Dr. Patrick Soon-Shiong
Chairman & CEO

JP Morgan Presentation 2018
January 9, 2018

Safe Harbor Statement

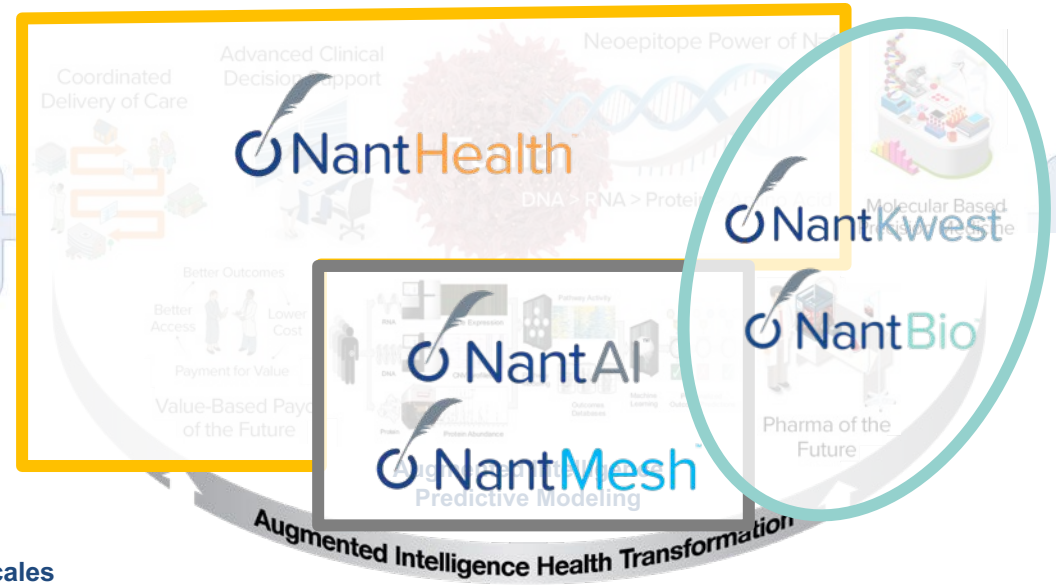
These slides and the accompanying oral presentation (the “Presentation”) include forward-looking statements, which are based on current expectations, estimates and projections of the management of NantKwest, Inc. and NantHealth, Inc.

Forward-looking statements include, among others, statements regarding NantKwest’s ability to pioneer immunotherapy, harness the power of the innate immune system, and change the current paradigm of cancer and other disease care; NantKwest’s expectations regarding the potential benefits of its strategy and technology; NantKwest’s expectations regarding its ability to utilize the Phase I aNK clinical trial data to support the development its other product candidates; the timing or likelihood of regulatory filings or other actions and related regulatory authority responses, including any planned IND filings or accelerated regulatory approval pathways; NantKwest’s beliefs regarding the potential markets for its product candidates and its ability to serve those markets; the evolving treatment paradigm for cancer, including physicians’ use of molecular information and targeted oncology therapeutics and the market size for molecular information products; physicians’ need for precision medicine products and any perceived advantage of our solutions over those of our competitors, including the ability of NantHealth’s comprehensive platform to help physicians treat their patients’ cancers; NantHealth’s ability to increase the commercial success of GPS Cancer; and NantHealth’s plans or ability to obtain reimbursement for GPS Cancer, including expectations as to its ability or the amount of time it will take to achieve successful reimbursement from third-party payors, such as commercial insurance companies and health maintenance organizations, and government insurance programs, such as Medicare and Medicaid. Factors that could cause NantKwest’s and NantHealth’s results to differ materially from those expressed in forward-looking statements include, without limitation, the fact that the foundation of NantKwest’s business is based upon the success of its aNK cells as a technology platform; NantKwest’s aNK platform and other product candidate families, including genetically modified taNK and haNK product candidates, will require significant additional clinical testing; NantKwest may not be able to file INDs, to commence additional clinical trials on the timelines it expects; and the fact that NantKwest’s and NantHealth’s Chairman and Chief Executive Officer and entities affiliated with him collectively own a significant percentage of NantKwest’s and NantHealth’s common stock and could exercise significant influence over matters requiring stockholder approval. This Presentation is dated as of January 9, 2017, and each of NantKwest and NantHealth undertakes no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law. No representation or warranty, express or implied, is given as to the completeness or accuracy of the information or opinions contained in this document and neither NantKwest, NantHealth nor any of their directors, stockholders, officers, employees, agents or advisers accepts any liability for any direct, indirect or consequential loss or damage arising from reliance on such information or opinions. Past performance should not be taken as an indication or guarantee of future performance, and no representation or warranty, express or implied, is made regarding future performance.

Harnessing the Power of Cognition and Augmented Intelligence: A Continuous Learning System Delivering Healthcare Transformation

Patients
Right Care -
Right Time -
Right Place -
Evidence Based -

Providers
Coordinated -
Integrated -
Evidence Based -
21st Century Medicine -



Payor of the Future
- Better Outcomes
- Better Access
- Better Safety
- Lower Cost

Pharma of the Future
- Molecular Based Medicine
- Personalized Medicine
- "The Power of N = 1"
- Transformational Innovation

To Cross the Chasm of Scales From N=1 to the Human Population Delivering Personalized Evidence Based Care

Unraveling the Mysteries of Cancer: The Power of N=1 Neoepitope Driven Immunotherapy

To Establish The Pharma of the Future Driving Molecular Based 21st Century Care

NANTWORKS

2018 – The NANT Cancer Vaccine

12 Novel Molecules in Phase II/III Clinical Trials in Over 20 Tumor Types

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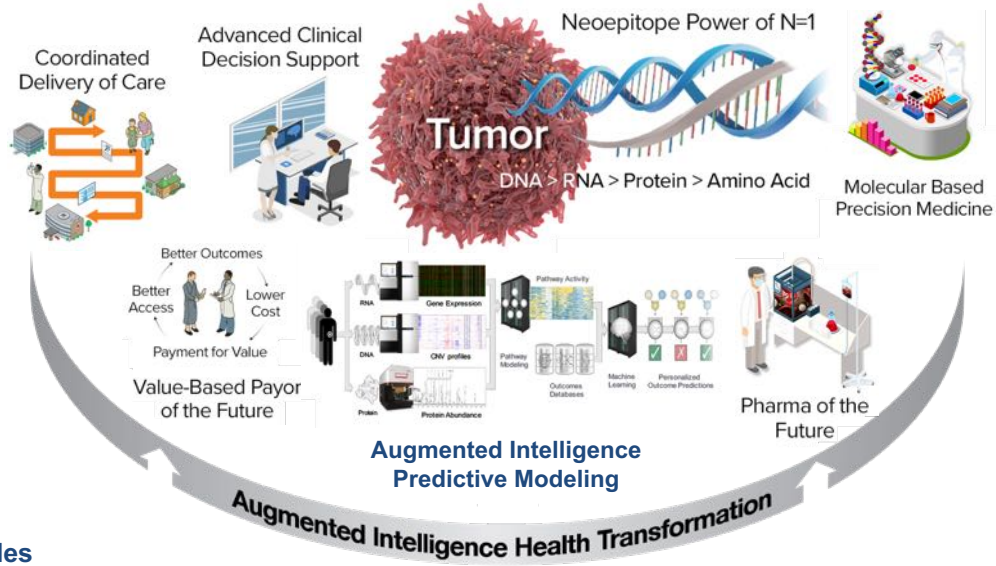

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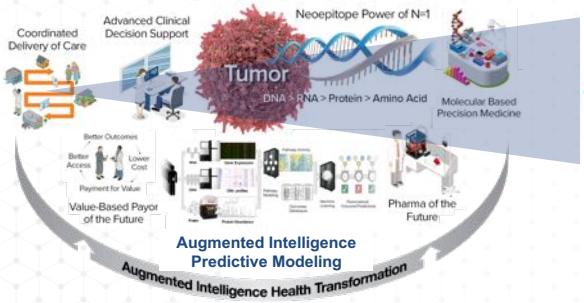
NantHealth
NASDAQ: NH

Status Year to Date 2017: By the Numbers

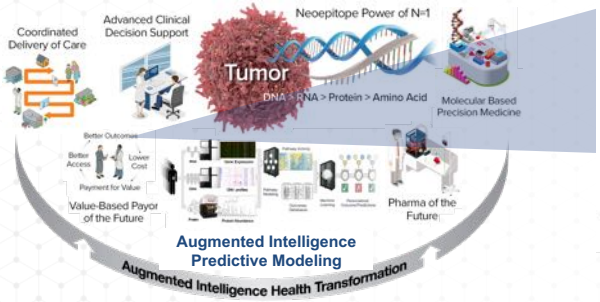


DeviceConX

- 13,000 Device Interfaces on DeviceConX
- 130+ Provider Clients at 370+ Sites
- 22,000+ DeviceConX Licenses Sold
- 10+ Billion Vital Signs Collected Annually
- Class 1 Regulated Medical Devices
- 18 EMRs Integrated
- 15,000 Daily Messages by VitalsConX

