HALOZYME THERAPEUTICS INC

FORM 8-K
(Current report filing)

Filed 01/07/15 for the Period Ending 01/07/15

Address	11388 SORRENTO VALLEY ROAD SAN DIEGO, CA 92121-1345
Telephone	(858) 794-8889
CIK	0001159036
Symbol	HALO
SIC Code	2836 - Biological Products, Except Diagnostic Substances
Industry	Biotechnology & Drugs
Sector	Healthcare
Fiscal Year	12/31

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

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

Date of Report (Date of Earliest Event Reported): **January 7, 2015**

HALOZYME THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**001-32335**	**88-0488686**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

11388 Sorrento Valley Road, San Diego, California	**92121**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: **(858) 794-8889**

Not Applicable
(Former name or former address, if changed since last report)

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

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

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

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

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

Item 7.01 Regulation FD Disclosure.

Attached hereto as Exhibits 99.1 and 99.2, which are incorporated herein by reference, are copies of the press release and certain slides used by Halozyme, Therapeutics, Inc. ("Halozyme") in making an investor presentation and that are expected to be used in subsequent presentations to interested parties, including analysts and stockholders.

This information is being furnished pursuant to Item 7.01 of this Report and shall not be deemed to be "filed" for the purposes of Section 18 of the Securities and Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that section and will not be incorporated by reference into any registration statement filed by Halozyme, under the Securities Act of 1933, as amended, unless specifically identified as being incorporated therein by reference. This Report will not be deemed an admission as to the materiality of any information in this Report that is being disclosed pursuant to Regulation FD.

Please refer to page 2 of Exhibit 99.2 for a discussion of certain forward-looking statements included therein and the risks and uncertainties related thereto.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press release, dated January 7, 2015
99.2	Halozyme Therapeutics, Inc. Investor Presentation, dated January 2015

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.

HALOZYME THERAPEUTICS, INC.

January 7, 2015

By: /s/ David Ramsay

Name: David Ramsay

Title: Vice President and Chief Financial Officer

EXHIBIT 99.1

Investor Contact:
Schond Greenway
Halozyme Therapeutics
858-704-8352
ir@halozyme.com

Media Contact:
Susan Neath Francis
212-301-7182
sfranciw2ogroup.com

Halozyme provides AGENDA highlights for analyst and investor meeting

- Discuss interim results for Study 202 evaluating PEGPH20 with gemcitabine and ABRAXANE ® in pancreatic cancer patients -
- Review current clinical development plan to evaluate PEGPH20 in two Non-Small Cell Lung Cancer trials, in combination with chemotherapy and then with a PD-1 inhibitor -
- Provide 2015 financial guidance -

SAN DIEGO, January 7, 2015 - Halozyme Therapeutics, Inc. (NASDAQ: HALO) today will review the PEGPH20 development program and provide 2015 financial guidance during a meeting for analysts and investors in New York at 10:00 a.m. ET/ 7:00 a.m. PT.

“We are committed to exploring the full potential of investigational new drug PEGPH20 which we believe may have utility in a range of solid tumors with accumulation of high levels of hyaluronan (HA). The interim analysis of Study 202 has provided insights into the potential clinical benefit of PEGPH20 in patients with metastatic pancreatic cancer with accumulation of high levels of HA. We plan to meet with regulatory authorities in the first half of 2015 to discuss these preliminary results and seek their feedback on our plans to initiate a registration study for PEGPH20 in metastatic pancreatic cancer,” stated Dr. Helen Torley, President and Chief Executive Officer.

“Additionally, we plan to further our clinical development plan for PEGPH20 by conducting two trials in non-small cell lung cancer (NSCLC). Patient screening for the first study (PRIMAL), designed to evaluate PEGPH20 in combination with docetaxel in second-line NSCLC patients, initiated in December 2014. The second study, which is in the planning phase, will examine PEGPH20 in combination with an immuno-oncology agent, specifically a PD-1 inhibitor. All of these efforts are being managed with a highly efficient infrastructure as evidenced by our projected 2015 net cash burn.”

Members of Halozyme's senior management, members of the research team and a renowned physician expert in pancreatic cancer will discuss the following topics as part of today's analyst and investor meeting:

PEGPH20 in Pancreatic Cancer

- Efficacy and safety data based on an interim analysis of HALO 109-202 (Study 202) will be presented. Study 202 is evaluating PEGPH20 in combination with gemcitabine and nab-paclitaxel (ABRAXANE ®) compared to gemcitabine and ABRAXANE alone in metastatic pancreatic cancer.
- The analysis is based on 146 patients who had been enrolled at the time of the temporary hold in April 2014 due to the observation of a potential imbalance in thromboembolic events between treatment arms.
- The interim analysis was conducted to evaluate the overall benefit:risk of adding PEGPH20 to standard chemotherapy, and to help identify the cut-off point for hyaluronan accumulation as we further the clinical development plan for PEGPH20 with a planned registration study in metastatic pancreatic cancer patients with high HA accumulation, and initiate two studies in NSCLC.
- The Company has requested a meeting with the FDA in 1H 2015 to discuss the current benefit:risk of PEGPH20 and the design of the registration study in metastatic pancreatic cancer.

PEGPH20 in Non-Small Cell Lung Cancer

- Management will review the PRIMAL study design, the ongoing global Phase 1b/2 randomized study evaluating PEGPH20 in combination with docetaxel as a second-line therapy for patients with locally advanced and metastatic NSCLC.
    - The Phase 1b portion includes both a dose escalation and dose expansion phase evaluating two different schedules and is projected to complete enrollment in the third quarter of 2015, pending the number of dose escalation cohorts of PEGPH20.
    - The Phase 2 randomized portion of the study will follow evaluation of the Phase 1b data.
- Management will also discuss the scientific rationale for combining PEGPH20 with immuno-oncology agents and plans to begin a study of PEGPH20 combined with a PD-1 inhibitor in patients with high-HA NSCLC tumors, in the second half of 2015.

Financial Guidance

The Company ended 2014 with approximately $135 million in cash, cash equivalents and marketable securities (these results are unaudited). For the full year 2015, the Company expects:

- Net revenues to be in the range of $85 million to $95 million.
- Operating expenses to be in the range of $145 million to $155 million.
- Net cash burn to be between $35 million and $45 million.

A webcast of the Analyst Day presentation can be accessed through the "Investors" section of Halozyme's corporate website at www.halozyme.com, and a recording will be made available for 90 days following the event. To access the live webcast, please log on to Halozyme's website approximately 15 minutes prior to the presentation to register and download any necessary audio software.

About PEGPH20
PEGPH20 is an investigational PEGylated form of Halozyme's proprietary recombinant human hyaluronidase under clinical development for the systemic treatment of tumors that accumulate hyaluronan.

About Halozyme
Halozyme Therapeutics is a biopharmaceutical company dedicated to developing and commercializing innovative products that advance patient care. With a diversified portfolio of enzymes that target the extracellular matrix, the Company's research focuses primarily on a family of human enzymes, known as hyaluronidases, which increase the dispersion and absorption of biologics, drugs and fluids. Halozyme's pipeline addresses therapeutic areas, including oncology, diabetes and dermatology that have significant unmet medical need today. The Company markets Hylenex ® recombinant (hyaluronidase human injection) and has partnerships with Roche, Pfizer, Janssen and Baxter. Halozyme is headquartered in San Diego, CA. For more information on how we are innovating, please visit our corporate website at www.halozyme.com.

Safe Harbor Statement
In addition to historical information, the statements set forth above include forward-looking statements (including, without limitation, statements concerning future actions relating to product development and regulatory events and goals, anticipated clinical trial results and strategies, product collaborations, our business intentions and financial estimates and results) that involve risk and uncertainties that could cause actual results to differ materially from those in the forward-looking statements. The forward-looking statements are typically, but not always, identified through use of the words "believe," "enable," "may," "will," "could," "intends," "estimate," "anticipate," "plan," "predict," "probable," "potential," "possible," "should," "continue," and other words of similar meaning. Actual results could differ materially from the expectations contained in forward-looking statements as a result of several factors, including delays in completion of clinical trials and other development activities, the possibility of safety events, unexpected expenditures and costs, unexpected results or delays in regulatory review, regulatory approval requirements, unexpected adverse events and competitive conditions. These and other factors that may result in differences are discussed in greater detail in Halozyme's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 10, 2014.

# # #

Halozyme THERAPEUTICS

Exhibit 99.2

PEGPH20: The Science & The Strategy

January 7, 2015

Forward-Looking Statements

All of the statements in this presentation that are not statements of historical facts constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Examples of such statements include future product development and regulatory events and goals, anticipated clinical trial results and strategies, product collaborations, our business intentions and financial estimates and results. These statements are based upon management's current plans and expectations and are subject to a number of risks and uncertainties which could cause actual results to differ materially from such statements. A discussion of the risks and uncertainties that can affect these statements is set forth in the Company's annual and quarterly reports filed from time to time with the Securities and Exchange Commission under the heading "Risk Factors." The Company disclaims any intention or obligation to revise or update any forward-looking statements, whether as a result of new information, future events, or otherwise.

Halozyme: Two Potential Drivers of Future Growth and Value

ENHANZE™ (rHuPH20)

Roche

Herceptin SC trastuzumab subcutaneous

MabThera SC Rituximab Subcutaneous

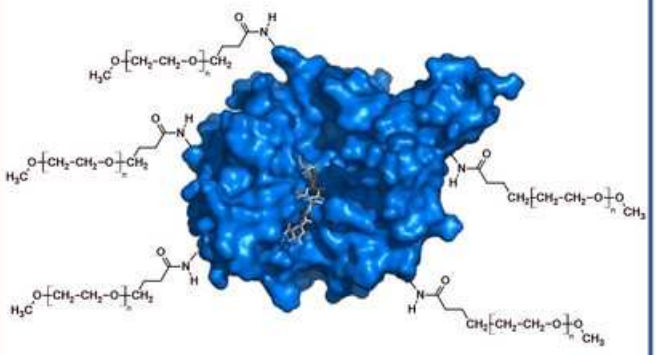
Baxter

HyQvia Human Normal Immunoglobulin (10%) Recombinant Human Hyaluronidase

Pfizer

janssen PHARMACEUTICAL COMPANIES OF Johnson & Johnson

PEGPH20



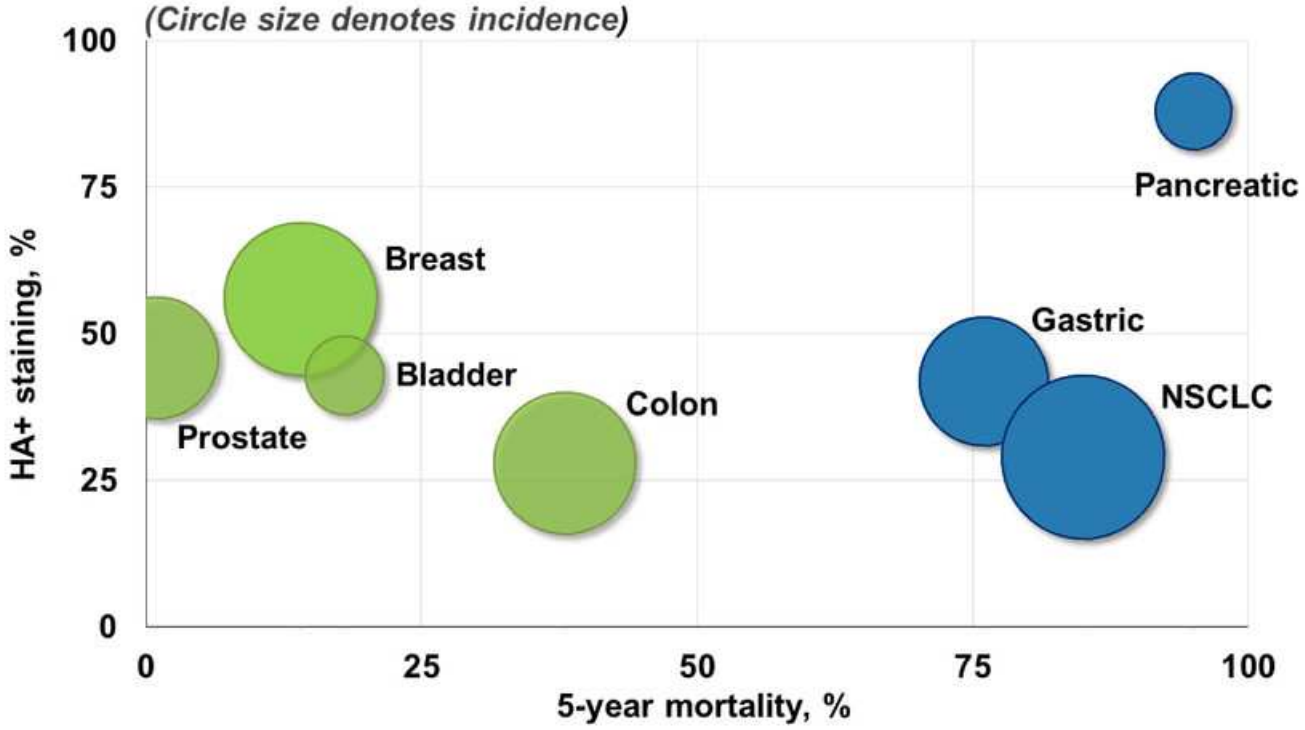
PEGylated form of rHuPH20
Investigational new drug in phase 2 development

PEGPH20 Goal: Improving Targeting of Co-Administered Cancer Drugs

- **PEGPH20**
  - Investigational new drug
  - Intended to target Hyaluronan (HA), a key component of the tumor microenvironment (TME)
  - Potential to increase tumor-selective access of co-administered anticancer therapy into tumors that accumulate high levels of hyaluronan (HA^{high})
    - Small molecule chemotherapy
    - Monoclonal antibody cancer therapies, including immunotherapy
    - Immune cells
  - Doubles survival in a number of animal models when combined with cancer therapy, compared to cancer therapy alone
- **Encouraging early efficacy data in Phase 1b and 2 trials of Stage IV pancreatic ductal adenocarcinoma when co-administered with**
  - Gemcitabine
  - Gemcitabine and Abraxane®

Clinical Focus Informed By HA^{high} Expression, 5-yr Mortality, and Incidence

Initial Focus Areas Highlighted in Blue



Jacobetz, et al. *Gut.* 2013;62:112–120. GLOBOCAN 2012, American Cancer Society; Halozyme Analysis.

Targeting Large Markets With Poor Survival Rates

	1L Stage IV Pancreatic Cancer	2L Stage IIIB/IV Non Small Cell Lung Cancer
Annual Incidence (US and EU 5)	~100,000	~80,000
Estimated % with HA^{high}	40-60%	35-45%
5 Year Survival	5%	16.8%
Overall Survival with Current Standard of Care	8.5 months (Abraxane® plus gemcitabine)	7-8 months (docetaxel, Alimta®, Tarceva®)

GLOBOCAN 2012, SEER 18, 2004-2010. Halozyme analysis.

2015 Financial Guidance

	2015E	Comments
Net Revenues	**$85M - $95M**	Royalties, sales of rHuPH20 to partners, Hylenex sales and collaboration revenues
Operating Expenses[1]	**$145M - $155M**	R&D driven by clinical trial enrollment
Cash Burn	**$35M - $45M**	Does not include new ENHANZE™ deals

Cash position end 2014: approximately $135M

Anticipated ENHANZE™ revenue funds operations without need for dilutive financing

NOTE: 1) Includes ~$20M in non-cash expenses, stock compensation and depreciation.

