai School of Medicine to evaluate the anti-fibrotic effects of carbohydrate compounds
  - Pre-clinical studies currently underway – results August 2007

# Regulatory Pathway: 505(b)(2)

# 505(b)(2) Regulatory Pathway

- 505(b)(1): "Typical" way most new drugs are approved; all investigations from sponsor

- 505(b)(2): Used for new formulations of existing drugs; applicant may rely on investigations to which it does not own or have the right of reference (e.g., information in the published literature or in approved NDAs for the RLD)

- 505(j): For generic drugs that are the same as the established drug (the "Reference Listed Drug" [RLD])

# FDA Position Regarding 505(b)(2)

- "FDA's longstanding interpretation of section 505(b)(2) … the Agency's approach is to use the 505(b)(2) drug approval pathway to avoid requiring drug sponsors to conduct and submit studies that are not scientifically necessary."

- "The conduct and review of duplicative studies would… slow the process for drug approval with no corresponding benefit to the public health."

# 505(b)(2) Avoids Significant Delays in Drug Approval

- "FDA has approved more than 80 section 505(b)(2) applications for drugs for indications ranging from cancer pain to attention deficit disorder.

- ...many of these drugs would never have reached the market, or would have been significantly delayed, without the 505(b)(2) pathway."

# DAVANAT®/5-FU Formulations: Historical Background

- 5-Fluorouracil, one of the most widely used cytotoxic agents
  - Less than desirable PK and side effect profile
  - Tiredness, fatigue, nausea, diarrhea, bone marrow depression (may lead to anemia), increased tendency to bruise, mouth sores, altered skin pigmentation
- In 2000, Pro-Pharmaceuticals embarked on developing a more effective, less toxic 5-FU by combining it with DAVANAT®
  - Pre-clinical studies subsequently demonstrated that DAVANAT® significantly improved the pharmacodynamic impact of 5-FU
  - Less toxicity due to "targeted delivery"
  - Higher intra-tumoral 5-FU concentration
  - Higher efficacy in multiple tumor types

# Benefits of Not Having Efficacy Trial

- Preservation of resources for other research
- Immediate availability of a less toxic 5-FU alternative
- Have more time to develop a strong marketing strategy, resulting in a brand consumers recognize and may prefer
- Exclusivity beyond 180 days when compared to ANDA approval

# Rationale for No Efficacy Trial

In clinical trials, DAVANAT® has been shown to be safe and non-toxic

In clinical trials, there is no increase in 5-FU toxicity w/ increased exposure of 5-FU w/ DAVANAT®

In preclinical studies, DAVANAT®/5-FU has greater anti-tumor activity than 5-FU alone

Galactomannans already approved by FDA (GRAS) NDA

DAVANAT® will be marketed as a 'stand-alone' vial- not as a combination product

**Based upon the data, there is no scientific basis to hypothesize that DAVANAT® /5-FU will be less effective as adjuvant therapy than 5-FU alone**

**Safely delivers a higher dose of 5-FU than already proven to be effective in adjuvant setting**