NantHealth
NASDAQ: NH

Status Year to Date 2017: By the Numbers

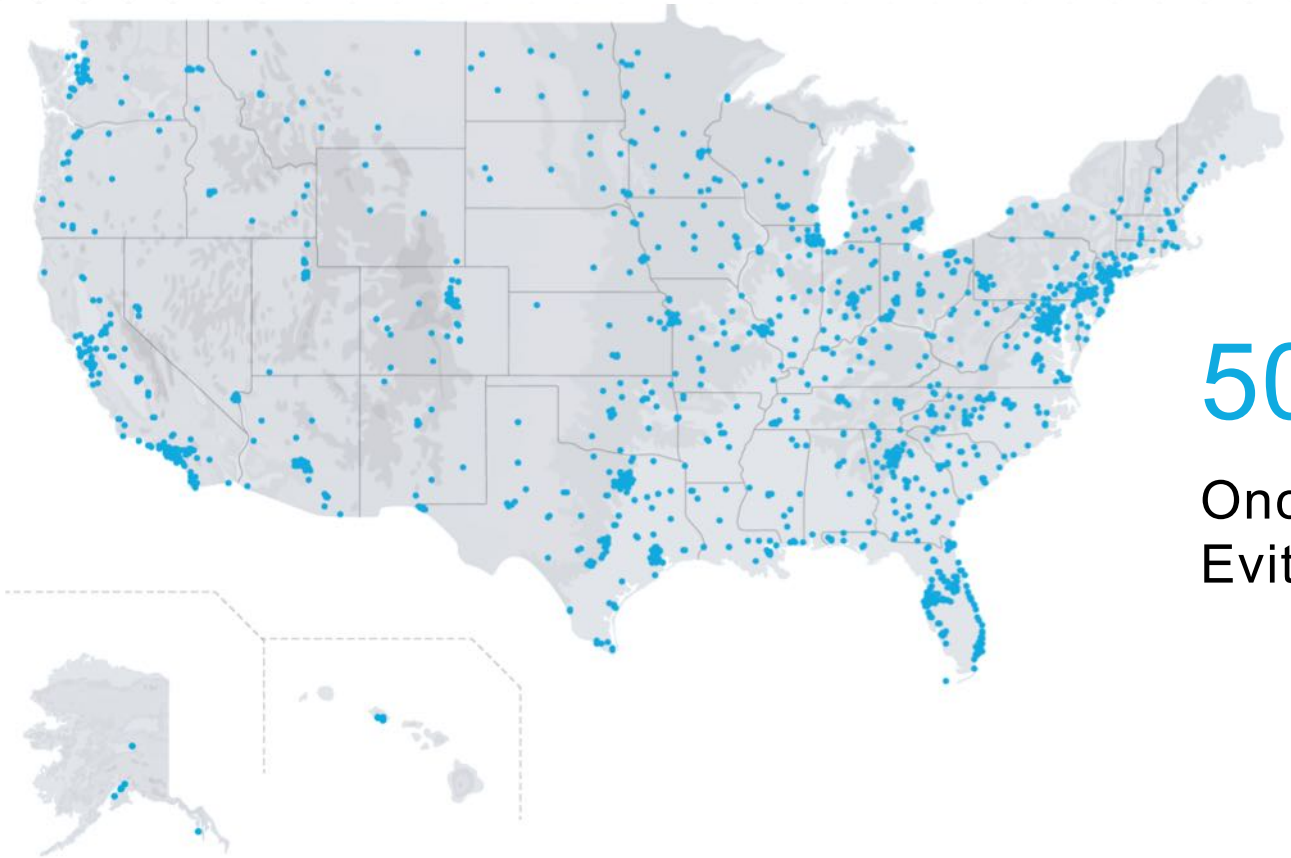


Eviti & NaviNet

- 22M Lives w/ Eviti Decision Support
- 3,000+ Cancer Treatment Regimens
- 5,000+ Oncology Practices Use Eviti
- 47M Lives Under NaviNet Payor Portal
- 40+ Health Plans on NaviNet
- 450K Active Daily Users on NaviNet
- 30M Monthly Transactions on NaviNet

Eviti Provider Network

NantHealth
NASDAQ: NH

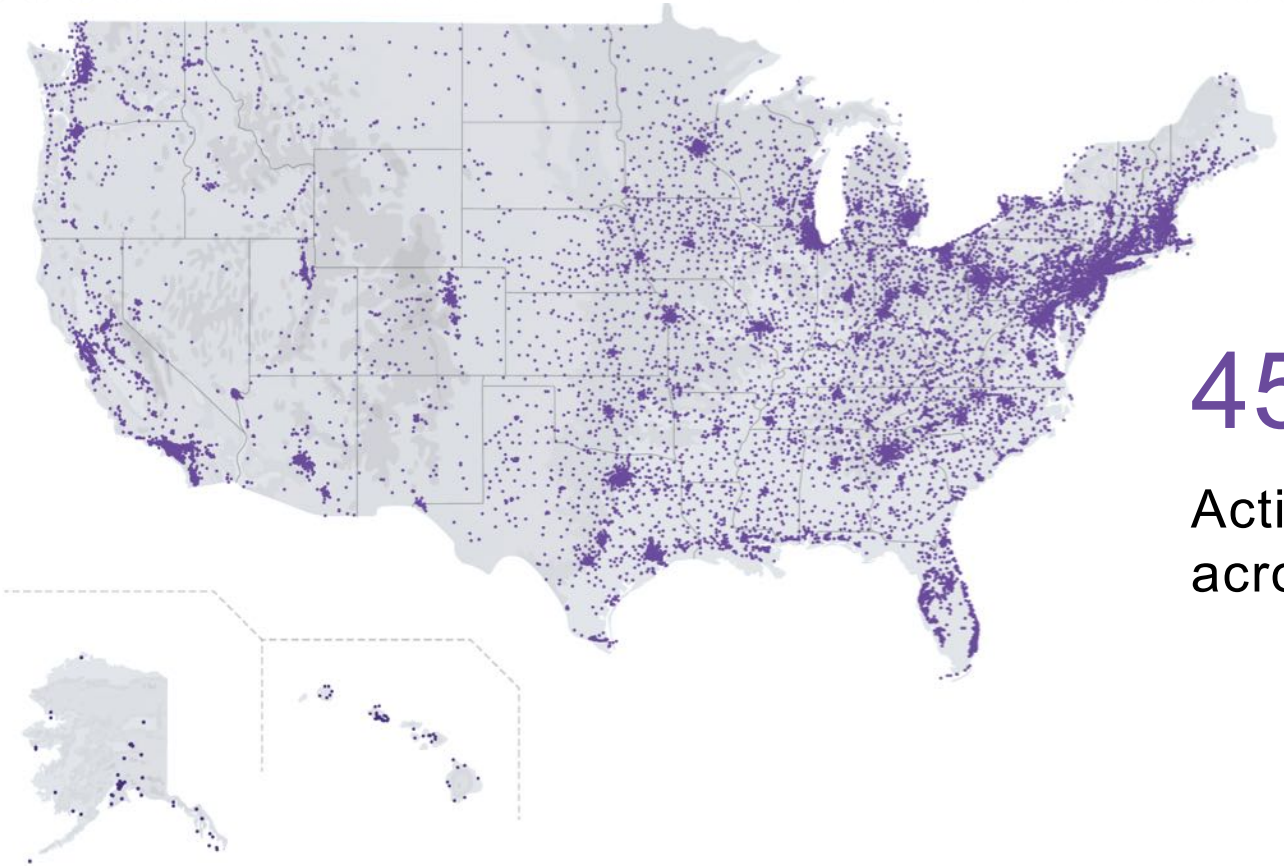


5000+

Oncology Practices Use Eviti across all 50 states

NaviNet Provider Network

NantHealth
NASDAQ: NH



450K

Active Daily Users
across all 50 States

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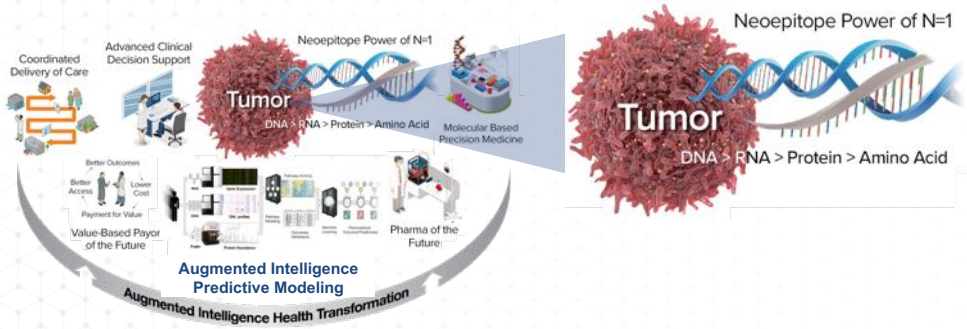
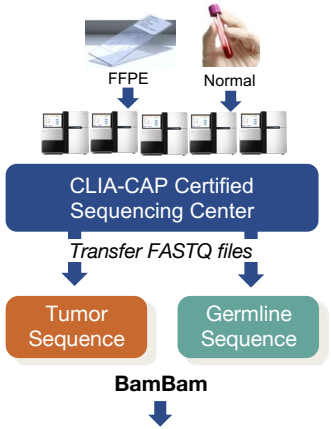
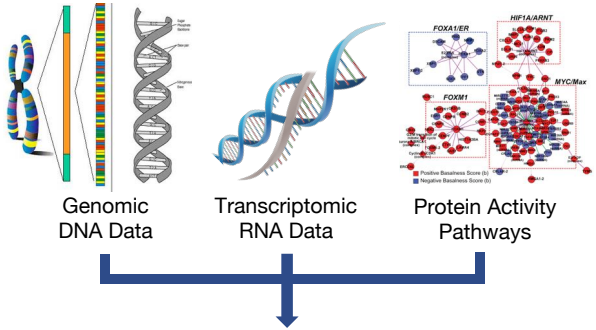