Today's Agenda

Introduction and Objectives	**Helen Torley, MB, ChB, MRCP** President and Chief Executive Officer Halozyme Therapeutics
PEGPH20 Mechanism of Action	**Christopher Thanos, PhD** Director, Biotherapeutics Halozyme Therapeutics
Exploring Combinations of PEGPH20 With Cancer Therapies	**Curt Thompson, PhD** Senior Director, Pharmacology Halozyme Therapeutics
From Theory to Initial Clinical Experience	**Sunil R. Hingorani, MD, PhD** Associate Member, FHCRC Director, Center for Accelerated Translation in Pancreas Cancer
Clinical Development Plan Update	**Athena Countouriotis, MD** Chief Medical Officer Halozyme Therapeutics
Q&A	

Today's Agenda

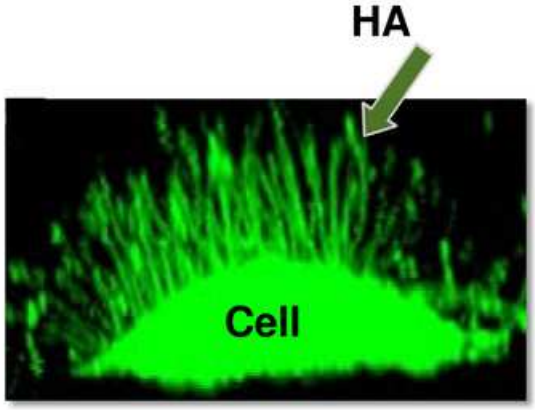
Introduction and Objectives	**Helen Torley, MB, ChB, MRCP** President and Chief Executive Officer Halozyme Therapeutics
PEGPH20 Mechanism of Action	**Christopher Thanos, PhD** Director, Biotherapeutics Halozyme Therapeutics
Exploring Combinations of PEGPH20 With Cancer Therapies	**Curt Thompson, PhD** Senior Director, Pharmacology Halozyme Therapeutics
From Theory to Initial Clinical Experience	**Sunil R. Hingorani, MD, PhD** Associate Member, FHCRC Director, Center for Accelerated Translation in Pancreas Cancer
Clinical Development Plan Update	**Athena Countouriotis, MD** Chief Medical Officer Halozyme Therapeutics
Q&A	

PEGPH20:
Mechanism of Action

Christopher Thanos, PhD
Director, Biotherapeutics
Halozyme Therapeutics

Hyaluronan (HA): A Physical Barrier to Cancer Therapy Access

- HA is a polysaccharide
- Stabilizes the TME via binding to extracellular and cell surface components
- Helps create a barrier to entry of cancer therapeutics into tumor
  - Increased tumor interstitial pressure [1,2]
  - Vasculature compression [3,4]
- HA-rich stroma "coat" can prevent host immune cell access to malignant cells



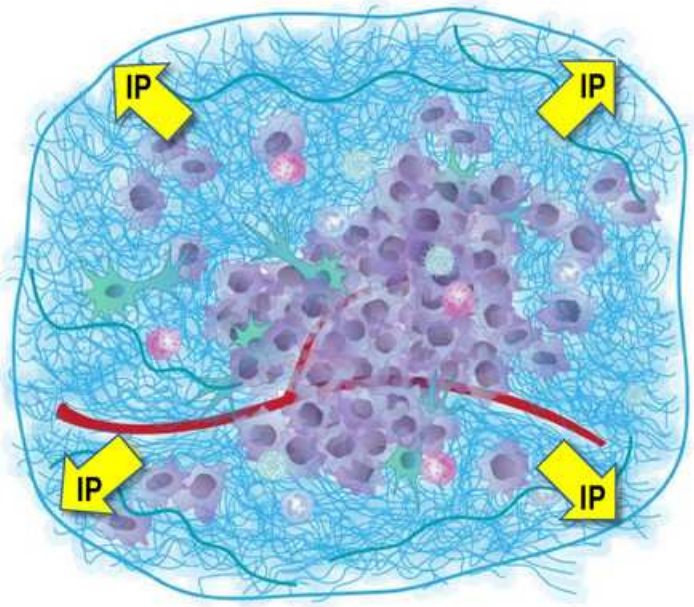
Protective 'spikes' of HA protrude from HA^{high} tumor cell in culture

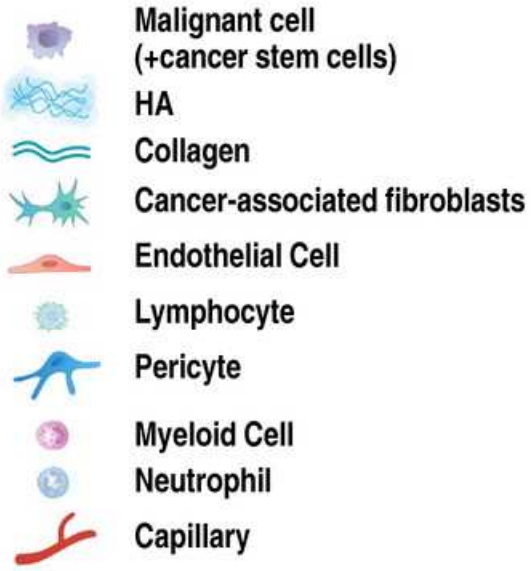
Kultti, et al. *JBC.* 2006,281:15821.

1. Brekken, et al. *Anticancer Res.* 2000,20:3503. 2. Provenzano and Hingorani, *Br. J. Cancer.* 2013,108:1. 3. Thompson, et al. *Mol Cancer Ther.* 2010,9:3052. 4. Stylianopoulos, et al. *PNAS. 2013,*110:18632.

HA^{high} Tumor Microenvironment

Illustration of TME





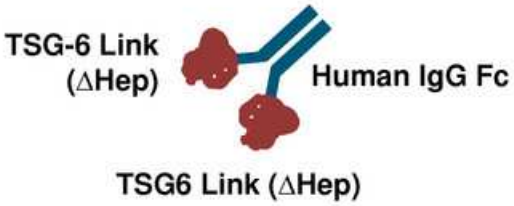
HA^{high} results in

- Increased tumor interstitial pressure (IP)
- Compression of blood vessels
- Poor anti-cancer therapy access to tumor

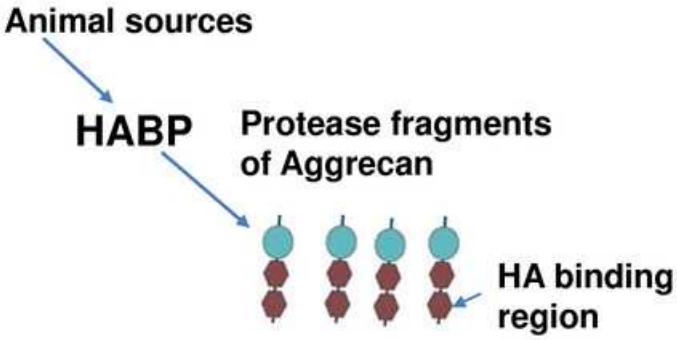
Measurement of HA Has Evolved Over the Clinical Development Program

PEGPH20 Phase 2

HTI-601 = biotin-TSG-6-ΔHep-Fc



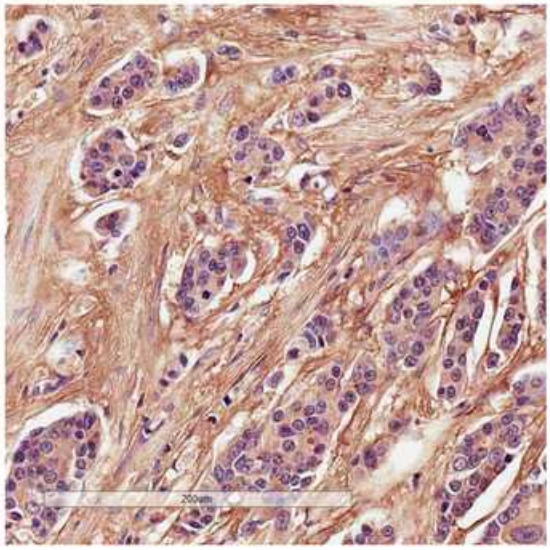
PEGPH20 Preclinical, Phase 1, 1b Trials

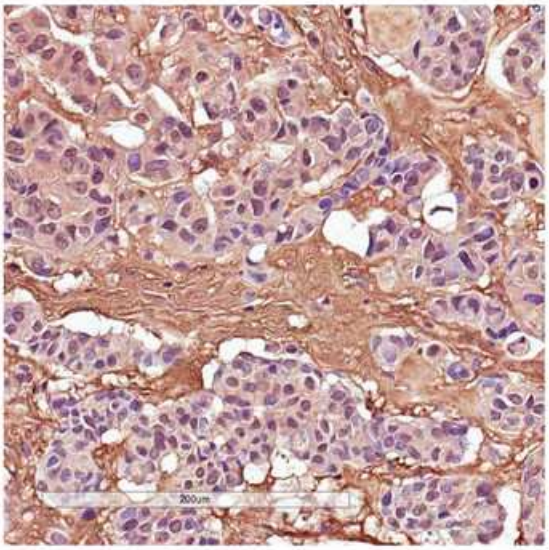


Recombinant Protein	Cartilage Derived
Higher specificity	Lower specificity
Pathologist assisted computer image analysis	Pathologist assessed
Lower inter-observer variability	Higher inter-observer variability

HA Accumulation Similar In Primary Tumor and Metastasis

HA^{high} Primary Breast Cancer	HA^{high} Paired Brain Metastasis



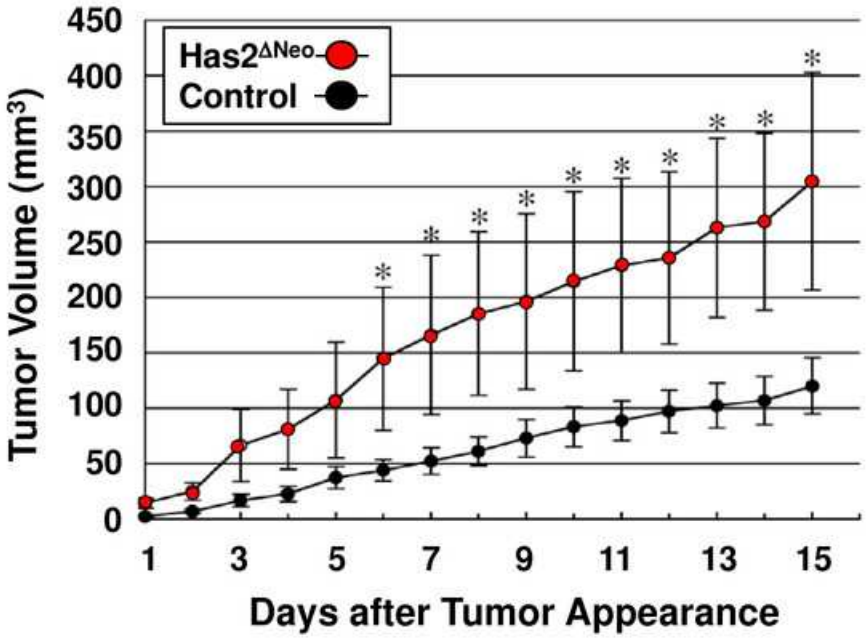


Archived biopsies from breast adenocarcinoma samples stained with HTI 601

Jadin, et al. Submitted for publication 2014.

Accumulation of HA Accelerates Tumor Progression In Animal Model

HER2/Neu/HAS2 Transgenic Mouse Model



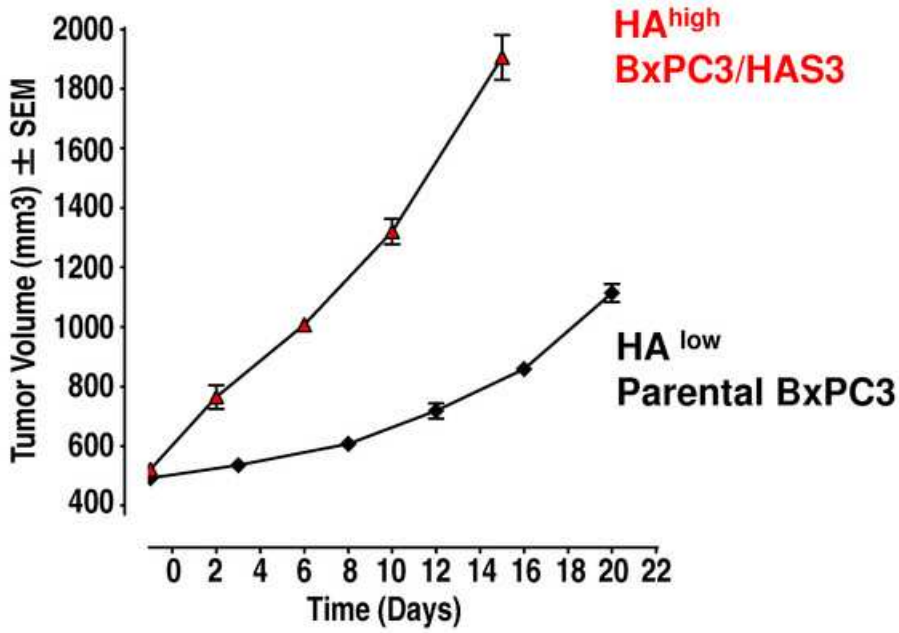
HA^{high} HER2/Neu/HAS2 Tumors

Control:HA ^{low} HER2/Neu Tumors

Koyama (Itano), et al. *Am. J. Pathol.* 2007,170:1086.

Accumulation of HA Drives Tumor Progression in HA^{high} Animal Model of Pancreatic Cancer

BxPC3 Pancreatic Human Xenografts

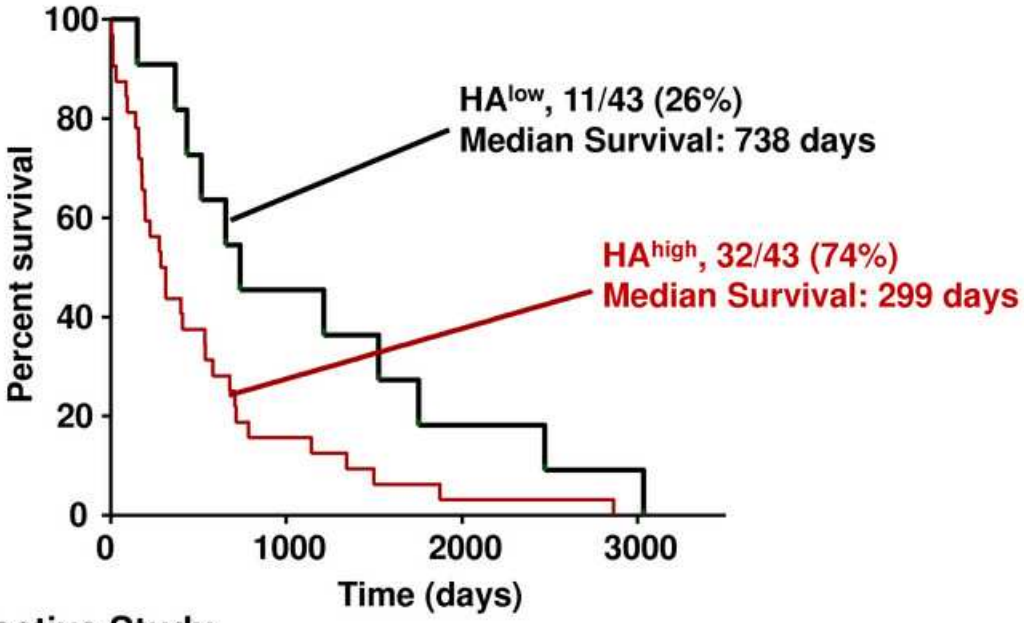


Mice were inoculated with either HA^{low} parental BxPC3 cells or HA^{high} BxPC3/HAS3 cells and tumor growth monitored.