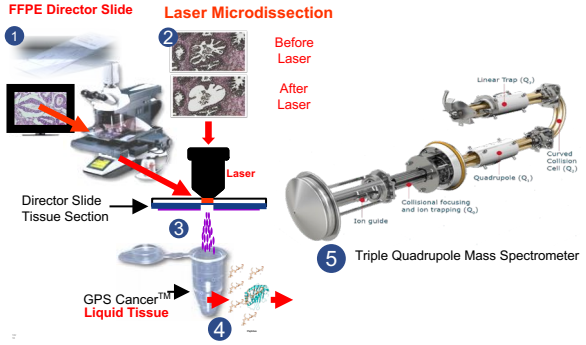
GPS Cancer

- 3 Billion Base Pairs (DNA) / 200,000 RNA
- 10,000 Protein Pathways
- Only WGS Test to Cover Tumor-Normal
- Over 7,000 Tumor-Normal Comparisons
- CLIA Certified/CAP-Accredited
- Over 20,000 Samples Processed
- Largest Cancer Whole Genome, Transcriptome Clinical Database
- 4 Seminal Patents Issued in 2017
- FDA Filing of GPS Cancer Jan 2018
- Launch of Liquid GPS DNA & RNA in 2018

GPS Cancer: Integrated Whole Genome, Transcriptome, Pathway Activity Quantitative Proteomic Solution







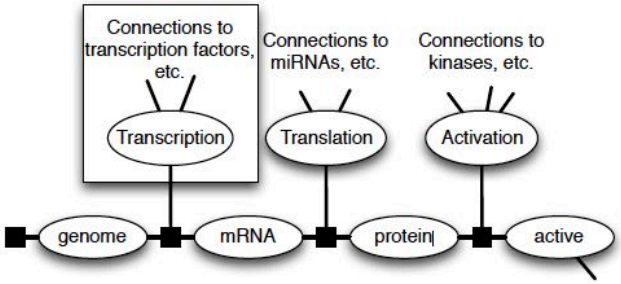
GPS Contrastor

State of the art algorithm that identifies mutations, indels, translocations in tumor vs. normal samples

Massively Parallel Custom-Designed Supercomputer on Layer 1 Fiber Optic Global Network

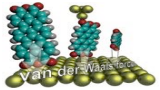
GPS Paradigm

State-of-the-art pathway algorithm that integrates genomic data with curated pathway knowledge and drug target information enabling next generation classification of tumor tissue into biologically active pathway based clusters and inflammatory status of tumor

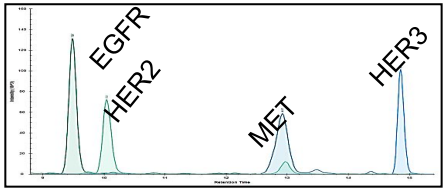


GPS Proteomics

Quantitative Targeted Proteomics by mass spectrometry with clinical utility at the Attomol (10^{-18} Molecules) level of detection in paraffin sections of tumor tissues and bone metastases



Attomol (10^{-18})



6 Personalized Chemotherapy, mAb and Targeted Proteins at the Attomol (10^{-18}) Level of Detection

GPS Cancer

The most comprehensive CLIA-CAP certified next generation molecular diagnostic test

Current Tumor Only Approved Genomic Tests Are Fundamentally Flawed

The Flaws in Current Tests

1. Analysis of selected 300+ genes while ignoring the remaining 19,000+
2. Ignoring normal (self) germline control as a comparator – the tumor-only test utilizes a reference genome as a proxy for the patient's own control
3. Using a database and reference genome as a proxy to normal control to call mutations

Clinical Consequences

- Impossible to precisely determine tumor mutation burden (TMB) of the whole genome – TMB based on 300+ genes is an assumption
- Over 90% false positive mutation calls – normal germline variants are erroneously assumed positive mutations with consequent inaccurate clinical treatment.
- Even with database filtration, mutation calls are still > 45% false positive – with the added error of false negatives

The Need for Evolution

Tumor-Only analysis of 300+ genes

300+ Genes

No (Self) Germline Control

Tumor-Only

Tumor-Normal
19,000+ genes

Tumor-Normal

+

19,000+ Genes

Normal Self Germline

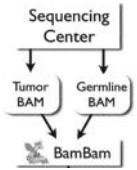
The Evolution of Genomic Testing in Cancer
From Tumor-Only to Tumor-Normal

Current Tumor-Only Tests Are Fundamentally Flawed

Tumor-Only

Vs.

Tumor-Normal



2008 — BamBam Algorithm Development for Tumor-Normal

NantOmics

2010 — Patent Filed Tumor-Normal Bioinformatics System

2012 — FOUNDATION MEDICINE FoundationOne Launch Tumor-Only Gene Panel

2013 — FOUNDATION MEDICINE FoundationOne Heme Launch

Clinical Demonstration in 5,000 Patients of Tumor-Normal Analysis in 10,000 Samples

ASCO

2015 — Roche Buys Majority Stake in Foundation

CLIA Lab Approval for Tumor-Normal GPS Cancer

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NantHealth NASDAQ: NH

NantHealth Launch of GPS Cancer

Clinical Evidence of False Positives with Tumor Only Testing

Memorial Sloan Kettering Cancer Center · JOHNS HOPKINS MEDICINE

Jan 2017 — Further Clinical Evidence of 90% False Positive with Tumor Only vs. Tumor-Normal in 621 Patients with 30 different cancer types

NantOmics

Mar 2017 — FOUNDATION MEDICINE FoundationOne Tumor Only Receives CMS Approval For NSCLC

Aug 2017 — Four Seminal Patents Issued Covering Tumor-Normal and Preventing False Positives

Nov 2017 — FOUNDATION MEDICINE FDA Approves Foundation Medicine's FoundationOne CDx Tumor-Only 328 Gene Panel

Memorial Sloan Kettering Cancer Center

MSK-Impact Receives FDA Approval for Tumor-Normal

Tumor-Only 90% False Positive Rate

Evolution to Tumor-Normal

Jan 2018 — **GPS Cancer** FDA Submitted For Tumor-Normal

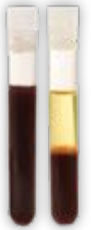
NantHealth NASDAQ: NH

Tumor-Normal

Tissue

2018 — **Liquid GPS™ DNA**

Liquid GPS™ RNA



The Evolution of Genomic Testing in Cancer
From Tumor-Only to Tumor-Normal

Tumor Only
Vs.
Tumor-Normal

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Tumor-Only 90% False Positive Rate

Evolution from Tumor-Only to Tumor-Normal

Jan 2018 — GPS Cancer FDA Submission For Tumor-Normal

2018 — Liquid GPS™ DNA

2018 — Liquid GPS™ RNA

April 2015: Tumor-Alone is Inaccurate

*"**Matched tumor-normal** sequencing analyses are **essential for precise** identification and interpretation of somatic and germline alterations"*

RESEARCH ARTICLE

CANCER

JOHNS HOPKINS MEDICINE

Personalized genomic analyses for cancer mutation discovery and interpretation

Siân Jones,[1] Valsamo Anagnostou,[2] Karli Lytle,[1] Sonya Parpart-Li,[1] Monica Nesselbush,[1] David R. Riley,[1] Manish Shukla,[1] Bryan Chesnick,[1] Maura Kadan,[1] Eniko Papp,[2] Kevin G. Galens,[1] Derek Murphy,[1] Theresa Zhang,[1] Lisa Kann,[1] Mark Sausen,[1] Samuel V. Angiuoli,[1] Luis A. Diaz Jr.,[2] Victor E. Velculescu[2]*

Massively parallel sequencing approaches are beginning to be used clinically to characterize individual patient tumors and to select therapies based on the identified mutations. A major question in these analyses is the extent to which these methods identify clinically actionable alterations and whether the examination of the tumor tissue alone is sufficient or whether matched normal DNA should also be analyzed to accurately identify tumor-specific (somatic) alterations. To address these issues, we comprehensively evaluated 815 tumor-normal paired samples from patients of 15 tumor types. We identified genomic alterations using next-generation sequencing of whole exomes or 111 targeted genes that were validated with sensitivities >95% and >99%, respectively, and specificities >99.99%. These analyses revealed an average of 140 and 4.3 somatic mutations per exome and targeted analysis, respectively. More than 75% of cases had somatic alterations in genes associated with known therapies or current clinical trials. Analyses of matched normal DNA identified germline alterations in cancer-predisposing genes in 3% of patients with apparently sporadic cancers. In contrast, a tumor-only sequencing approach could not definitively identify germline changes in cancer-predisposing genes and led to additional false-positive findings comprising 31% and 65% of alterations identified in targeted and exome analyses, respectively, including in potentially actionable genes. These data suggest that matched tumor-normal sequencing analyses are essential for precise identification and interpretation of somatic and germline alterations and have important implications for the diagnostic and therapeutic management of cancer patients.

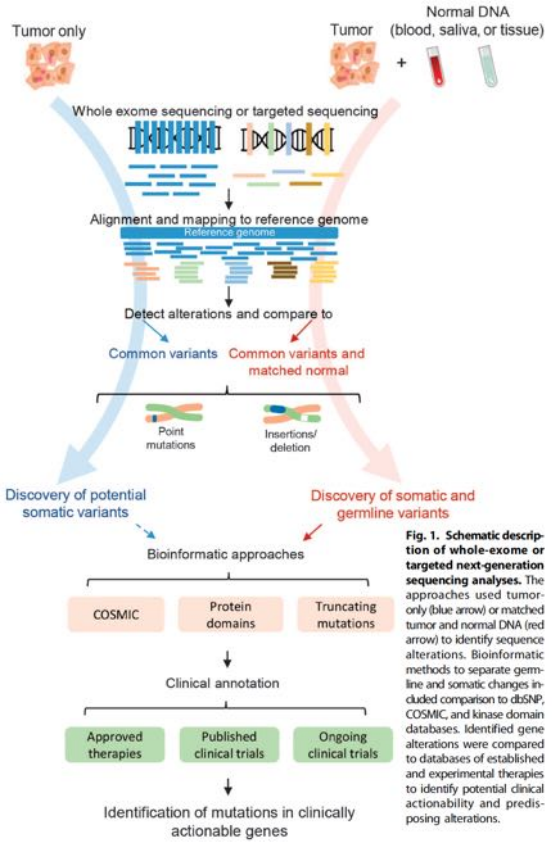
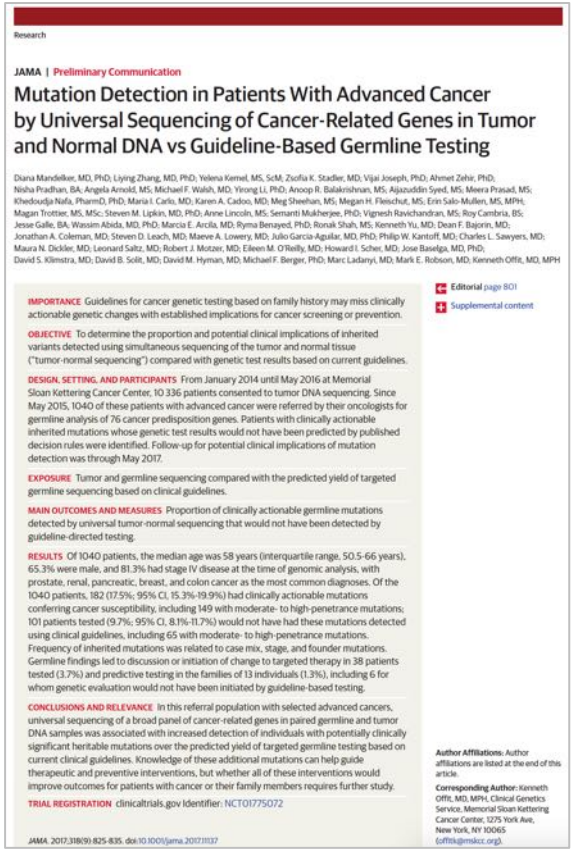


Fig. 1. Schematic description of whole-exome or targeted next-generation sequencing analyses. The approaches used tumor-only (blue arrow) or matched tumor and normal DNA (red arrow) to identify sequence alterations. Bioinformatic methods to separate germline and somatic changes included comparison to dbSNP, COSMIC, and kinase domain databases. Identified gene alterations were compared to databases of established and experimental therapies to identify potential clinical actionability and predisposing alterations.

2017 – Clinical Value of Tumor-Normal vs. Tumor-Alone



Research

JAMA | Preliminary Communication

Mutation Detection in Patients With Advanced Cancer by Universal Sequencing of Cancer-Related Genes in Tumor and Normal DNA vs Guideline-Based Germline Testing

Diana Mandelker, MD, PhD; Liying Zhang, MD, PhD; Yelena Kemel, MS, ScM; Zsofia K. Stadler, MD; Vijai Joseph, PhD; Ahmet Zehir, PhD; Nisha Pradhan, BA; Angela Arnold, MS; Michael F. Walsh, MD; Yirong Li, PhD; Anoop R. Balakrishnan, MS; Aijazuddin Syed, MS; Meera Prasad, MS; Khedoudja Nafa, PharmD, PhD; Maria I. Carlo, MD; Karen A. Cadoo, MD; Meg Sheehan, MS; Megan H. Fleischut, MS; Erin Salo-Mullen, MS, MPH; Magan Trottier, MS, MSc; Steven M. Lipkin, MD, PhD; Anne Lincoln, MS; Semanti Mukherjee, PhD; Vignesh Ravichandran, MS; Roy Cambria, BS; Jesse Galle, BA; Wassim Abida, MD, PhD; Marcia E. Arcila, MD; Ryma Benayed, PhD; Ronak Shah, MS; Kenneth Yu, MD; Dean F. Bajorin, MD; Jonathan A. Coleman, MD; Steven D. Leach, MD; Maeve A. Lowery, MD; Julio Garcia-Aguilar, MD, PhD; Philip W. Kantoff, MD; Charles L. Sawyers, MD; Maura N. Dickler, MD; Leonard Saltz, MD; Robert J. Motzer, MD; Eileen M. O'Reilly, MD; Howard I. Scher, MD; Jose Baselga, MD, PhD; David S. Klimstra, MD; David B. Solit, MD; David M. Hyman, MD; Michael F. Berger, PhD; Marc Ladanyi, MD; Mark E. Robson, MD; Kenneth Offit, MD, MPH

Editorial page 801

Supplemental content

IMPORTANCE Guidelines for cancer genetic testing based on family history may miss clinically actionable genetic changes with established implications for cancer screening or prevention.

OBJECTIVE To determine the proportion and potential clinical implications of inherited variants detected using simultaneous sequencing of the tumor and normal tissue ("tumor-normal sequencing") compared with genetic test results based on current guidelines.

DESIGN, SETTING, AND PARTICIPANTS From January 2014 until May 2016 at Memorial Sloan Kettering Cancer Center, 10 336 patients consented to tumor DNA sequencing. Since May 2015, 1040 of these patients with advanced cancer were referred by their oncologists for germline analysis of 76 cancer predisposition genes. Patients with clinically actionable inherited mutations whose genetic test results would not have been predicted by published decision rules were identified. Follow-up for potential clinical implications of mutation detection was through May 2017.

EXPOSURE Tumor and germline sequencing compared with the predicted yield of targeted germline sequencing based on clinical guidelines.

MAIN OUTCOMES AND MEASURES Proportion of clinically actionable germline mutations detected by universal tumor-normal sequencing that would not have been detected by guideline-directed testing.

RESULTS Of 1040 patients, the median age was 58 years (interquartile range, 50.5-66 years), 65.3% were male, and 81.3% had stage IV disease at the time of genomic analysis, with prostate, renal, pancreatic, breast, and colon cancer as the most common diagnoses. Of the 1040 patients, 182 (17.5%; 95% CI, 15.3%-19.9%) had clinically actionable mutations conferring cancer susceptibility, including 149 with moderate- to high-penetrance mutations; 101 patients tested (9.7%; 95% CI, 8.1%-11.7%) would not have had these mutations detected using clinical guidelines, including 65 with moderate- to high-penetrance mutations. Frequency of inherited mutations was related to case mix, stage, and founder mutations. Germline findings led to discussion or initiation of change to targeted therapy in 38 patients tested (3.7%) and predictive testing in the families of 13 individuals (1.3%), including 6 for whom genetic evaluation would not have been initiated by guideline-based testing.

CONCLUSIONS AND RELEVANCE In this referral population with selected advanced cancers, universal sequencing of a broad panel of cancer-related genes in paired germline and tumor DNA samples was associated with increased detection of individuals with potentially clinically significant heritable mutations over the predicted yield of targeted germline testing based on current clinical guidelines. Knowledge of these additional mutations can help guide therapeutic and preventive interventions, but whether all of these interventions would improve outcomes for patients with cancer or their family members requires further study.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT01775072

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Kenneth Offit, MD, MPH, Clinical Genetics Service, Memorial Sloan Kettering Cancer Center, 1275 York Ave, New York, NY 10065 (offitk@mskcc.org).

JAMA. 2017;318(9):825-835. doi:10.1001/jama.2017.11037

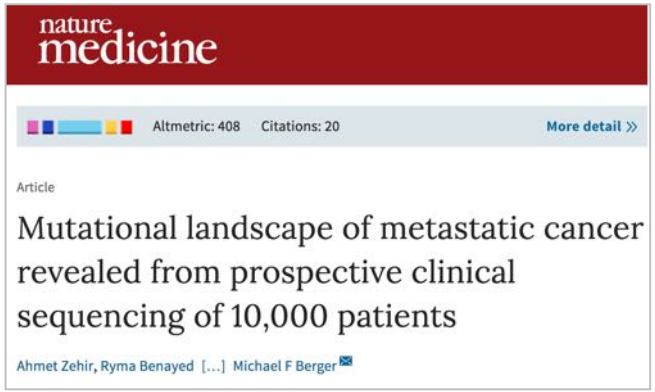
*"…universal sequencing of a broad panel of cancer-related genes in paired **germline** and **tumor DNA** samples was associated with **increased detection** of individuals with potentially clinically significant heritable mutations over the predicted yield of targeted germline testing based on current clinical guidelines. Knowledge of these additional mutations can help guide therapeutic and preventive interventions."*

1884

Memorial Sloan Kettering Cancer Center

2017 – Clinical Value of Tumor-Normal vs. Tumor-Alone

*"By sequencing DNA from both **tumor and normal** blood, we were able to **unambiguously call somatic mutations with greater sensitivity and specificity** through the elimination of rare germline variants"*



Memorial Sloan Kettering Cancer Center

"We report the overall experience of a large institution-wide, prospective clinical sequencing effort to guide the selection of genomically matched therapies for patients spanning all solid tumor malignancies. We demonstrate that enterprise-scale sequencing of tumors and patient-matched blood samples using a comprehensive cancer panel is feasible and achievable within a turnaround time that permits clinical interpretation and utilization.