Modified from Kultti, et al. *Biomed Res Int.* 2014

Tumor HA Accumulation Associated with Shorter Survival

Pancreatic Cancer



Retrospective Study

Survival of pancreatic cancer patients categorized according to staining intensity for HA in tumor biopsies. N=43

Whatcott, et al. AACR. 2013

Non-Clinical Approach: Validated Methods, Confirmation in Independent Labs

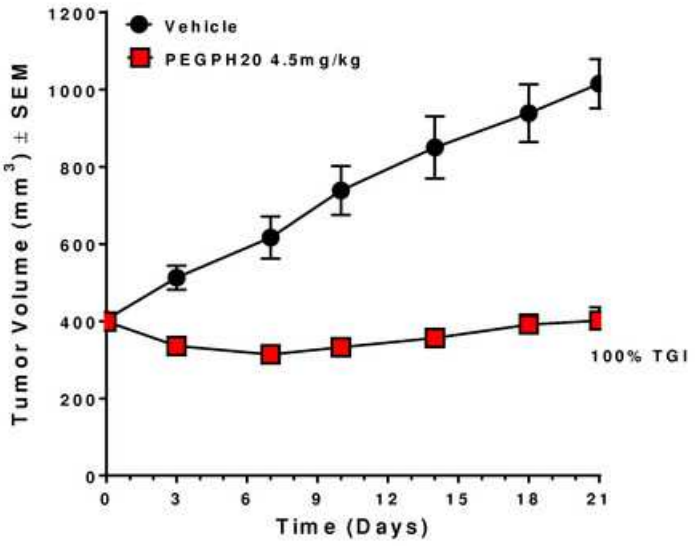
- **Assessment of PEGPH20 (single agent and enhanced combination) antitumor activity in validated models**
  - **HA^{high} human xenograft models**
  - **Patient derived (PDx) HA^{high} tumor models**
  - **Genetically engineered mouse models of pancreatic ductal adenocarcinoma**

- **Independent Laboratories confirmed observations**
  - **Dr. S. Hingorani, Fred Hutchinson Cancer Center**
  - **Dr. D. Diamond, City of Hope**
  - **Dr. N. Itano, Kyoto Sangyo University**
  - **Dr. D. Tuveson, Cold Spring Harbor**

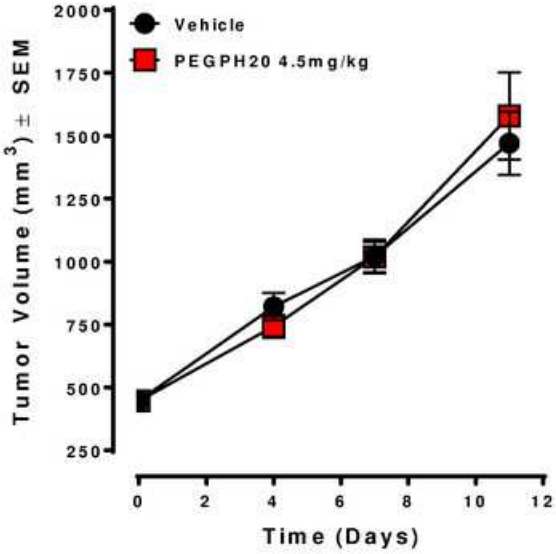
PEGPH20-Mediated HA Depletion Selectively Impacts HA^{high} Tumors In Animal Model

NSCLC PDx Model Example

HA^{high}



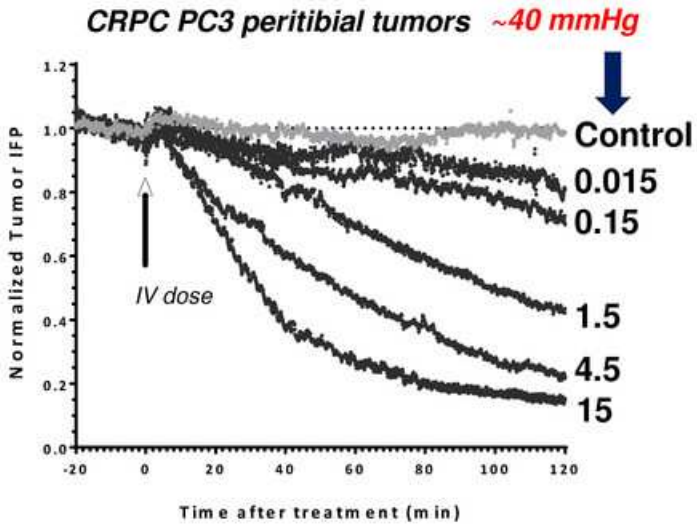
HA^{low}



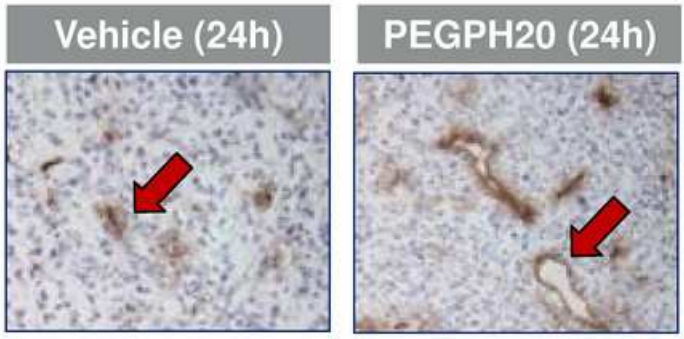
Jiang, et al. Halozyme Therapeutics, Inc. unpublished data, experiments completed 2014.

PEGPH20-Mediated HA Removal In Animal Model Reduces Tumor Interstitial Pressure, Decompressing Vessels

Normalization of Tumor IP



PEGPH20-mediated Vessel Expansion

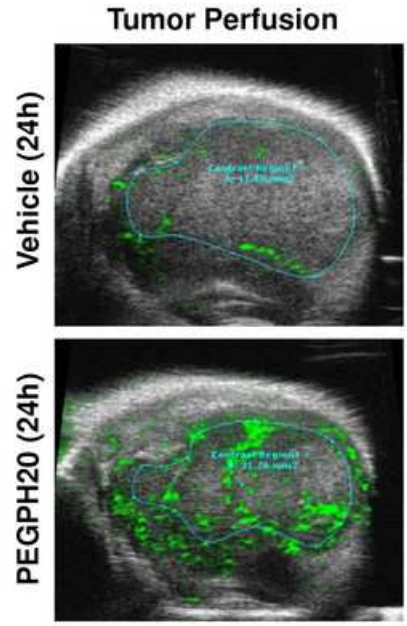


Endothelial labeling

Thompson, et al. *Mol. Cancer Ther.* 2010,9:3052.

Tumor Reperfusion Post PEGPH20 Administration Results In Increased Drug Accumulation in Tumor Animal Model

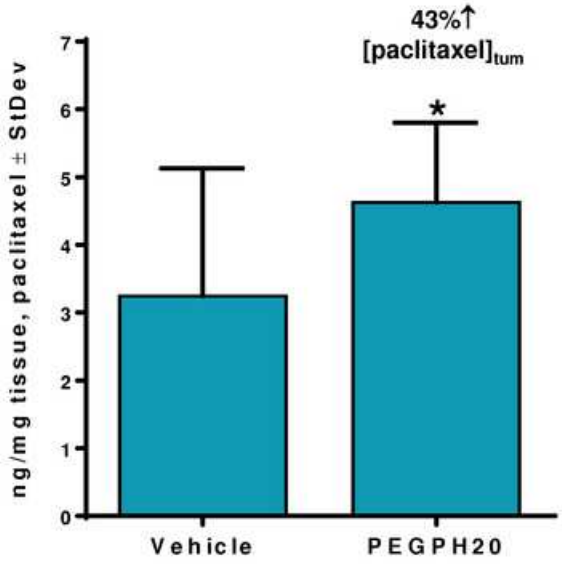
PC3 Prostate Xenograft Tumors



Hyperechoic microbubbles to visualize vasculature "space" or vascular area of peritibial PC3 tumors ± PEGPH20 (15 mg/kg, IV). Blue tracing is tumor area.

Thompson et al. Mol Cancer Ther. 2010,9:3052.

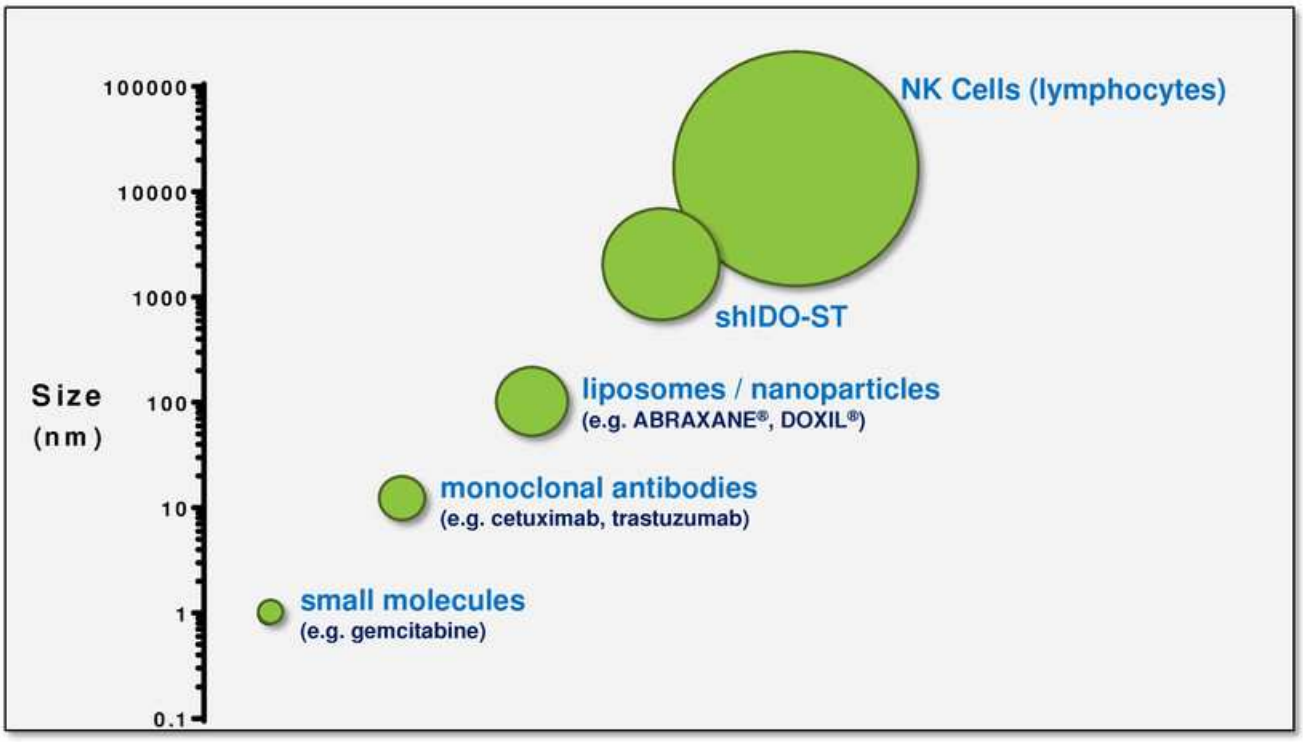
ABRAXANE® Treated BxPC3/HAS3 Pancreatic Xenograft Tumors



Mice (n≥4) received nab-paclitaxel (10 mg/kg, IV) ± PEGPH20 (1 mg/kg, IV). Mice sacrificed 1h post-nab-paclitaxel.

Osgood et al., AACR, Pancreatic Cancer Mtg., May 2014

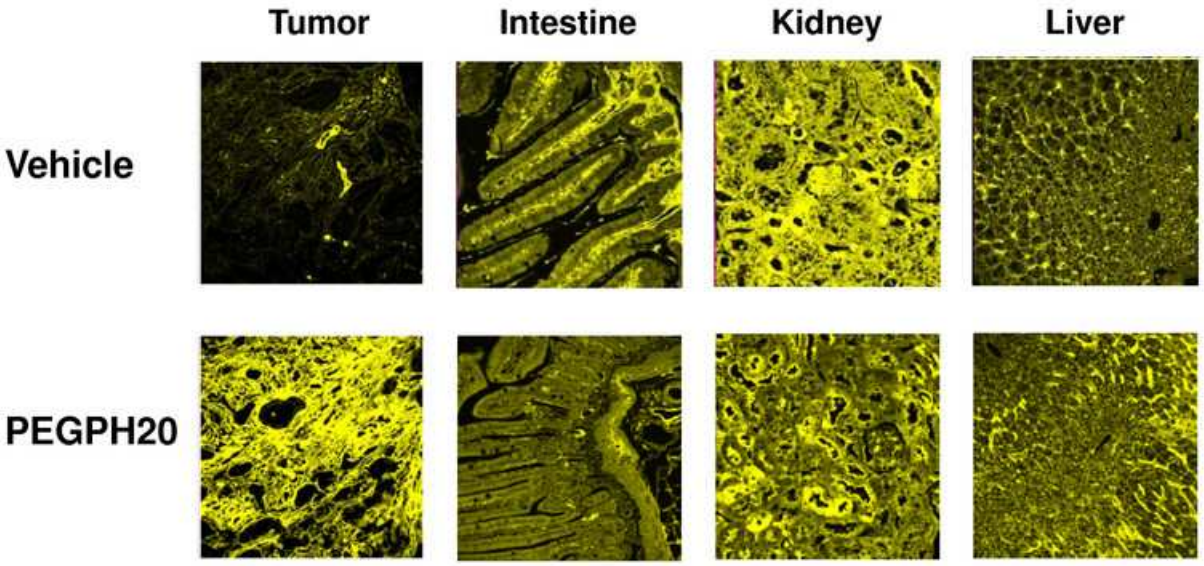
PEGPH20 Evaluated With Multiple Cancer Therapeutics Across Broad Range of Sizes



In preclinical studies, PEGPH20 was shown to improve therapeutic efficacy independent of size, charge or PK of the therapeutic.

PEGPH20 Enhances Penetration Into HA^{high} Tumor but Not Normal Tissue In Animal Model

KPC Genetically Engineered Mouse Model of PDA

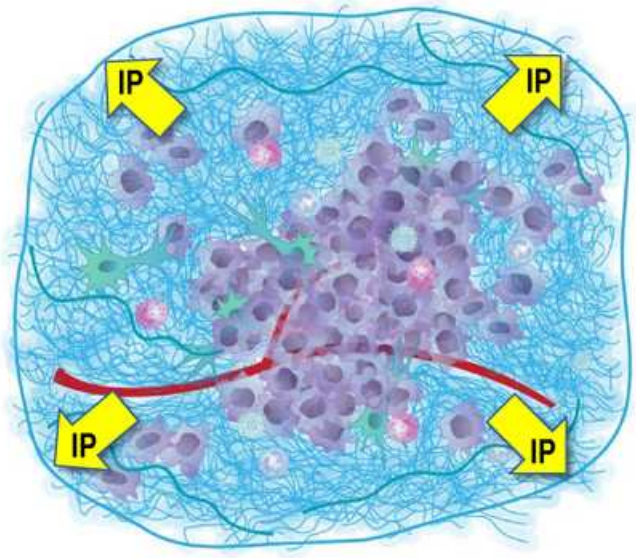


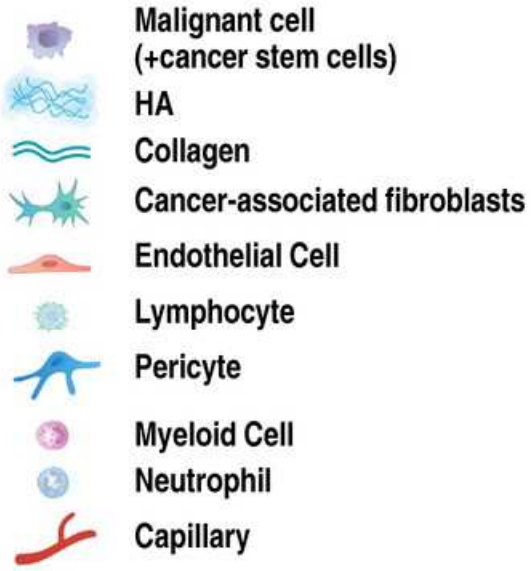
Fluorophore-labelled dextrans (2,000,000 Da) were injected into tumor-bearing KPC mice.

Jacobetz, et al, *Gut*. 2013

HA^{high} Tumor Microenvironment

Illustration of TME



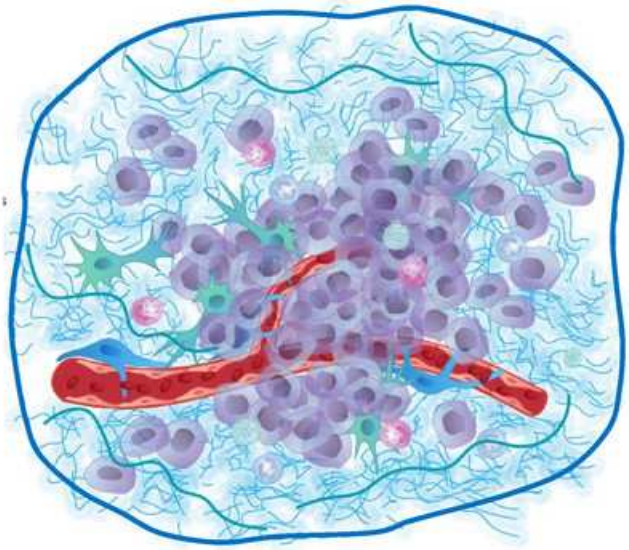


HA^{high} results in

- Increased tumor interstitial pressure (IP)
- Compression of blood vessels
- Poor anti-cancer therapy access to tumor

PEGPH20 Has Been Shown In Animal Models to Drive Multiple Changes In the Tumor Microenvironment

Illustration of TME (Post PEGPH20)



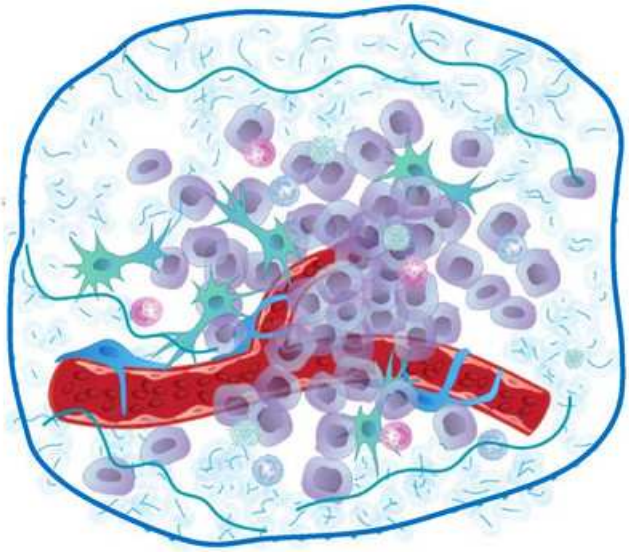
- Malignant cell (+cancer stem cells)
- HA
- Collagen
- Cancer-associated fibroblasts
- Endothelial Cell
- Lymphocyte
- Pericyte
- Myeloid Cell
- Neutrophil
- Capillary

Expected TME Post PEGPH20 Administration:

- **Reduced** tumor interstitial pressure
- **Expansion** of blood vessels

PEGPH20 Has Been Shown In Animal Models to Drive Multiple Changes In the Tumor Microenvironment

Illustration of TME (Post PEGPH20)



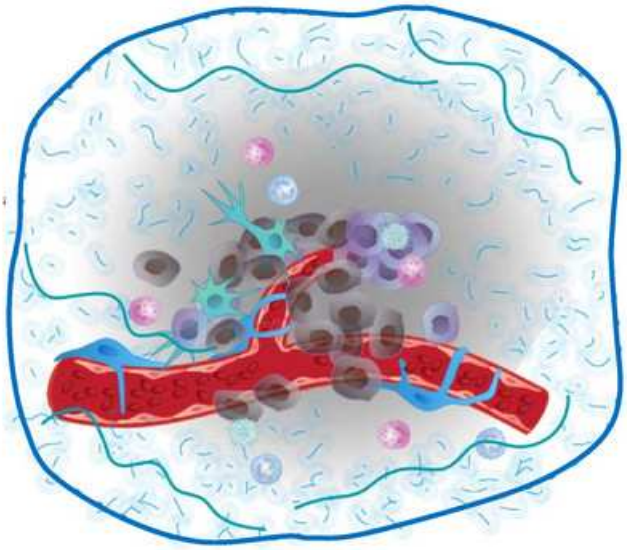
- Malignant cell (+cancer stem cells)
- HA
- Collagen
- Cancer-associated fibroblasts
- Endothelial Cell
- Lymphocyte
- Pericyte
- Myeloid Cell
- Neutrophil
- Capillary

Expected TME Post PEGPH20 Administration:

- Reduced tumor interstitial pressure
- Expansion of blood vessels

PEGPH20 Plus Chemotherapy Can Result in Increased Tumor Cell Death In Animal Models

Illustration of TME (Post PEGPH20 plus Chemotherapy)



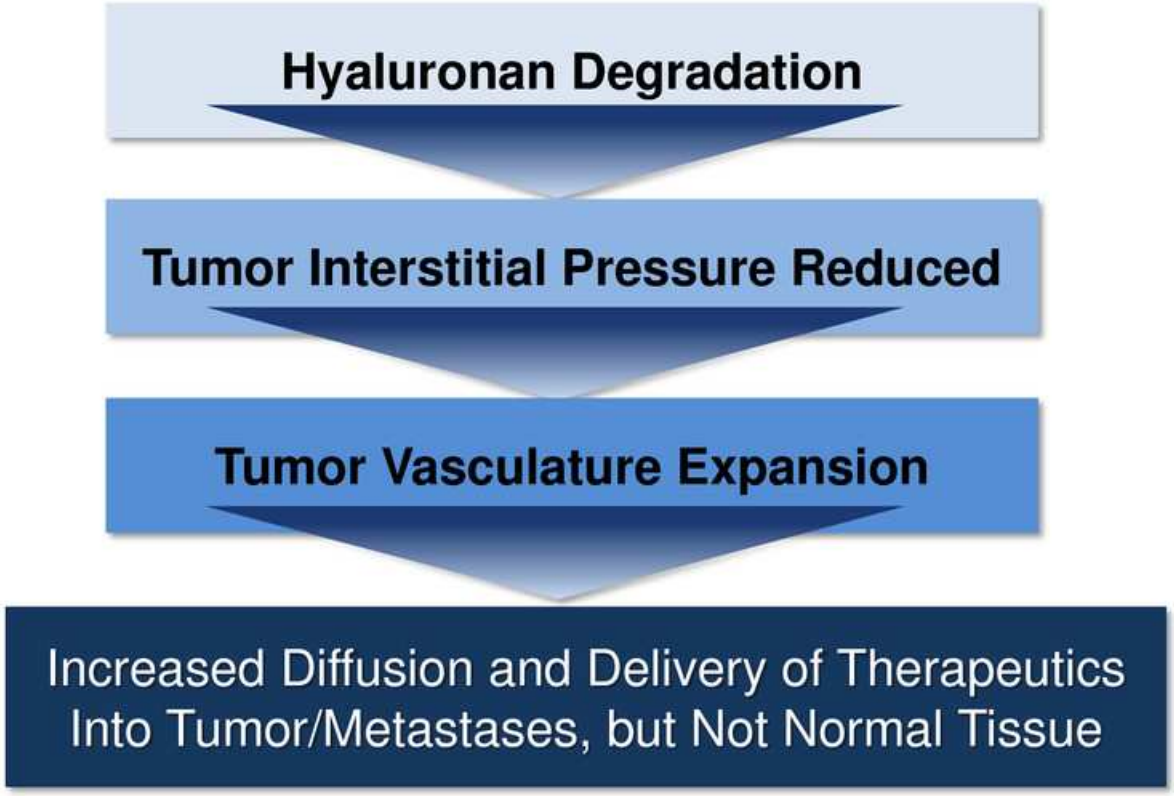
- Malignant cell (+cancer stem cells)
- HA
- Collagen
- Cancer-associated fibroblasts
- Endothelial Cell
- Lymphocyte
- Pericyte
- Myeloid Cell
- Neutrophil
- Capillary

Expected TME Post PEGPH20 plus Chemotherapy Administration:

- Reduced tumor interstitial pressure
- Expansion of blood vessels
- Increased anti-cancer therapy access to tumor and increased tumor cell death

PEGPH20 In Animal Models Rapidly Reverses High Tumor Pressure Allowing Increased Anti-Cancer Drug Access to Tumor

PEGPH20 In Animal Models



Today's Agenda

Introduction and Objectives	**Helen Torley, MB, ChB, MRCP** President and Chief Executive Officer Halozyme Therapeutics
PEGPH20 Mechanism of Action	**Christopher Thanos, PhD** Director, Biotherapeutics Halozyme Therapeutics
Exploring Combinations of PEGPH20 With Cancer Therapies	**Curt Thompson, PhD** Senior Director, Pharmacology Halozyme Therapeutics
From Theory to Initial Clinical Experience	**Sunil R. Hingorani, MD, PhD** Associate Member, FHCRC Director, Center for Accelerated Translation in Pancreas Cancer
Clinical Development Plan Update	**Athena Countouriotis, MD** Chief Medical Officer Halozyme Therapeutics
Q&A	

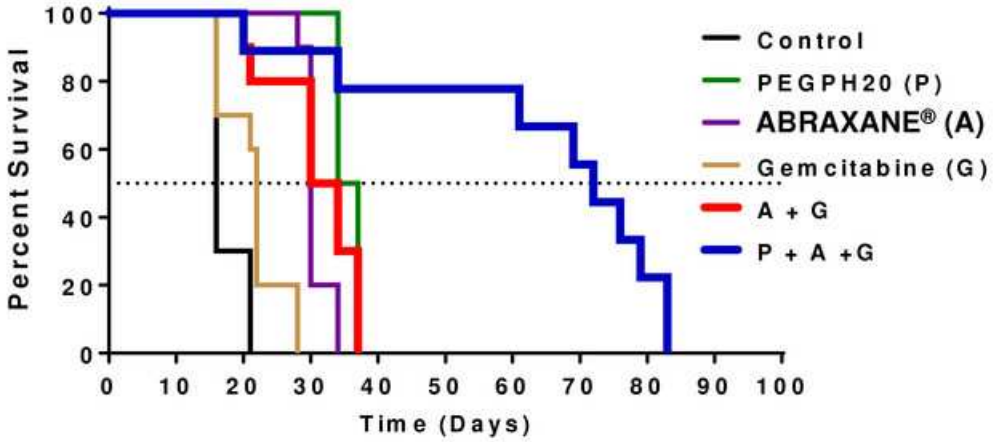
Nonclinical Exploration of Combinations of PEGPH20 With Cancer Therapies

Curt Thompson, PhD
Senior Director, Pharmacology
Halozyme Therapeutics

In Pancreatic Cancer Animal Model, PEGPH20 Increased Survival When Combined with Gemcitabine and Abraxane®

HA^{high} AsPC1/HAS3 Pancreatic Xenografts

	C	A + G	P + A + G
Median survival (days)	30	48	74



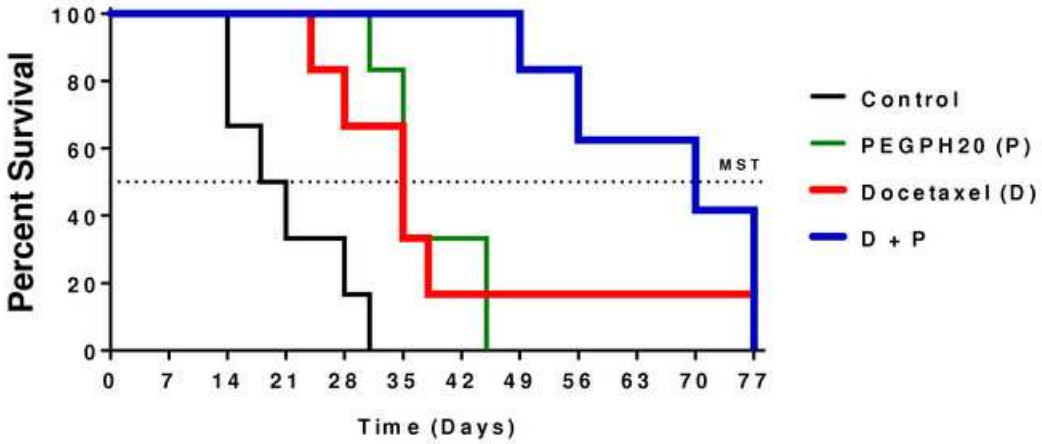
Mice (n≥12) received PEGPH20 (37.5 µg/kg, IV, 2x/wk) ± A (10 mg/kg, IV, q7d) ± G (180 mg/kg, IP; 24h after PEGPH20 ± A, q7d). Percent survival defined as (a) time to tumor volume ≥ 2000 mm^3, (b) time to ≥ 20% bodyweight loss, or (c) time to animal duress or death.

Osgood, et al. AACR, Pancreatic Cancer: Innovations in Research and Treatment, May 2014, in New Orleans.

In NSCLC Animal Model, PEGPH20 Doubled Survival When Combined with Docetaxel

HA^{high} LUM697 NSCLC Patient Derived Human Xenografts

	C	D	D + P
Median survival (days)	19.5	35	70

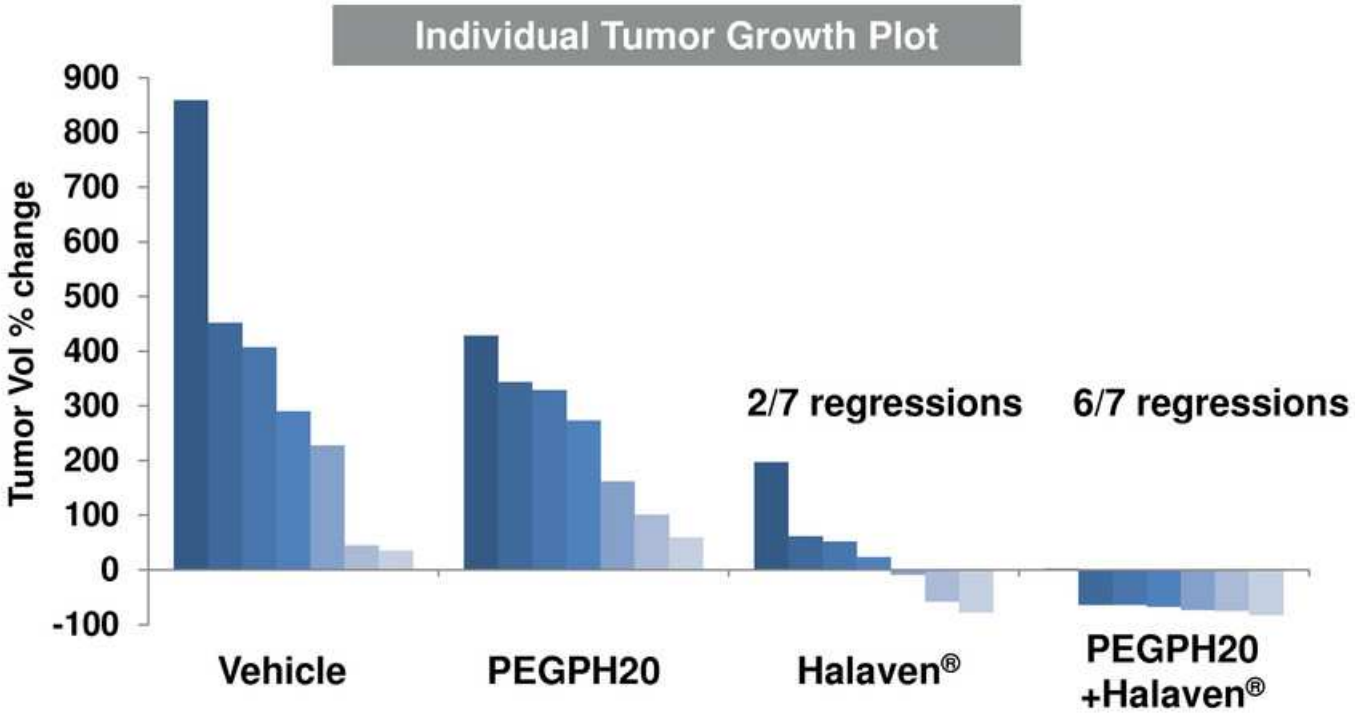


Mice (n≥12) received PEGPH20 (37.5 µg/kg, IV, 2x/wk) ± D (5 mg/kg, IV, q7d). Percent survival defined as (a) time to tumor volume ≥2000 mm^3, (b) time to ≥20% bodyweight loss, or (c) time to animal duress or death.

Jiang, et al. Halozyme Therapeutics, Inc. unpublished data, experiments completed in 2014.

In Triple Negative Breast Cancer Animal Model, PEGPH20 Resulted In Tumor Regression Combined with Halaven®

HA^{high} HCC1806/HAS3 Xenografts

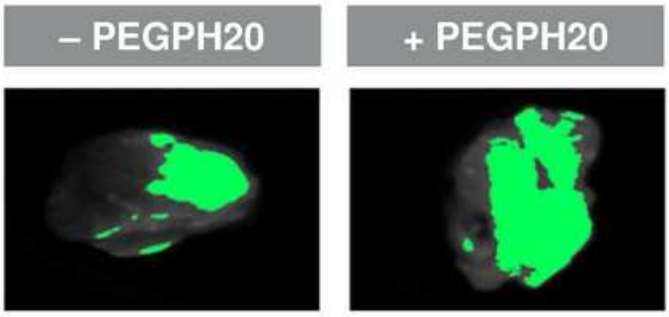


Huang, et al. Halozyme Therapeutics, Inc. unpublished data, experiments completed in 2014.