Given the diversity of tumor types that can harbor potentially actionable mutations, broad molecular profiling is necessary to provide all patients the opportunity to receive a genomically matched therapy.

Further enriching the clinical utility of our approach is the inclusion of patient-matched normal DNA for every tumor that is profiled. ***By sequencing DNA from both tumor and normal blood, we were able to unambiguously call somatic mutations with greater sensitivity and specificity through the elimination of rare germline variants."***

The Evolution of Genomic Testing in Cancer
From Tumor-Only to Tumor-Normal

Tumor Only

Vs.

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2008 2010 2012 2013 2015 2016 Jan 2017 Mar 2017 Aug 2017 Nov 2017 Jan 2018 2018

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- Tumor BAM
- Germline BAM
- BamBam
- BamBam Algorithm Development for Tumor-Normal
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- FoundationOne Tumor Only Receives CMS Approval For NSCLC

Aug 2017
- Four Seminal Patents Issued Covering Tumor-Normal and Preventing False Positives

Nov 2017
- FOUNDATION MEDICINE
- FDA Approves Foundation Medicine's FoundationOne CDx Tumor-Only 328 Gene Panel
- Memorial Sloan Kettering Cancer Center
- MSK-Impact Receives FDA Approval for Tumor-Normal

Jan 2018
- GPS Cancer
- FDA Submission For Tumor-Normal
- NantHealth
- NASDAQ: NH
- Tumor-Normal
- Tissue

2018
- Liquid GPS™ DNA
- Liquid GPS™ RNA

Tumor-Only 90% False Positive Rate

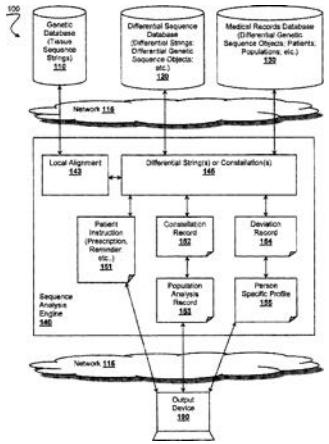
Evolution from Tumor-Only to Tumor-Normal

Four Seminal Patents for NantHealth GPS Cancer Covering Tumor-Normal Analysis of NGS

(12) **United States Patent**

(10) **Patent No.: US 9,646,134 B2**
(45) **Date of Patent: *May 9, 2017**

(54) **BAMBAM: PARALLEL COMPARATIVE ANALYSIS OF HIGH-THROUGHPUT SEQUENCING DATA**



1. A processor-based method of deriving a differential genetic sequence object, the method comprising:

providing access to a genetic database storing (a) a first genetic sequence string representing a first tissue and (b) a second genetic sequence string representing a second tissue, wherein the first and second sequence strings have a plurality of corresponding sub-strings;

providing access to a sequence analysis engine coupled with the genetic database; producing, using the sequence analysis engine, a local alignment using a known position of at least one of a plurality of corresponding sub-strings;

determining base probabilities of possible locations of sequence reads in the first and second genetic sequence strings as a function of error rates of at least one sequencer;

identifying a difference between the first set and the second set of genetic sequence strings by comparing genotypes from the first and the second sets that,

. . .

4. The method of claim 1 wherein the first and second genetic sequence strings represent substantially the entire genome, transcriptome, or proteome of the first and second tissues, respectively.

6. The method of claim 1 wherein the first tissue is a healthy tissue and wherein the second is a diseased tissue.

7. The method of claim 6 wherein the diseased tissue comprises a tumor tissue.

(12) **United States Patent**

(10) **Patent No.: US 9,652,587 B2**
(45) **Date of Patent: May 16, 2017**

(54) **BAMBAM: PARALLEL COMPARATIVE ANALYSIS OF HIGH-THROUGHPUT SEQUENCING DATA**

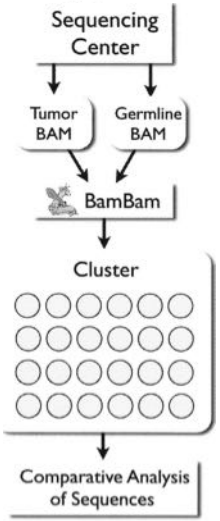
What is claimed:

1. A method of deriving a differential genetic sequence object, the method comprising:

accessing a genetic database storing a first set of genetic sequence strings and associated reads representing a first tissue and a second set of genetic sequence strings and associated reads representing a second tissue, wherein the first set and the second set include genomic location information, wherein the accessing is executed by a hardware processor;

aligning the first set of genetic sequence strings and the second set of genetic sequence strings using the genomic location information in at least one of the first set or the second set, the first set of genetic sequence strings and the second set of genetic sequence strings being analyzed against each other, wherein the aligning is executed by the hardware processor the analyzing comprising:

determining base probabilities of possible locations of



6. The method of claim 1 wherein the first tissue is a healthy tissue and wherein the second is a diseased tissue.

7. The method of claim 6 wherein the diseased tissue comprises a tumor tissue.

Four Seminal Patents for NantHealth GPS Cancer Covering Tumor-Normal Analysis of NGS

(12) **United States Patent**

(10) **Patent No.: US 9,721,062 B2**
(45) **Date of Patent: Aug. 1, 2017**

(54) **BAMBAM: PARALLEL COMPARATIVE ANALYSIS OF HIGH-THROUGHPUT SEQUENCING DATA**

What is claimed:

1. A computer-based sequence analysis system comprising:

a computer readable memory configured to store at least a first and a second genomic sequence datasets, the sequence datasets comprising genomic reads associated with respective first and second tissues; and

a sequence analysis engine having a processor coupled with the computer readable memory and configured to:

determine a common genomic location in the first and second genomic sequence datasets;

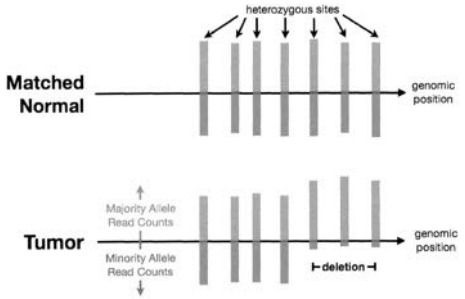
generate at least a pair of pileups by:

reading a first set of pileups that includes genomic reads from the first genomic sequence dataset and that overlap the common genomic location; and

reading a second set of pileups that includes genomic reads from the second genomic sequence dataset and that also overlap the common genomic location;

infer at least a pair of genotypes for the common genomic location based on the at least the pair of pileups, the at least the pair of genotypes including a first genotype associated with the first tissue and a second genotype associated with the second tissue;

identify a genomic difference between the first genotype and the second genotype in the at least the pair



7. The system of claim 1, wherein the first tissue and the second tissue are from the same patient.

8. The system of claim 1, wherein the first tissue comprises a tumor tissue and the second tissue comprises a matched normal tissue.

(12) **United States Patent**

(10) **Patent No.: US 9,824,181 B2**
(45) **Date of Patent: Nov. 21, 2017**

(54) **BAMBAM: PARALLEL COMPARATIVE ANALYSIS OF HIGH-THROUGHPUT SEQUENCING DATA**

What is claimed:

1. A parallel genomic comparative analysis system comprising:

a memory; and

an sequence analysis engine coupled with the memory and configured to:

identify a genomic position within a reference genome;

access a first file storing tumor sequence data including short reads associated with a tumor tissue;

access a second file storing match normal sequence data short reads associated with a matched normal tissue;

store in the memory a tumor dataset having tumor short read sequences from the first file where the tumor short read sequences overlap the genomic position;

store in the memory a matched normal dataset having matched normal short read sequences from the second file and that overlap the genomic position;

select a tumor genotype and a matched normal genotype that maximize a joint probability as a function of the tumor short read sequences and the match normal short read sequences at the genomic position, wherein the joint probability depends on one of a probability calculated as a multinomial operating as a function of the matched normal genotype or as a probability calculated as a multinomial operating as a function of the tumor genotype; and

store a difference between the tumor genotype and the matched normal genotype in a device memory.

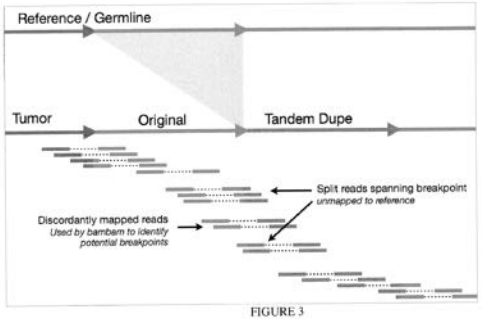


FIGURE 3

13. The system of claim 1, wherein the tumor sequence data of the tumor tissue and the matched normal sequence data of the matched normal tissue originate from the same person.