In Ovarian Cancer Animal Model, PEGPH20 Enhanced Antibody Access

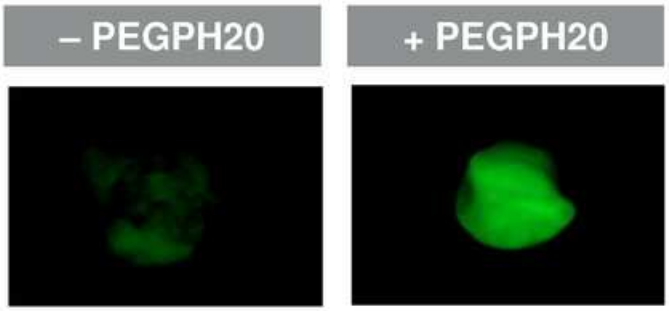
HA^{high} SK-OV3/HAS2 Xenograft Tumor

Increased Trastuzumab Accumulation



Trastuzumab labeled with AF488 48h post treatment

Increased Anti-PD-L1 Accumulation

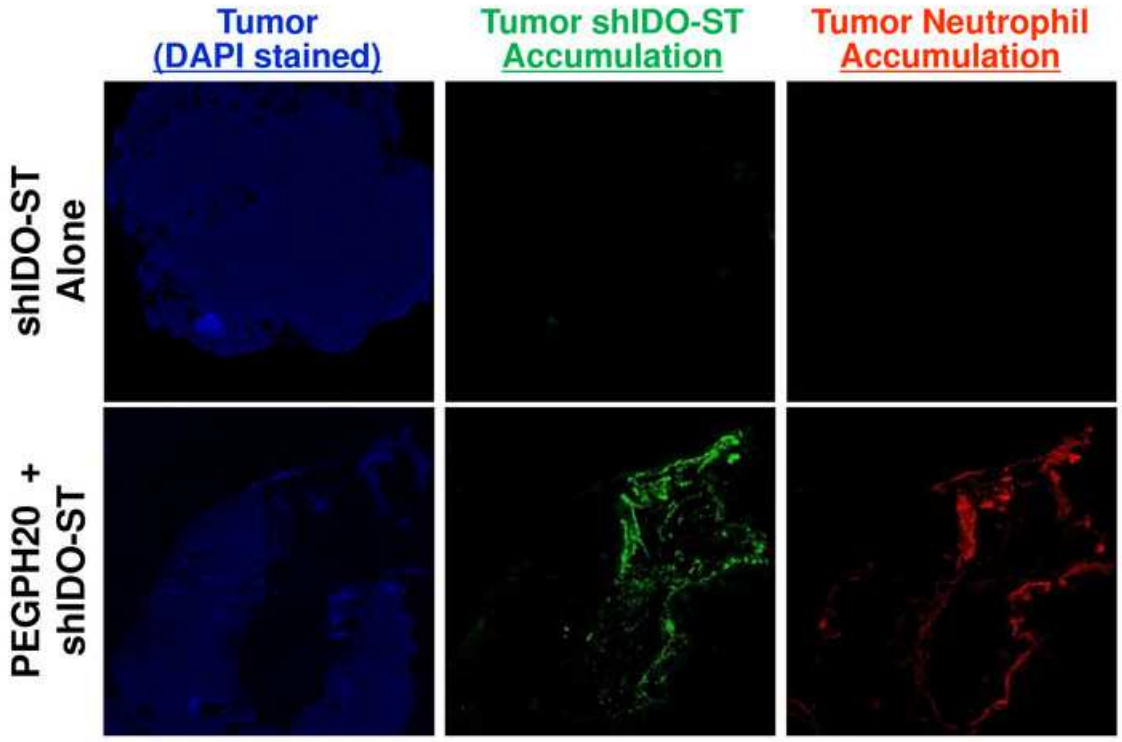


Anti-PD-L1 labeled with AF488 48h post treatment

Singha, et al. *Mol Cancer Ther.* Epub Dec 2014.

In Pancreatic Cancer Animal Model, PEGPH20 Enhanced shIDO-ST and Neutrophil Influx

Luc-expressing Orthotopic PDA Tumors (KPC Derived)

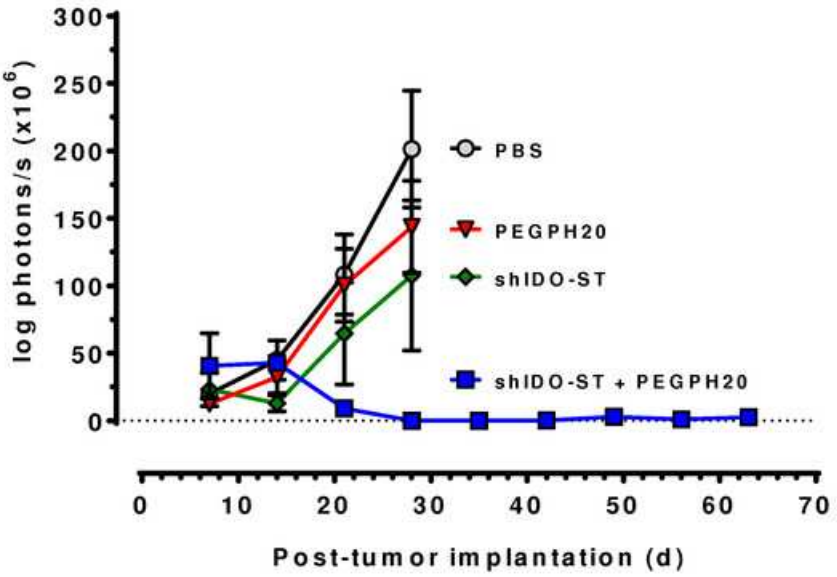


Immuno-fluorescence staining (5x) w/Mab against ST or neutrophils, 96h post-treatment

Manuel, et al. (City of Hope), AACR, Pancreatic Cancer Mtg, May 2014, in New Orleans

In Pancreatic Cancer Animal Model, PEGPH20 Facilitated shIDO-ST-mediated Tumor Regression

Luc-expressing Orthotopic PDA Tumors (KPC Derived)



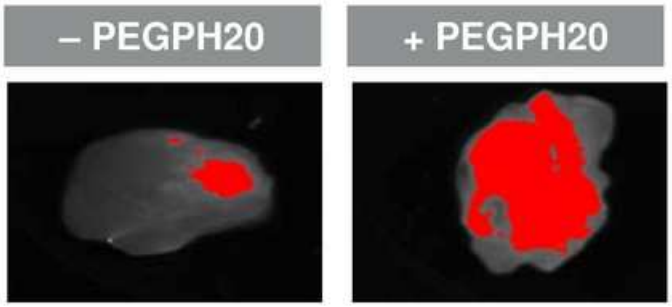
shIDO-ST (5e6 CFU/mouse, qd3x, d14-16), PEGPH20 (2.25 mg/kg, 1x d13)

Manuel, et al. (City of Hope), AACR, Pancreatic Cancer Mtg, May 2014, in New Orleans

In Ovarian Cancer Animal Model, PEGPH20 Enhanced Immune Cell Access into HA^{high} Tumor

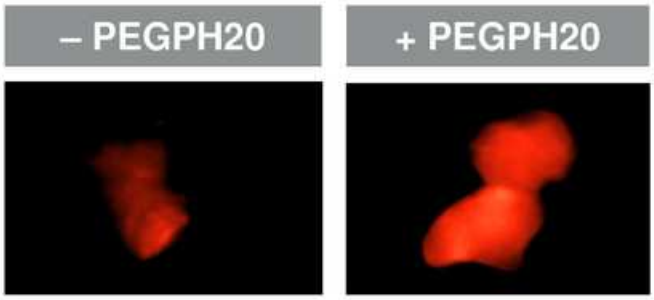
HA^{high} SK-OV3/HAS2 Xenograft tumor

Increased Natural Killer (NK) Cell Accumulation



Human primary NK cells labeled with PKH26 co-injected with trastuzumab, 48h post

Increased Primary T Cell Accumulation

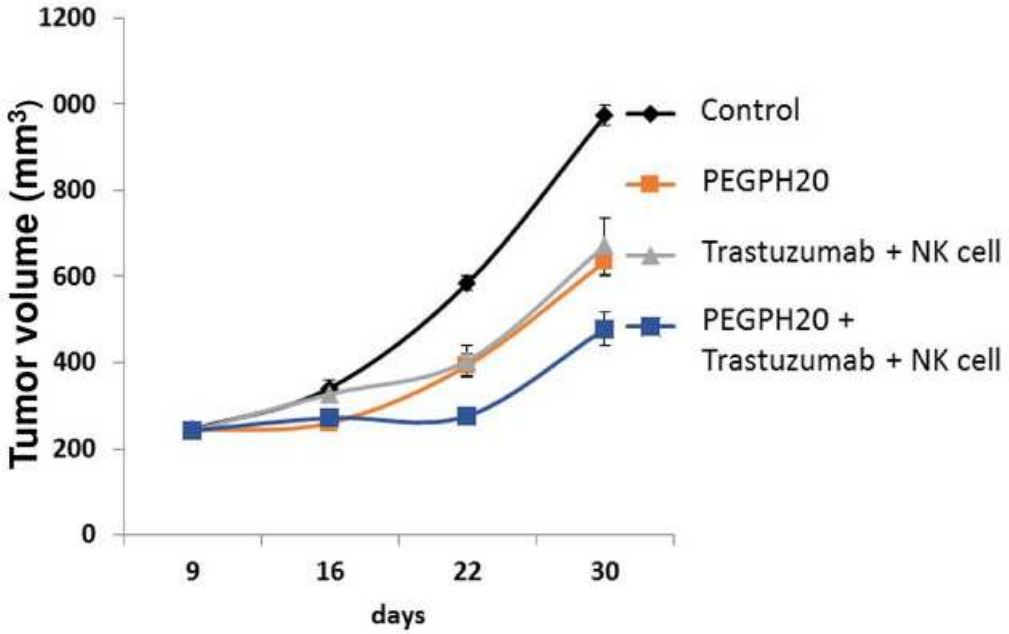


Human primary T cells labeled with PKH26, 48h post-treatment

Singha, et al. *Mol Cancer Ther.* Epub Dec 2014.

In Ovarian Cancer Animal Model, PEGPH20 Plus Trastuzumab and NK Cells Inhibited Tumor Growth

SKOV3/HAS2 Tumor Xenografts



Increased Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC)

Singha, et al. *Mol Cancer Ther.* Epub Dec 2014.

PEGPH20 Nonclinical Summary

- PEGPH20, an investigational drug, depletes HA content of tumors in animal studies
  - Reduced tumor interstitial pressure resulting in increased tumor perfusion
  - Increased tumor access of
    - Small molecules
    - Monoclonal antibodies including immune checkpoint inhibitors
    - Immune cells
- Depletion of HA in nonclinical studies demonstrated to:
  - Inhibit tumor growth
  - Improve survival
  - Decrease metastasis
- No increase in tested cancer therapy penetration to normal tissues

Today's Agenda

Introduction and Objectives	**Helen Torley, MB, ChB, MRCP** President and Chief Executive Officer Halozyme Therapeutics
PEGPH20 Mechanism of Action	**Christopher Thanos, PhD** Director, Biotherapeutics Halozyme Therapeutics
Exploring Combinations of PEGPH20 With Cancer Therapies	**Curt Thompson, PhD** Senior Director, Pharmacology Halozyme Therapeutics
From Theory to Initial Clinical Experience	**Sunil Hingorani, MD, PhD** Associate Member, FHCRC Director, Center for Accelerated Translation in Pancreas Cancer
Clinical Development Plan Update	**Athena Countouriotis, MD** Chief Medical Officer Halozyme Therapeutics
Q&A	

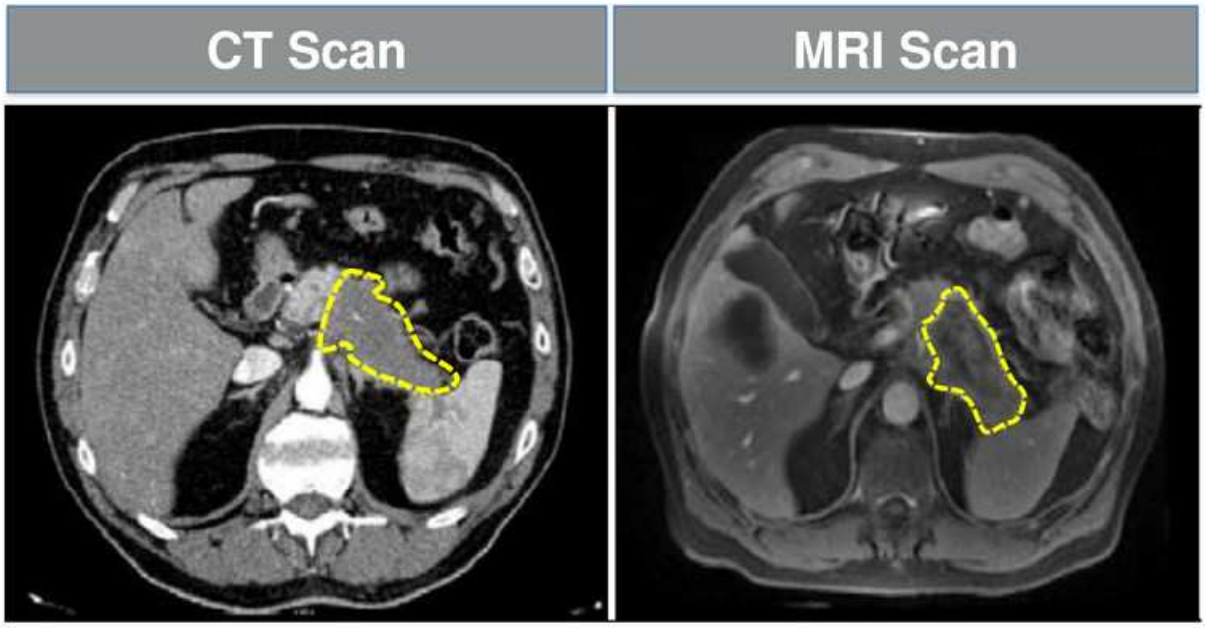
From Theory to Initial Clinical Experience

Sunil R. Hingorani, MD, PhD
Associate Member, FHCRC
Director, Center for Accelerated Translation in Pancreas Cancer

Sobering Realities of Pancreas Cancer

- Increasing incidence with unabated mortality
- Eludes detection until late stages
- Metastasizes early and widely during disease progression
- Modest survival improvement in last 3 decades
- Highest 1, 5, and 10 year mortalities of any cancer

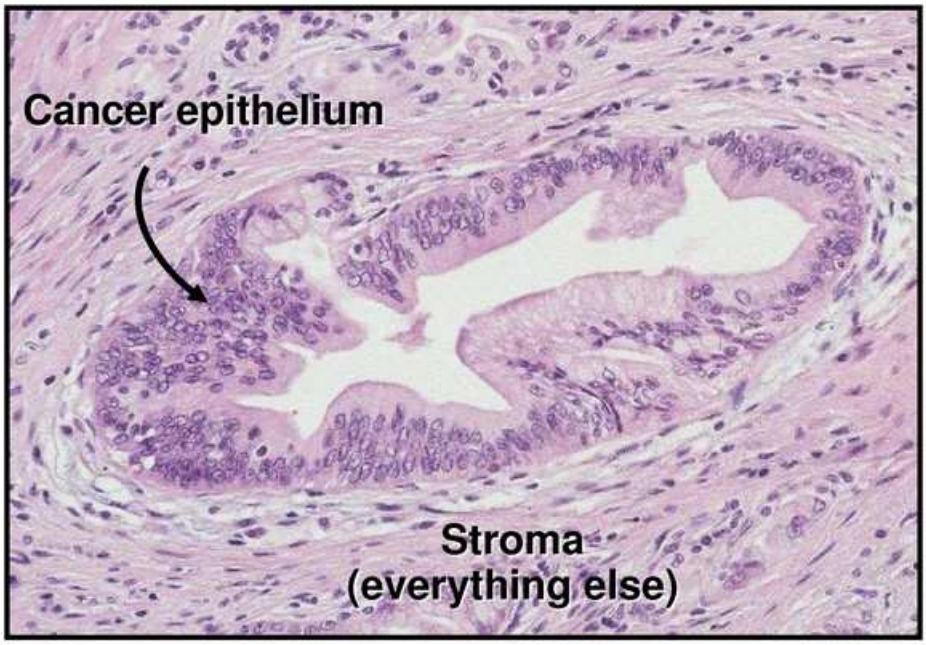
Pancreas Cancers are Hypoperfused: They Have a *Decreased* Blood Supply