Four Seminal Patents for NantHealth GPS Cancer
Covering Tumor-Normal Analysis and Avoiding False Positives of NGS

(12) **United States Patent**

(10) **Patent No.: US 9,721,062 B2**
(45) **Date of Patent: Aug. 1, 2017**

(54) **BAMBAM: PARALLEL COMPARATIVE ANALYSIS OF HIGH-THROUGHPUT SEQUENCING DATA**

What is claimed:

1. A computer-based sequence analysis system comprising:

a computer readable memory configured to store at least a first and a second genomic sequence datasets, the sequence datasets comprising genomic reads associated with respective first and second tissues; and

a sequence analysis engine having a processor coupled with the computer readable memory and configured to:

determine a common genomic location in the first and second genomic sequence datasets;

generate at least a pair of pileups by:

reading a first set of pileups that includes genomic reads from the first genomic sequence dataset and that overlap the common genomic location; and

reading a second set of pileups that includes genomic reads from the second genomic sequence dataset and that also overlap the common genomic location;

infer at least a pair of genotypes for the common genomic location based on the at least the pair of pileups, the at least the pair of genotypes including a first genotype associated with the first tissue and a second genotype associated with the second tissue;

identify a genomic difference between the first genotype and the second genotype in the at least the pair

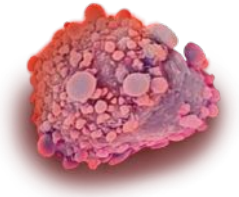
type and the second genotype in the at least the pair of genotypes;

filter false positives based on a skewing from a random distribution; and

store the genomic difference in a device memory.

GPS Product Suite for 2018

Tumor-Normal



GPS Cancer

- All Solid Tumors
- CLIA-CAP Accredited 2016
- FDA Filed January 2018

Liquid GPS DNA

- CLIA-CAP accredited
- Stable and easy blood collection and shipping from point of care
- Quantitative monitoring of resistance to TKIs (eg EGFR targeted therapies)
- Quantitative measurement of targeting BRAF V600E
- FDA filing Q1 2018

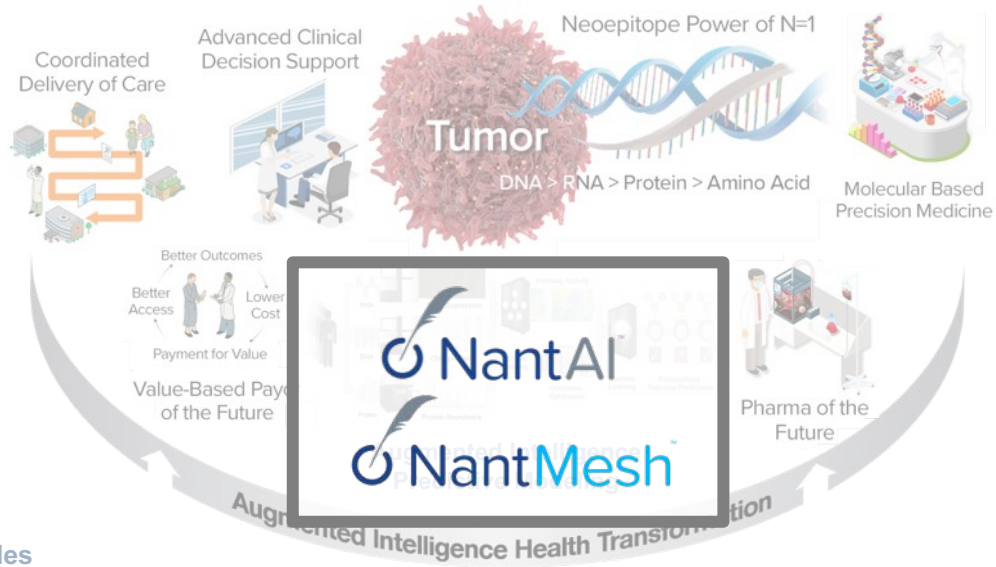
Liquid GPS RNA

- CLIA-CAP accredited
- Proprietary methodology and technology
- Stable and easy blood collection and shipping from point of care
- Quantitation of the expression of biomarkers predictive of drug response
- Guided use of targeted and immunotherapies
- Ongoing monitoring of response to therapies

Harnessing the Power of Cognition and Augmented Intelligence: A Continuous Learning System Delivering Healthcare Transformation

Patients
Right Care -
Right Time -
Right Place -
Evidence Based -

Providers
Coordinated -
Integrated -
Evidence Based -
21st Century Medicine -



Payor of the Future
- Better Outcomes
- Better Access
- Better Safety
- Lower Cost

Pharma of the Future
- Molecular Based Medicine
- Personalized Medicine
- "The Power of N = 1"
- Transformational Innovation

To Cross the Chasm of Scales
From N=1 to the Human Population
Delivering Personalized
Evidence Based Care

Unraveling the Mysteries of Cancer: The Power of N=1
Neoepitope Driven Immunotherapy

To Establish
The Pharma of the Future
Driving Molecular Based
21st Century Care

NANTWORKS

2018 – The NANT Cancer Vaccine

12 Novel Molecules in Phase II/III Clinical Trials in Over 20 Tumor Types

NantAI
Private

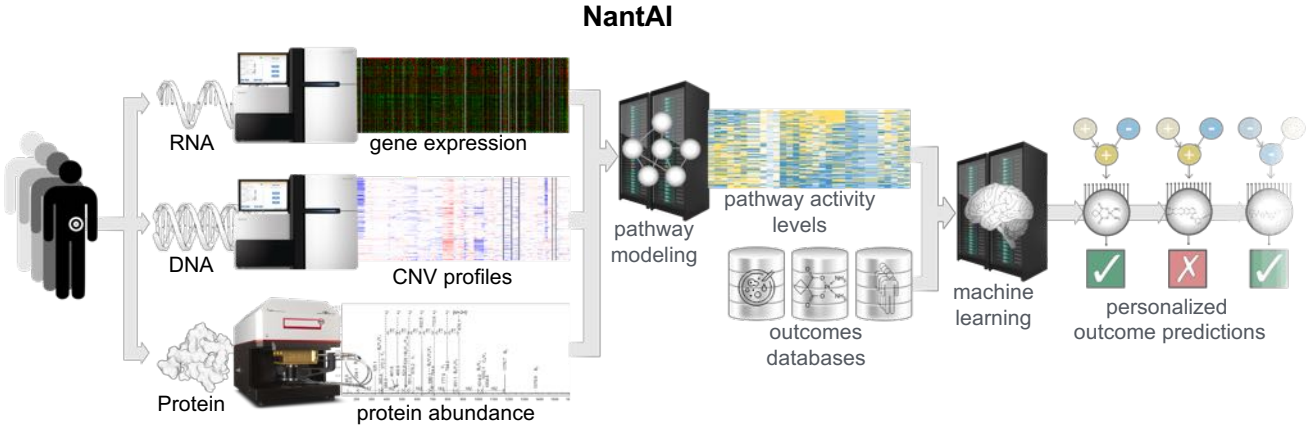
By The Numbers

NantAI - Neoepitope

- 40 Petabytes of Genomic Storage
- 5+ Compute Years Generated for Cancer
- Over 21 Million Outcomes Analyzed
- Over 1,000 Issued Claims on AI

NantMesh

- Next Generation Layer 2 Carrier Network
- 150+ Datacenters in 17 Metro Markets
- 398 Tbps Routing Capacity
- 76.2Tbps of Capacity per Fiber Pair
- 4,150 Active Network Interfaces
- 12,000 Fiber Miles / 70,000 Optical Miles
- Lowest Latency Global Fiber Network
- Key Provider of Broadband Fiber for US & Asia for High Frequency Traders



Currently host >31K fully trained outcome predictors
~5 compute-years required to generate
Over 21 million outcomes have been analyzed

NantAI

The Reasoning Engine is Our Core to Augmented Intelligence

US009262719B2

(12) **United States Patent**
Soon-Shiong

(10) **Patent No.: US 9,262,719 B2**
(45) **Date of Patent: Feb. 16, 2016**

(54) **REASONING ENGINES**

(76) Inventor: **Patrick Soon-Shiong**, Los Angeles, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 318 days.

(21) Appl. No.: **14/006,932**

(22) PCT Filed: **Mar. 22, 2012**

(86) PCT No.: **PCT/US2012/030052**
§ 371 (c)(1),
(2), (4) Date: **Jan. 3, 2014**

(87) PCT Pub. No.: **WO2012/129371**
PCT Pub. Date: **Sep. 27, 2012**

(65) **Prior Publication Data**

US 2014/0129504 A1 May 8, 2014

Related U.S. Application Data

(60) Provisional application No. 61/466,367, filed on Mar. 22, 2011, provisional application No. 61/466,398, filed on Mar. 22, 2011.