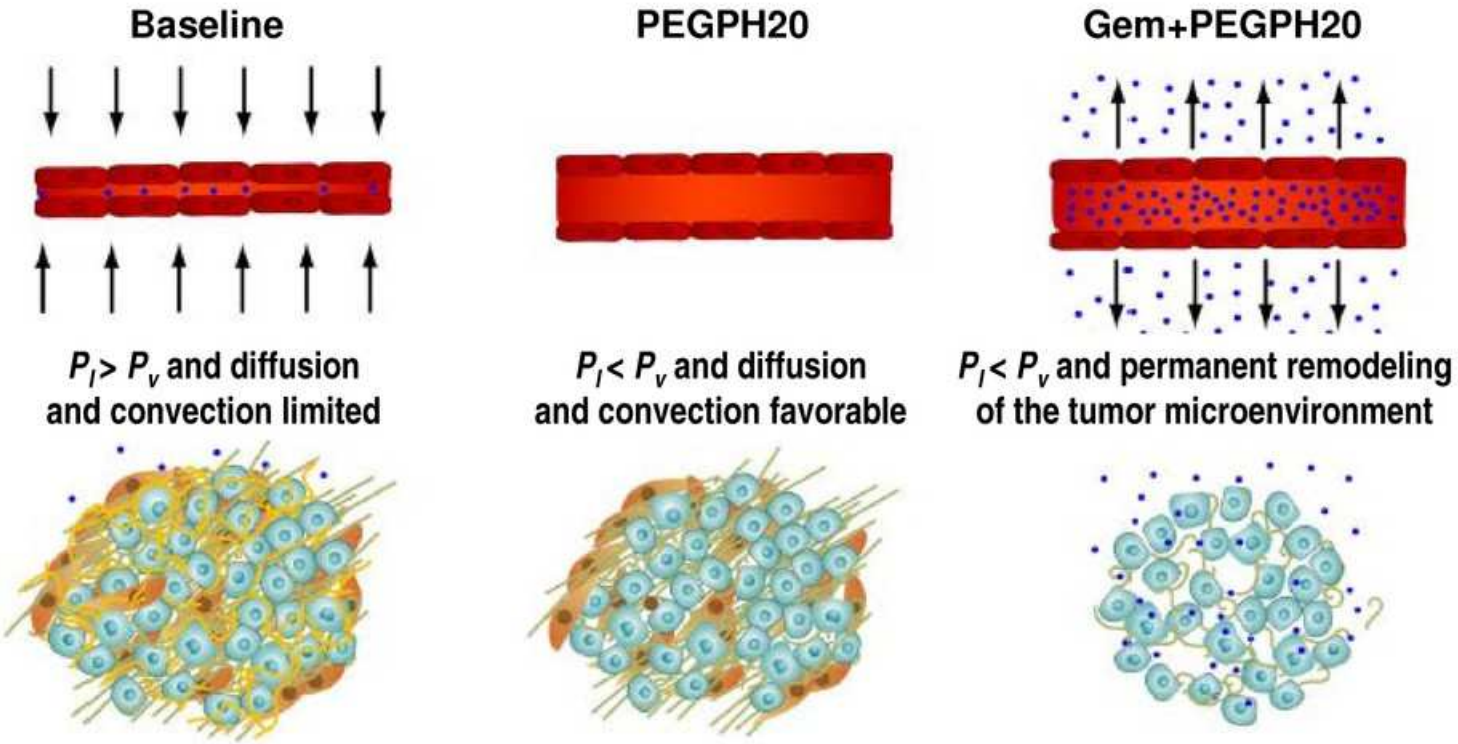
Von Hoff, et al. *Cancer Cell.* 2009,16:708.

Pancreas Cancer as a "Solid Tumor Organ": Multi-faceted Desmoplastic Response

Pancreas Cancer Histology



Changing the Game: Altering Intratumoral Physical Dynamics to Advantage in Pancreas Cancer

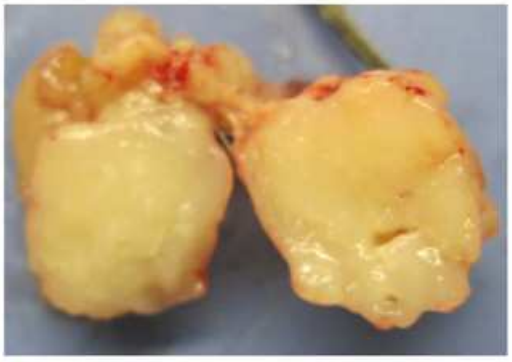


Provenzano, et al. *Cancer Cell.* 2012,21(3):418.

Breaching the Pancreas Cancer Sanctuary: Changing Disease Biology with PEGPH20

KPC Mouse Model

Before

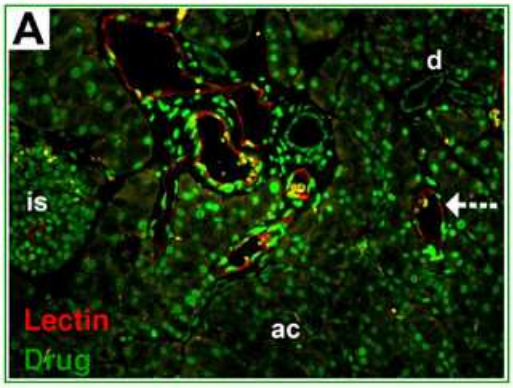


- **Hard**
- **Fibrotic**
- **Hypovascular**

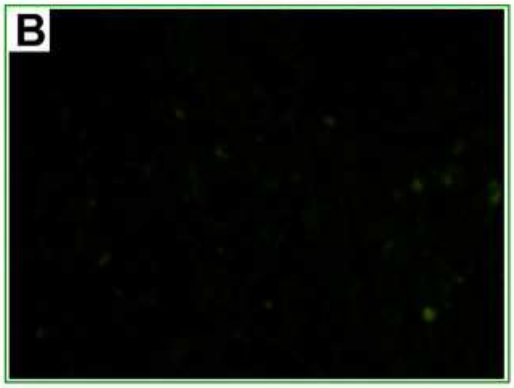
Provenzano, et al. *Cancer Cell.* 2012,21(3):418.

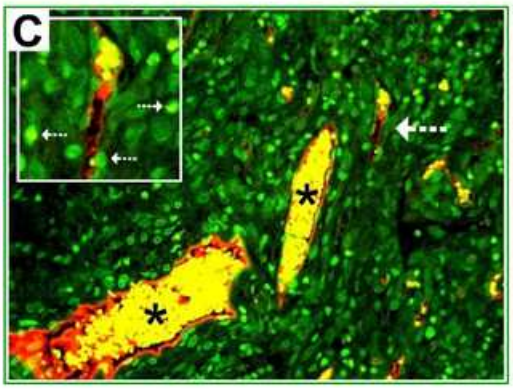
Breaching the Pancreas Cancer Sanctuary: Creating a Newly Vulnerable Disease

Normal Pancreas



Pancreas Cancer



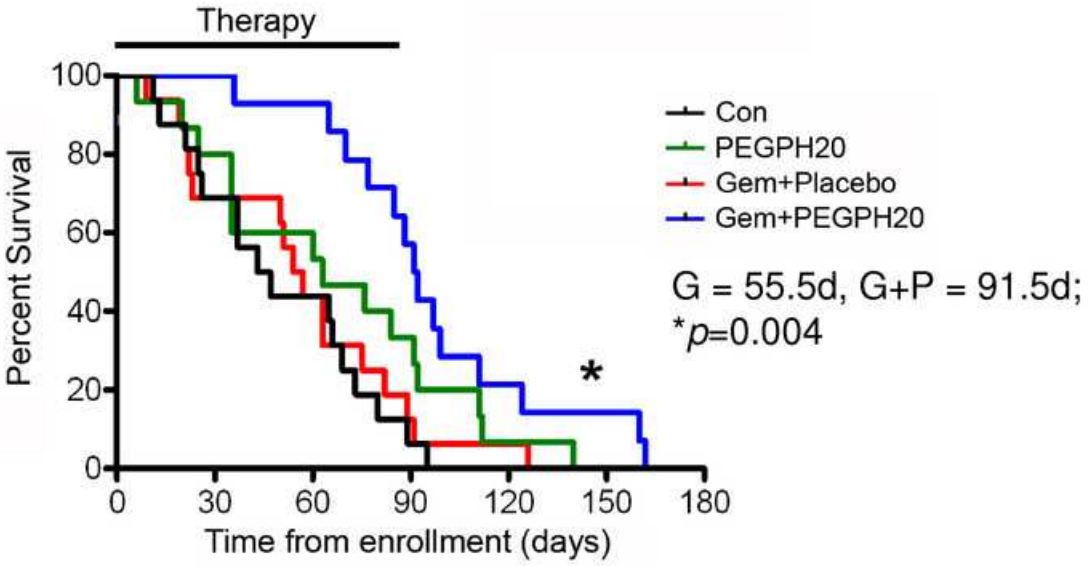


Pancreas Cancer Treated with PEGPH20

Provenzano, et al. *Cancer Cell.* 2012,21(3):418.

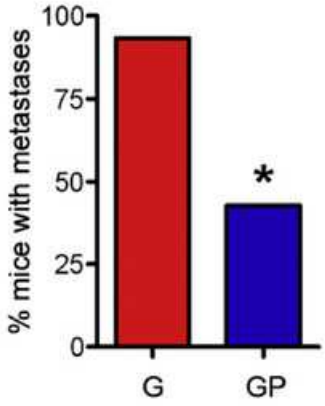
Randomized, Blinded, Placebo-controlled Preclinical Trial in KPC Pancreas Cancer Model

Combination Therapy Significantly Improves Survival in KPC Mice



Provenzano, et al. *Cancer Cell.* 2012.

Decreased Metastatic Burden With PEGPH20 + Gemcitabine Therapy in KPC Mice



Treatment (n=10)	% Met Disease	% Liver Mets	% Lung Mets	% Lymph Node Mets
GEM + Vehicle	93	73	40	73
GEM + PEGPH20	43	43	21	36

Gemcitabine dosed 1x/wk @ 3-wk on / 1-wk off schedule; PEGPH20 dosed 24 hr prior to gemcitabine.

Provenzano, et al. *Cancer Cell.* 2012.

Clinical Proof of Concept Demonstrated in Phase 1b Trial in Advanced Pancreatic Cancer

Halozyme Study 201 Study Objectives

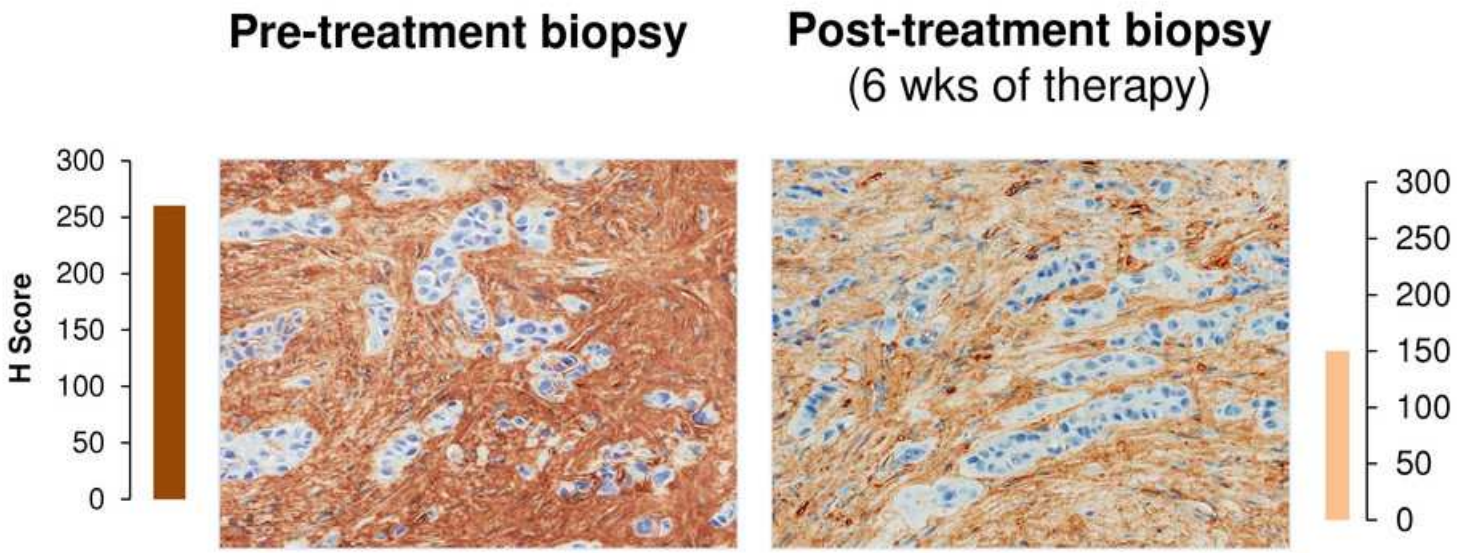
- **Primary**
  - Assess safety and tolerability of PEGPH20 in combination therapy
  - Establish recommended phase 2 dose (RP2D) of PEGPH20 in combination with gemcitabine in patients with Stage IV previously untreated Pancreatic Ductal Adenocarcinoma
- **Secondary**
  - Assess tumor response using RECIST 1.1 criteria
  - Assess pharmacokinetic (PK) profile and evaluate pharmacodynamic activity of PEGPH20
  - Assess treatment effect based on tumor HA status

Study 201 PEGPH20 Treatment-Related AEs (≥10% in Total Incidence)

Adverse Events N = 28	Grade 3/4	All Grades
	Incidence, %	
Any AE	7 (25.0)	24 (85.7)
Muscle spasms	2 (7.1)	15 (53.5)
Myalgia	0	11 (39.3)
Arthralgia	0	8 (28.6)
Edema peripheral	1 (3.6)	8 (28.6)
Fatigue	1 (3.6)	7 (25.0)
Pain in extremity	0	5 (17.9)
Asthenia	0	3 (10.7)

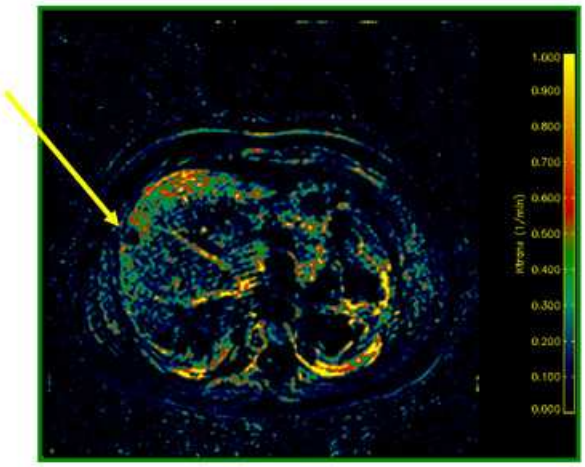
*One Grade 5 event reported: cerebrovascular accident.

Study 201: Example of HA Target Modulation

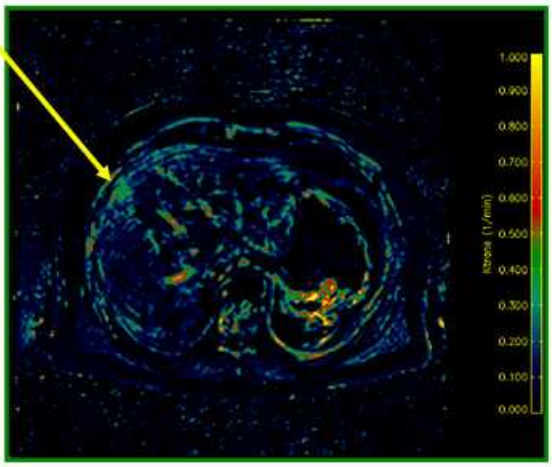


Hingorani, et al. ASCO 2013 (abstract 4010).

Study 201: Example of Increased Perfusion (K_{trans}) after PEGPH20



Baseline:
Mean = 0.14 min^{-1}
Median = 0.10 min^{-1}

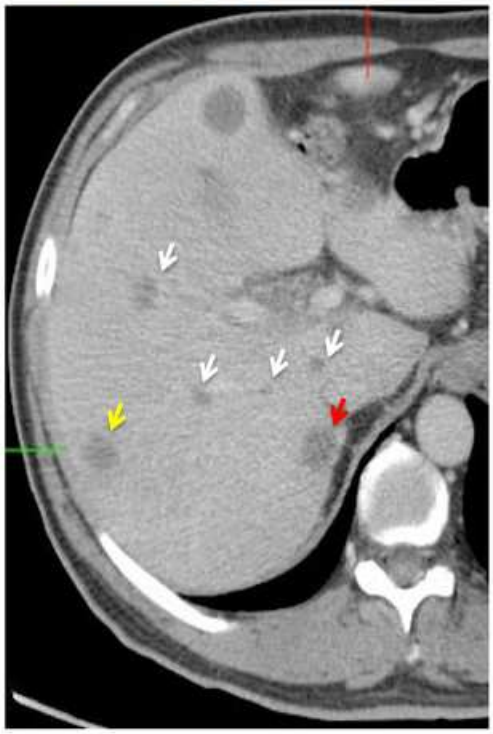


24-hr Post 1st Dose:
Mean = 0.20 min^{-1}
Median = 0.17 min^{-1}

Hingorani et al., *ECCO* 2013 (abstr 2598)
Hingorani et al., *J Clin Oncol* 2013 (abstr 4010)

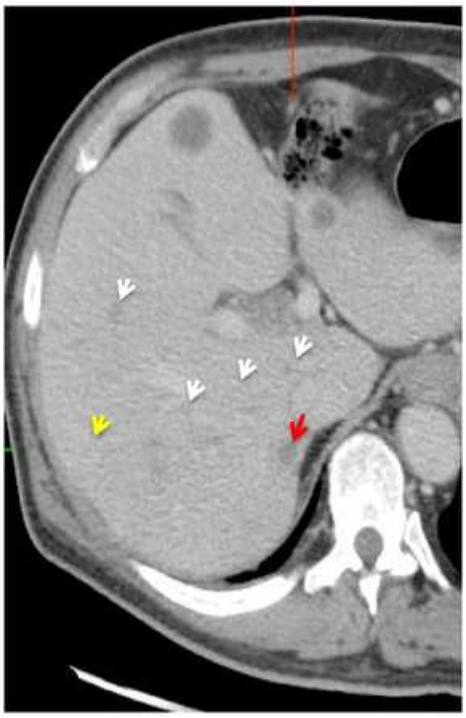
Study 201: Example of Radiographic Response (PR) at EOC1

Baseline
Sum Target L = 83.2 mm



TL3
Diameter:
19.3 mm
Volume:
1.5 cm^3

EOC1
Sum Target L = 56.1 mm



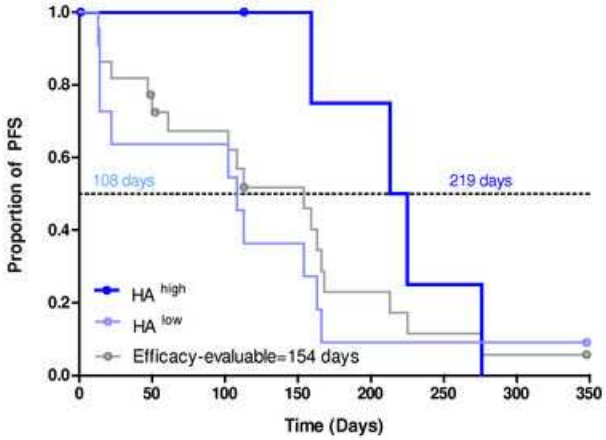
TL3
Diameter:
10.2 mm
Volume:
0.33 cm3

Hingorani, et al. ASCO 2013 (abstr 4010)

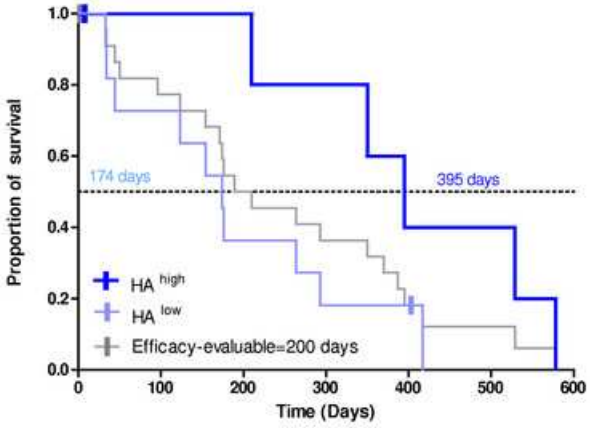
Final Results of Study 201 Exploratory Analyses Support Potential for HA^{high} as Response Predictor

Single-arm Phase1b Evaluation PEGPH20+gemcitabine in Stage IV Metastatic Pancreatic Ductal Adenocarcinoma

Progression-Free Survival (PFS)



Overall Survival (OS)



	ORR% (n)*	Median PFS (days)	OS (days)
Gem+PEGPH20	29% (7/24)	154	200
HA^{high}	67% (4/6)	219	395
HA^{low}	27% (3/11)	108	174

Source: Study 201 Final Report

(*confirmed PR per RECIST1.1)

Summary: PEGH20+Gemcitabine in Models and Patients

- Pancreas cancer primary tumors and metastases effectively exclude chemotherapeutics
- PEGPH20 alters unfavorable hydrodynamics to promote drug penetration
- PEGPH20 seems well-tolerated in patients
- Patients with high intratumoral HA levels appear to benefit most from PEGPH20

Today's Agenda

Introduction and Objectives	**Helen Torley, MB, ChB, MRCP** President and Chief Executive Officer Halozyme Therapeutics
PEGPH20 Mechanism of Action	**Christopher Thanos, PhD** Director, Biotherapeutics Halozyme Therapeutics
Exploring Combinations of PEGPH20 With Cancer Therapies	**Curt Thompson, PhD** Senior Director, Pharmacology Halozyme Therapeutics
From Theory to Initial Clinical Experience	**Sunil R. Hingorani, MD, PhD** Associate Member, FHCRC Director, Center for Accelerated Translation in Pancreas Cancer
Clinical Development Plan Update	**Athena Countouriotis, MD** Chief Medical Officer Halozyme Therapeutics
Q&A	

Clinical Development Plan Update

Athena Countouriotis, MD
Chief Medical Officer
Halozyme Therapeutics

Robust Non-Clinical Observations Inform Our Clinical Development Strategy

HA^{high} present in many patients with common solid tumors

- **Evaluate PEGPH20 in multiple tumor types**

PEGPH20 inhibits tumor growth in HA^{high} animal tumor models

- **Select HA^{high} patients through development of Companion Diagnostic**

PEGPH20 Increases intratumor concentration of anticancer treatments in animal tumor models

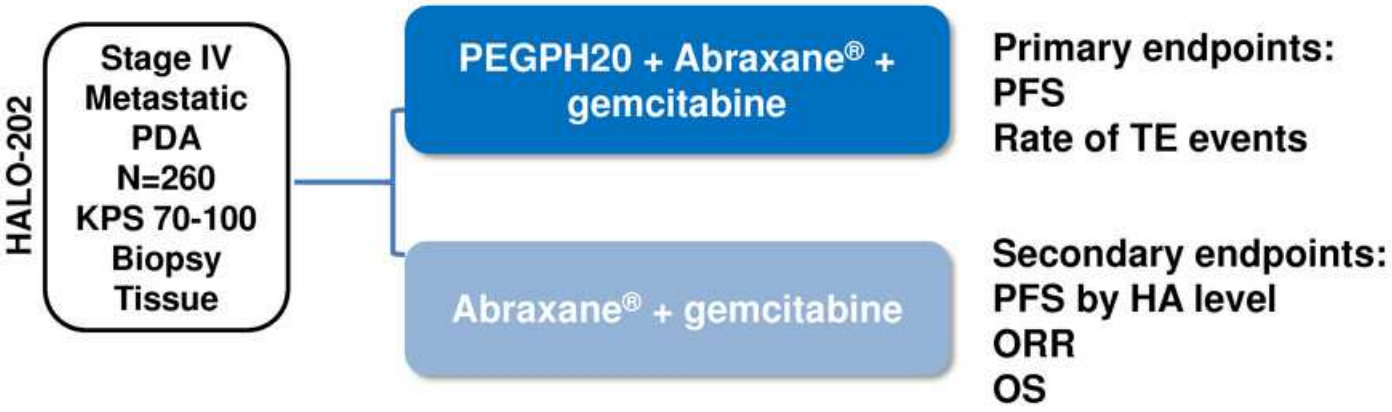
- **Study combination of PEGPH20 with Standard of care chemotherapies AND Immune Checkpoint Inhibitor Antibodies**

Hypothesized Results for PEGPH20 in Combination with Abraxane® and Gemcitabine In Pancreatic Cancer

	PEGPH20 + AG (PAG)	Abraxane® + gemcitabine (AG)
High HA	Highest PFS *(HA^{high})*	Lowest PFS *(Poor prognosis - HA^{high})*
Low HA	Moderate PFS *(Low HA, likely = AG)*	Moderate PFS *(Better prognosis - Low HA)*

PEGPH20 is an investigational product

Study 202: Ongoing Trial of PEGPH20 with Abraxane® and Gemcitabine

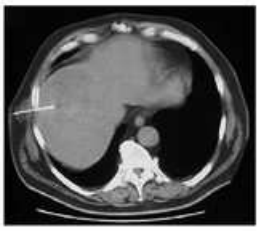


Total Sites	44 (US only)
First patient enrolled	March 2013
Expected last patient enrolled	2H 2015
Expected top line data	Event driven, estimate Q4 2015-Q1 2016
HA status	Retrospective assessment at central lab of tissue biopsy with HTI601/StainMap™

Current Approach Designed With Goal of Meeting FDA Standards and Expectations for a Companion Diagnostic

Referring Institution	CURRENT Central Lab	FUTURE Companion Diagnostic

Diagnostic Biopsy

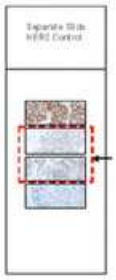


Embed Process Section

Unstained Section

Stained Slide

IHC-based Stain



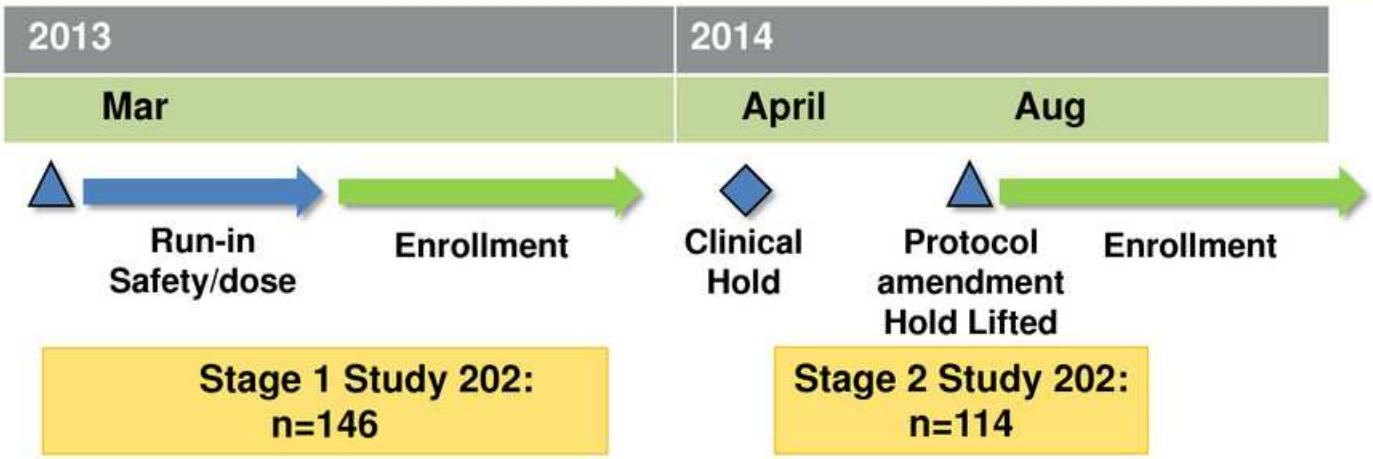
Scan

Digital Image Score

With Partner

U.S. Patent No. 8,846,034 issued for patient selection with an anti-hyaluronan agent, such as PEGPH20, diagnostic agents for detection and quantification of hyaluronan in a biological sample and combinations and kits for use in practicing the methods.

Study 202 History and Status



Clinical Hold: based on DMC finding of potential imbalance in TE events between treatment arms

Protocol Amendment

- Add ~100 patients
- 2:1 PAG to AG randomization
- Exclude high Thromboembolic Event risk patients
- Add LMWH to both arms
- Additional primary endpoint: evaluation of TE events Stage 2 vs Stage 1

Interim Analysis Study 202

- Conducted to evaluate further the level of HA accumulation (ie HA^{high}) to assist in the development of our companion diagnostic and our clinical development plan in pancreatic and NSCLC

- Important caveats
  - Open database, ongoing study
  - Data verification ongoing

Study 202: Response Rate Analysis Populations

Populations Evaluated	PAG n=	AG n=	Analysis
Randomized to Trial in Stage 1	**77**	**69**	
Response Rate Population			
Safety population: received study drug prior to Clinical Hold	**74**	**61**	**Overall Response Rate**
HA response rate population: received study drug, had at least one post-baseline tumor assessment and have HA data	**35**	**27**	**Overall Response Rate by HA level**

Data Through April 9th, 2014

Results: Early Data Suggest Higher ORR with PEGPH20 Particularly in HA^{high}

Study 202 Interim Analysis: ORR (RECIST 1.1 for controlled trial)				
Analysis Population	PAG Arm Responders/ total patients (%)	AG Arm Responders/ total patients (%)	Rate Ratio	P-value PAG vs AG
Safety	25/74 (34)	14/61 (23)	1.5	0.17
HA Overall Response Rate	21/35 (60)	10/27 (37)	1.6	0.090
HA High	12/17 (71)	5/17 (29)	2.4	0.016
HA Low	9/18 (50)	5/10 (50)	1.0	0.94

- ORR based on independent, blinded central review
- Safety data presented on slides 71-73

MPACT Study ORR Results: Von Hoff D. *NEJM*. 2013,369:1691

- Abraxane® plus gemcitabine, 23% vs gemcitabine, 7%

Results: Early Data Suggests Increased PFS In HA^{high} Patients Treated with PEGPH20

Progression Free Survival

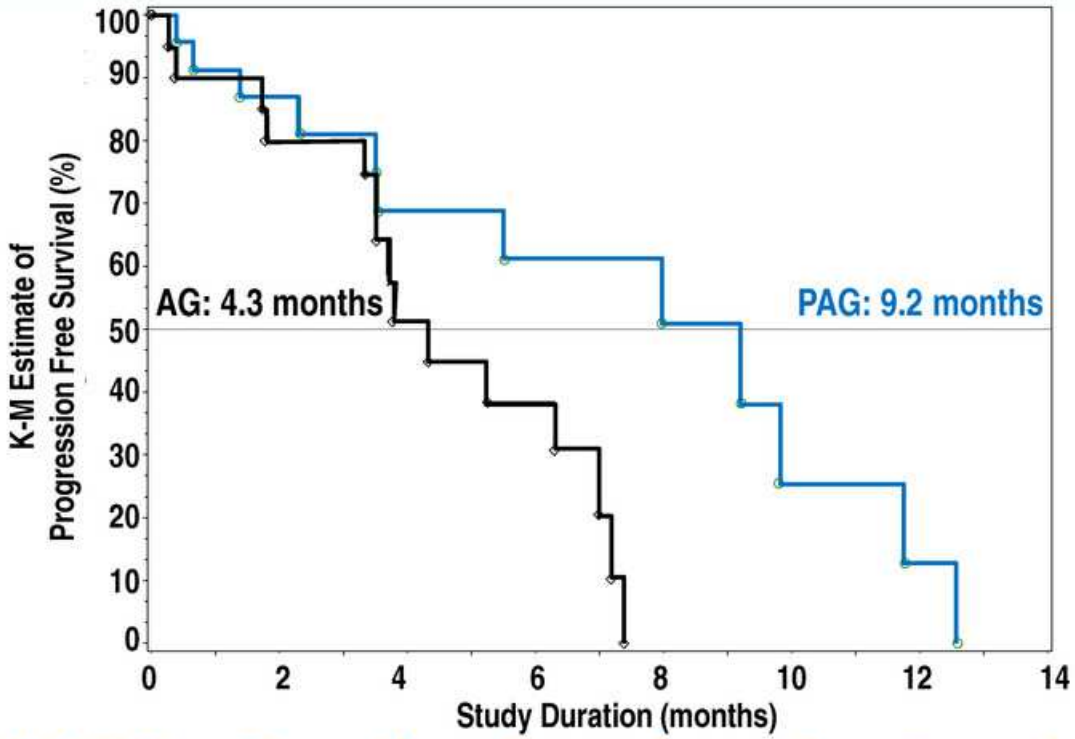
Study 202 Interim Results: Analysis Population	No. with events / total evaluated patients; median PFS in months			
	PAG arm n=61	AG arm n=45	HR	P-value PAG vs AG
Safety w/HA	34/61; 5.5	30/45; 4.8	0.64	0.086
HA High	12/25; 9.2	15/23; 4.3	0.38	0.031
HA Low	22/36; 4.8	15/22; 5.6	0.92	0.81