(51) **Int. Cl.**

G06F 17/00	(2006.01)
G06N 5/04	(2006.01)
G06T 9/00	(2006.01)
G06K 9/00	(2006.01)
G06F 17/30	(2006.01)
G06N 5/02	(2006.01)

(52) **U.S. Cl.**
CPC ***G06N 5/046*** (2013.01); ***G06F 17/3087*** (2013.01); ***G06K 9/00624*** (2013.01); ***G06N 5/025*** (2013.01); ***G06N 5/043*** (2013.01); ***G06T 9/00*** (2013.01)

(58) **Field of Classification Search**
None
See application file for complet

(56) **References Cite**

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(Continued)

Primary Examiner — Jeffrey A Gaffin
Assistant Examiner — David H Kim
(74) *Attorney, Agent, or Firm* — Maur
LLP; Michael Mauriel; Andrew A. Nc

(57) **ABSTRACT**

A reasoning engine is disclosed. Co
engines acquire data relating to one or
environments. Inference engines
engines review the acquire data, histor
erate one or more hypotheses about
environments might be correlated, if
engine can attempt to validate the hy
trolling acquisition of the environmen

30 Claims, 4 Drawing

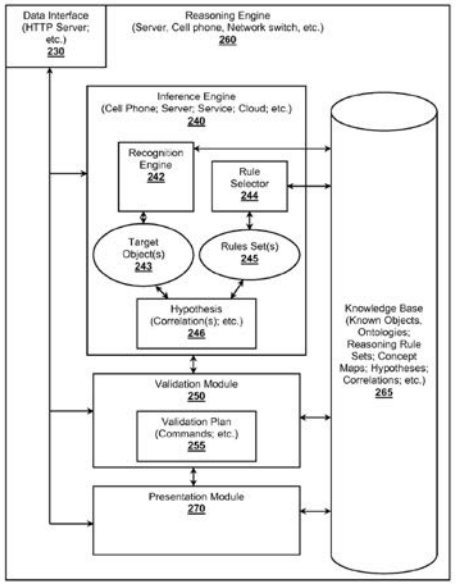


Figure 2

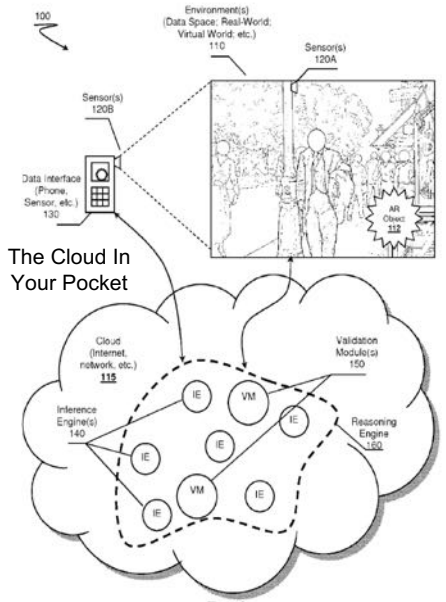
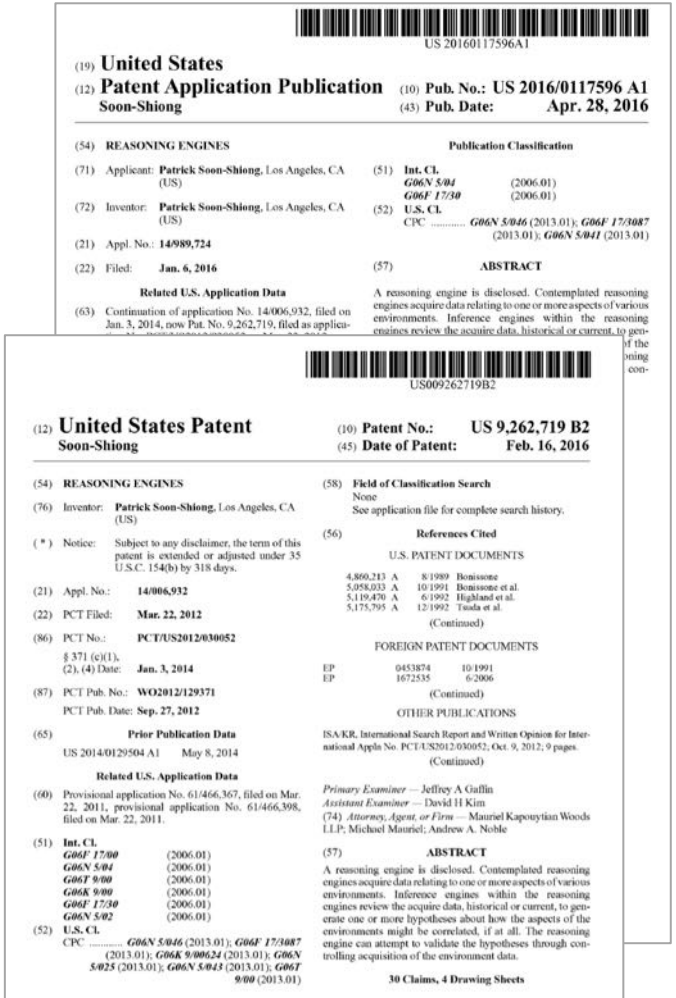


Figure 1



US 20160117596A1

(19) **United States**

(12) **Patent Application Publication**
Soon-Shiong

(10) **Pub. No.: US 2016/0117596 A1**
(43) **Pub. Date: Apr. 28, 2016**

(54) **REASONING ENGINES**

(71) Applicant: **Patrick Soon-Shiong**, Los Angeles, CA (US)

(72) Inventor: **Patrick Soon-Shiong**, Los Angeles, CA (US)

(21) Appl. No.: **14/989,724**

(22) Filed: **Jan. 6, 2016**

Related U.S. Application Data

(63) Continuation of application No. 14/006,932, filed on Jan. 3, 2014, now Pat. No. 9,262,719, filed as applica-

Publication Classification

(51) **Int. Cl.**
G06N 5/04 (2006.01)
G06F 17/30 (2006.01)

(52) **U.S. Cl.**
CPC ***G06N 5/046*** (2013.01); ***G06F 17/3087*** (2013.01); ***G06N 5/041*** (2013.01)

(57) **ABSTRACT**

A reasoning engine is disclosed. Contemplated reasoning engines acquire data relating to one or more aspects of various environments. Inference engines within the reasoning engines review the acquire data, historical or current, to gen-

US009262719B2

(12) **United States Patent**
Soon-Shiong

(10) **Patent No.: US 9,262,719 B2**
(45) **Date of Patent: Feb. 16, 2016**

(54) **REASONING ENGINES**

(76) Inventor: **Patrick Soon-Shiong**, Los Angeles, CA (US)

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G06T 9/00 (2006.01)
G06K 9/00 (2006.01)
G06F 17/30 (2006.01)
G06N 5/02 (2006.01)

(52) **U.S. Cl.**
CPC ***G06N 5/046*** (2013.01); ***G06F 17/3087*** (2013.01); ***G06K 9/00624*** (2013.01); ***G06N 5/025*** (2013.01); ***G06N 5/043*** (2013.01); ***G06T 9/00*** (2013.01)

(58) **Field of Classification Search**
None
See application file for complete search history.

(56) **References Cited**

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5,058,033 A 10/1991 Bonissone et al.
5,119,470 A 6/1992 Highland et al.
5,175,795 A 12/1992 Tsuda et al.
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ISA/KR, International Search Report and Written Opinion for International Appln No. PCT/US2012/030052; Oct. 9, 2012; 9 pages.
(Continued)

Primary Examiner — Jeffrey A Gaffin
Assistant Examiner — David H Kim
(74) *Attorney, Agent, or Firm* — Mauriel Kapouytian Woods LLP; Michael Mauriel; Andrew A. Noble

(57) **ABSTRACT**

A reasoning engine is disclosed. Contemplated reasoning engines acquire data relating to one or more aspects of various environments. Inference engines within the reasoning engines review the acquire data, historical or current, to generate one or more hypotheses about how the aspects of the environments might be correlated, if at all. The reasoning engine can attempt to validate the hypotheses through controlling acquisition of the environment data.

30 Claims, 4 Drawing Sheets

NantAI

Reasoning Engines

Claim 31: A computer-based **medical reasoning engine** comprising:

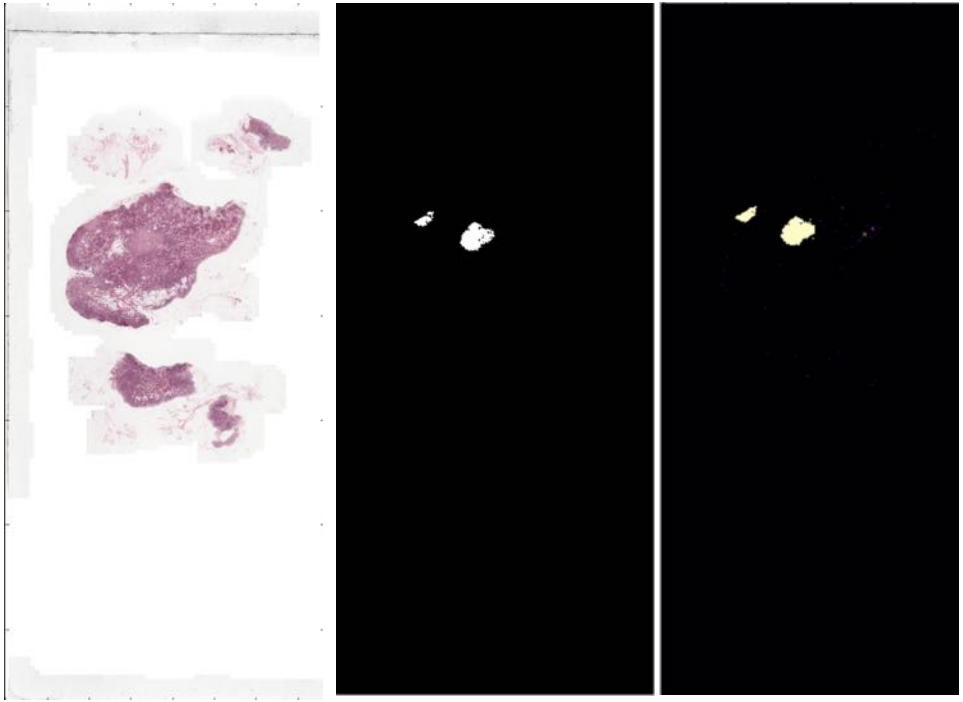
- A medical data interface configured to acquire medical data associated with treatment of a patient; and
- At least one medical inference server coupled with the medical data interface and configured to:
  - Obtain the medical data via the medical data interface;
  - Recognize, from the medical data, a treatment protocol and result related to the treatment of the patient, the treatment protocol and result each comprising object attributes;
  - select a reasoning rules set from available reasoning rules sets as a function of the medical data and object attributes of the treatment protocol and results;
  - Establish at least one outcome hypothesis according to the selected reasoning rules set as a function of patient data, the at least one outcome hypothesis representing that the treatment protocol and result have a suspected correlation with respect to the patient; and
  - Configure an output device to present the at least one outcome hypothesis along with reasoning supporting the at least one outcome hypothesis.