MPACT Study PFS Results: Von Hoff D. *NEJM.* 2013,369:1691

- Abraxane® plus gemcitabine 5.5 months vs gemcitabine 3.7 months

Results: Early Data Suggests Increased PFS In HA^{high} Patients Treated with PEGPH20

PFS In Patients with HA^{high}



At Risk PAG: 25	20	11	8	5	2	1	0
AG: 23	16	8	6	0	0	0	0

Study 202: Interim ORR and PFS Data Summary

	PAG	AG
High HA	ORR: 71% PFS: 9.2 months	ORR: 29% PFS: 4.3 month
Low HA	ORR: 50% PFS: 4.8 months	ORR: 50% PFS: 5.6 months

ORR data through April 9th and reflects PAG or AG treatment
PFS data through December 5th and reflects PAG → AG treatment in PAG arm

Overall Safety Profile
Treatment Related AEs >25% Patients

	PAG N=74 Patients, n (%)		AG N=61 Patients, n (%)	
Preferred Term	**Grade 3+**	**Any Grade**	**Grade 3+**	**Any Grade**
Any AE	61 (82.4)	73 (98.6)	45 (73.8)	57 (93.4)
Fatigue	13 (17.6)	50 (67.6)	11 (18.0)	39 (63.9)
Nausea	5 (6.8)	41 (55.4)	2 (3.3)	27 (44.3)
Anemia	14 (18.9)	30 (40.5)	10 (16.4)	32 (52.5)
Edema peripheral	2 (2.7)	43 (58.1)	3 (4.9)	17 (27.9)
Diarrhea	5 (6.8)	31 (41.9)	2 (3.3)	22 (36.1)
Alopecia	0	24 (32.4)	0	25 (41.0)
Decreased appetite	4 (5.4)	26 (35.1)	2 (3.3)	15 (24.6)
Muscle spasms	6 (8.1)	40 (54.1)	0	1 (1.6)
Platelet count decreased	5 (6.8)	21 (28.4)	4 (6.6)	18 (29.5)
Vomiting	4 (5.4)	23 (31.1)	0	16 (26.2)
Neutropenia	18 (24.3)	24 (32.4)	9 (14.8)	11 (18.0)

Adverse Events Leading to Discontinuation

	Adverse Event	PAG	AG
AE leading to discontinuation		13/74 (18%)	13/61 (21%)
AEs resulting in discontinuation occurring in >1 patient, either arm	Pneumonitis	3	0
	Pulmonary embolism	2	0
	Acute renal failure	0	2

Study 202: Stage 1 Interim Results Thromboembolic Events Through 12/1/14

Parameters	PAG	AG
Patients, N	74	61
Patients with TEs, n (%)	31 (41.9)	15 (24.6)
Patients with PE, n (%)	16 (21.6)	6 (9.8)
Patients with DVT, n (%)	16 (21.6)	9 (14.7)
Patients with Arterial TE, n (%)	7 (9.4)	0
Grade 1 and 2 events, (% of N)	21	15
Grade ≥3 events (% of N)	23	5

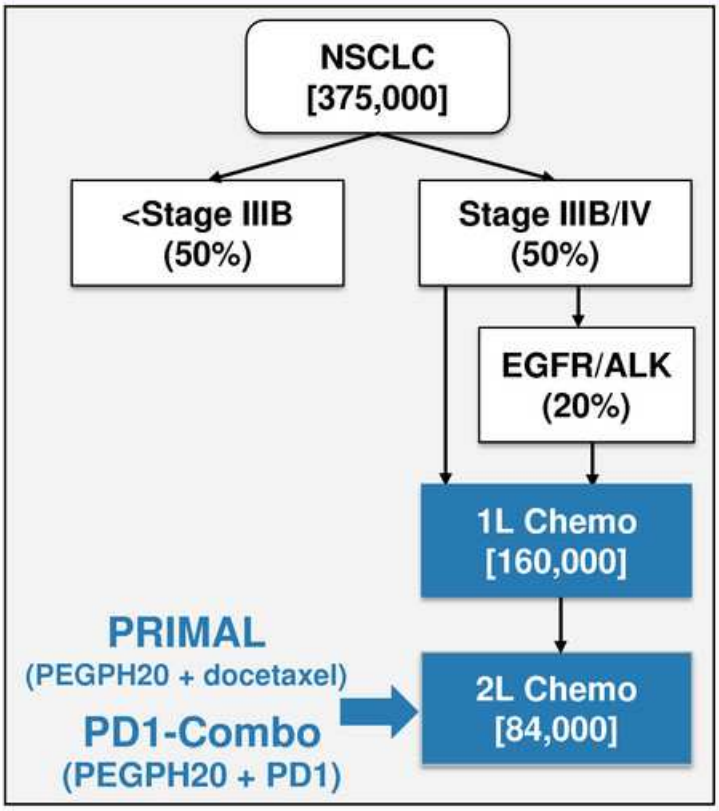
TE events in Stage 1 managed through dose interruption, with majority of patient reinitiating PAG/AG post anticoagulation. Patients may have had more than one event

Pancreatic Cancer: Planned Next Steps

- **Meeting with FDA (end Q1 target)**
  - **Discuss potential registration-seeking trial in HA^{high} Stage 4 Pancreatic Ductal Adenocarcinoma patients**
- **Gain EMA scientific advice on proposed protocol**

Non Small Cell Lung Cancer – Significant Unmet Medical Need

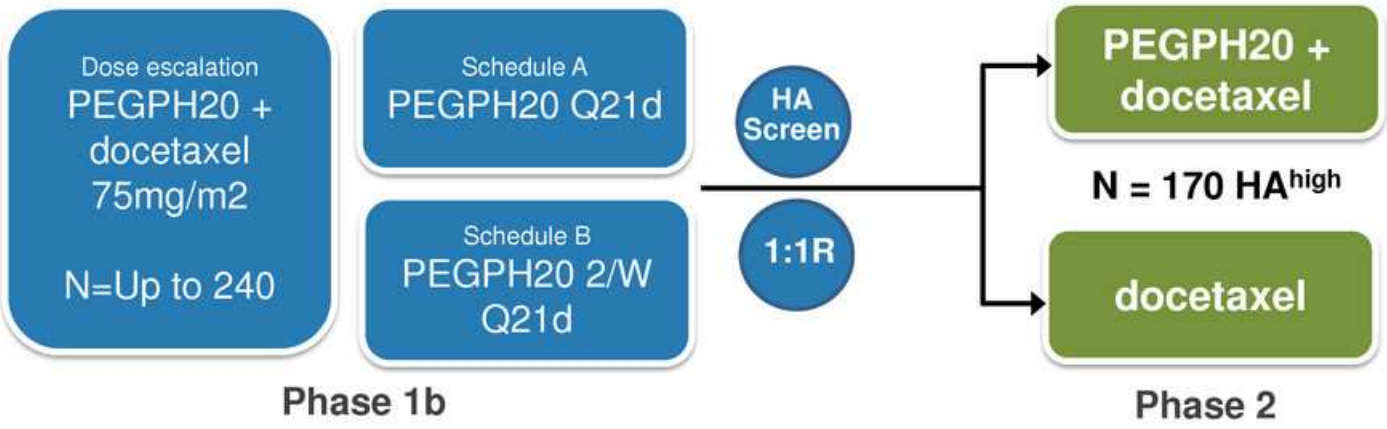
- Over 160K newly diagnosed 1L and 84K 2L patients annually (US & 5EU)
- Survival times remain low with no curative therapy
  - In 1st line non-biomarker population OS is 10-12 months and PFS is 4-6 months
  - In 2nd line OS is 7-8 months and PFS 3-4 months
- Immunotherapy may offer hope for some but opportunity remains to do more



References: GLOBOCAN 2012 (IARC) - 3.7.2014; "Lung Cancer", American Cancer Society, 2014.
2 Scagliotti, et al. *J Clin Oncol.* 2008; 26:3543-51, Halozyme analysis.

Phase 1b/2 PRIMAL Study in NSCLC Initiated

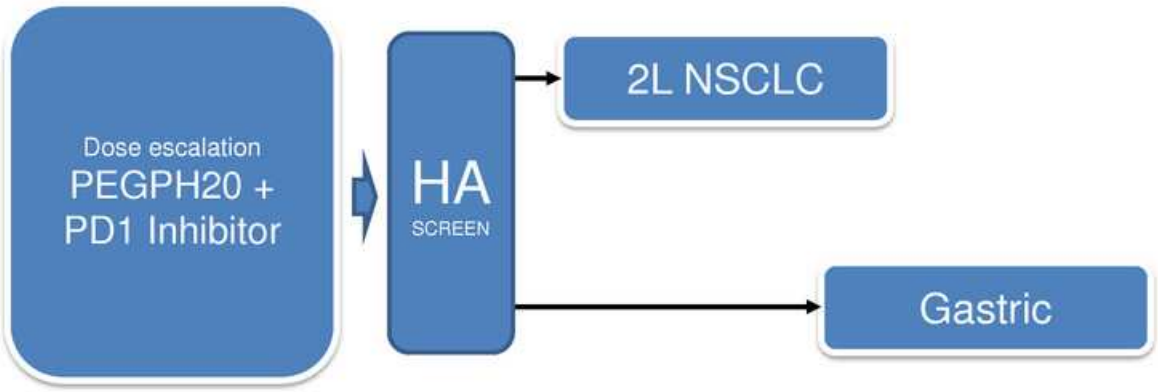
PEGPH20 + docetaxel in HA^{high} Platinum Failed NSCLC Patients



Total Sites	**Phase 1b ~10, Phase 2 50-75; Global**
Study Status	**Sites opening: patient screening underway**
Study Objectives	**Phase 1b: Dose finding: schedule options** **Phase 2: Efficacy in HA ^{high} patients**
Primary Endpoint	**PFS**
Secondary Endpoints	**ORR, DOR, DCR, OS**

Exploring Combination of PEGPH20 with an Anti PD1 Antibody in HA^{high} Tumors—HALO 107-101

Phase 1b Study in Multiple Tumors: 20 HA ^{high} Subjects Each



Dose Escalation

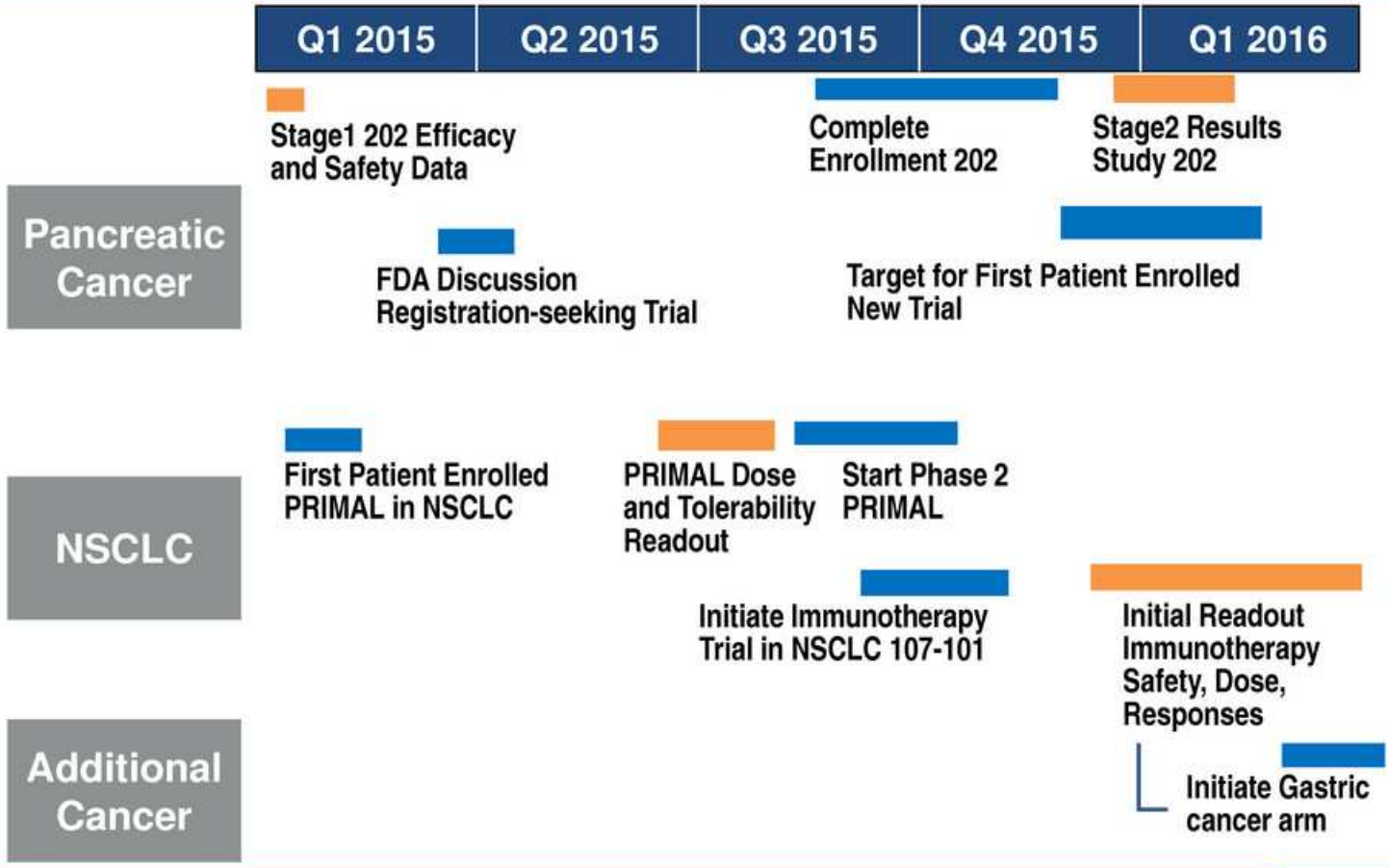
Endpoints: DLT, MTD, RP2D, PK of PEGPH20 and safety profile

Dose Expansion

Phase 1b expansion end points:

- **ORR, DCR, DOR, PFS**
- **Plan to initiate study Q3 2015**

Key Projected Program and Data Milestones



Today's Agenda

Introduction and Objectives	**Helen Torley, MB, ChB, MRCP** President and Chief Executive Officer Halozyme Therapeutics
PEGPH20 Mechanism of Action	**Christopher Thanos, PhD** Director, Biotherapeutics Halozyme Therapeutics
Exploring Combinations of PEGPH20 With Cancer Therapies	**Curt Thompson, PhD** Senior Director, Pharmacology Halozyme Therapeutics
From Theory to Initial Clinical Experience	**Sunil R. Hingorani, MD, PhD** Associate Member, FHCRC Director, Center for Accelerated Translation in Pancreas Cancer
Clinical Development Plan Update	**Athena Countouriotis, MD** Chief Medical Officer Halozyme Therapeutics
Q&A	

Robust Non-Clinical Observations Inform Our Clinical Development Strategy

HA^{high} present in many patients with common solid tumors

- **Evaluate PEGPH20 in multiple tumor types**

PEGPH20 inhibits tumor growth in HA^{high} animal tumor models

- **Select HA^{high} patients through development of Companion Diagnostic**

PEGPH20 Increases intratumor concentration of anticancer treatments in animal tumor models

- **Study combination of PEGPH20 with Standard of care chemotherapies AND Immune Checkpoint Inhibitor Antibodies**

PEGPH20 Goal: Improving Targeting of Co-Administered Cancer Drugs

- Encouraging data from Phase1b and 2 pancreatic cancer trials supportive of potential for efficacy benefit in HA^{high} tumors
  - FDA and EMA feedback sought for registration trial initiation 2015
- Clinical testing underway in additional tumor
  - Non-small cell lung cancer
    - PRIMAL trial with docetaxel in 2L patients initiated
    - Trial with PD1 inhibitor to commence 2015

Question and Answer

Halozyme
THERAPEUTICS