The engine of claim 31, wherein the medical data comprises **genomic data.**

Unsupervised Machine Learning Combined with Machine Vision

Leading to Computer Based Tumor Cell Identification

Deep Learning for Identifying Metastatic Cancer



Digital Whole Slide Image of Biopsy Tissue

Pathologist Ground Truth of Tumor Cells

Successful Prediction by NantWorks Machine Vision Platform

NantAI

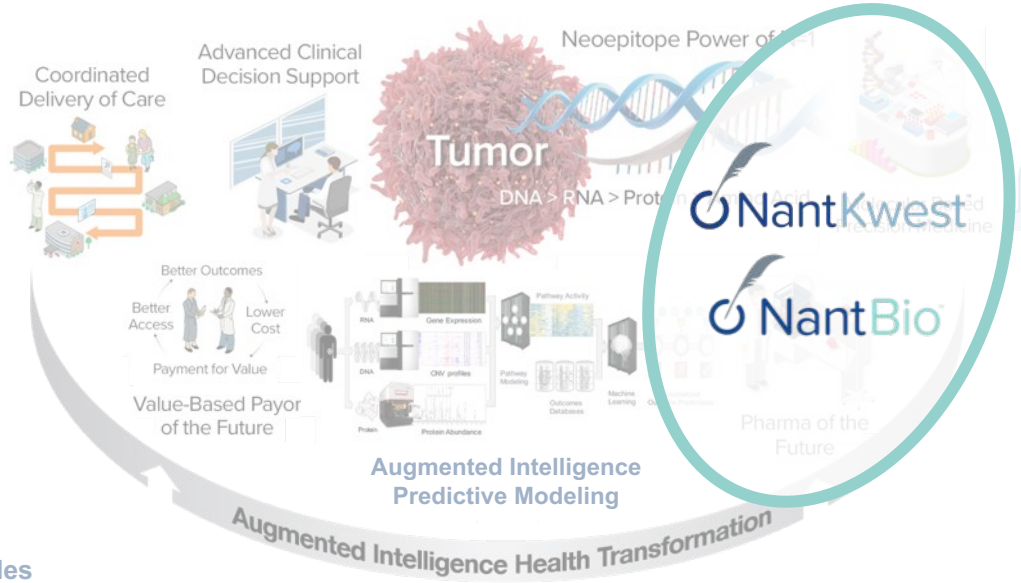
NantMesh: Layer 1 Network

UPPER LAYERS →	7	**Application Layer** ✓ Message format, Human-Machine Interfaces
	6	**Presentation Layer** ✓ Coding into 1s and 0s; encryption, compression
	5	**Session Layer** ✓ Authentication, permissions, session restoration
TRANSPORT SERVICE →	4	**Transport Layer** ✓ End-to-end error control
	3	**Network Layer** ✓ Network addressing; routing or switching
	2	**Data Link Layer** ✓ Error detection, flow control on physical link
	1	**Physical Layer** ✓ Bit stream: physical medium, method of representing bits

Harnessing the Power of Cognition and Augmented Intelligence: A Continuous Learning System Delivering Healthcare Transformation

Patients
Right Care -
Right Time -
Right Place -
Evidence Based -

Providers
Coordinated -
Integrated -
Evidence Based -
21st Century Medicine -



Payor of the Future
- Better Outcomes
- Better Access
- Better Safety
- Lower Cost

Pharma of the Future
- Molecular Based Medicine
- Personalized Medicine
- "The Power of N = 1"
- Transformational Innovation

To Cross the Chasm of Scales
From N=1 to the Human Population
Delivering Personalized
Evidence Based Care

Unraveling the Mysteries of Cancer: The Power of N=1
Neoepitope Driven Immunotherapy

To Establish
The Pharma of the Future
Driving Molecular Based
21st Century Care

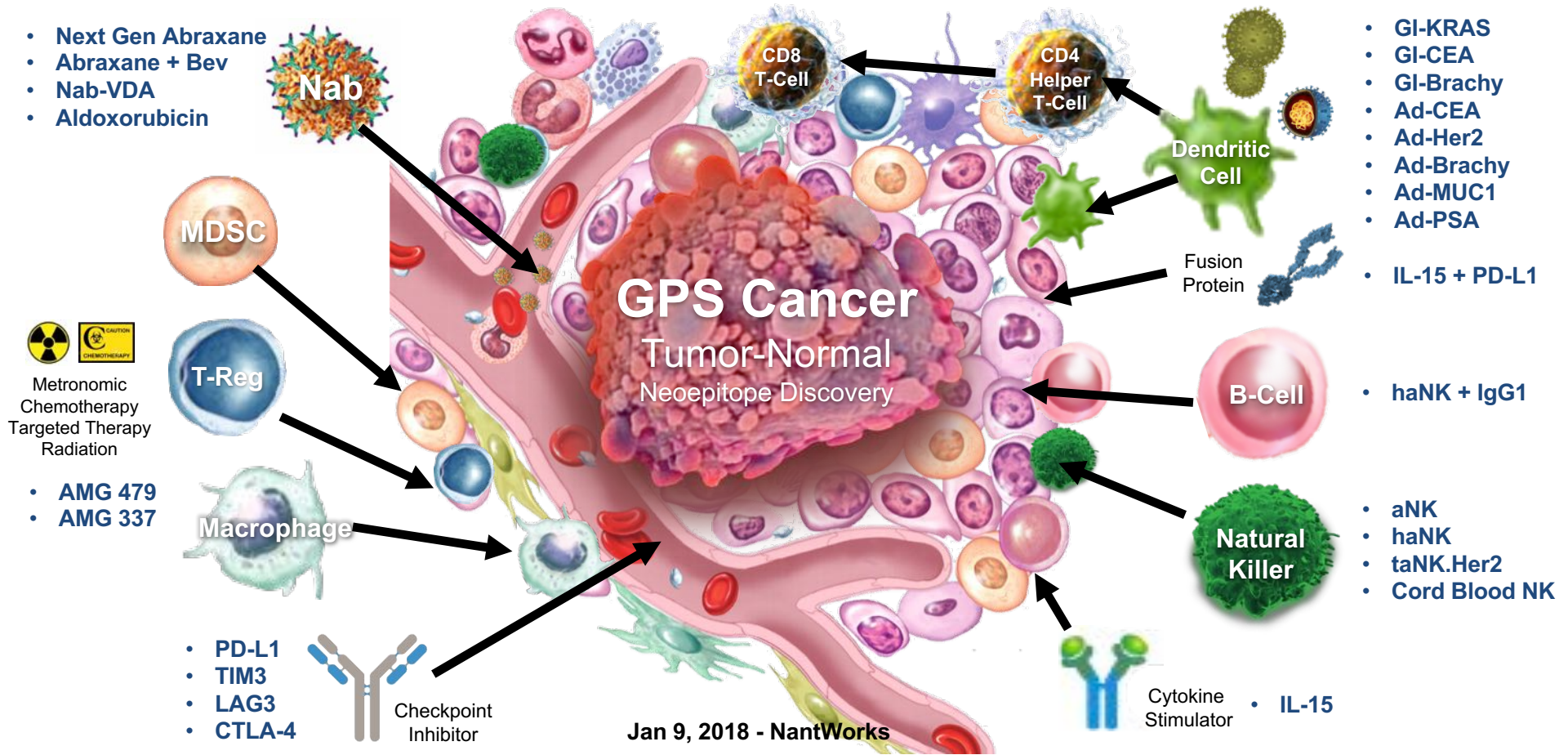
NANTWORKS

2018 – The NANT Cancer Vaccine

12 Novel Molecules in Phase II/III Clinical Trials in Over 20 Tumor Types

The NANT Cancer Vaccine: 12 Orchestrated Novel Biological Molecules in Phase II/III Trials

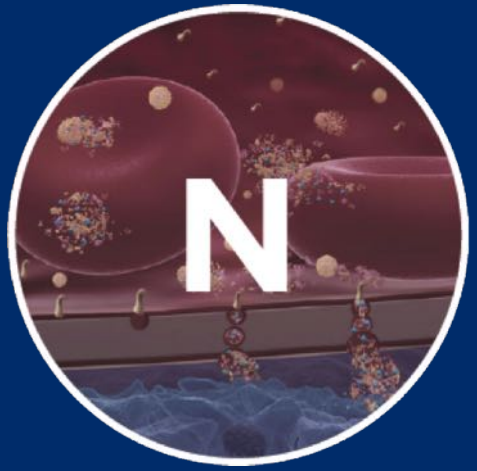
Immuno-Suppressed Tumor Microenvironment + **Innate & Adaptive Effectors**



Jan 9, 2018 - NantWorks

The NANT Cancer Vaccine

Nab



Immune Suppressor & ICD Signal Inducer Platform

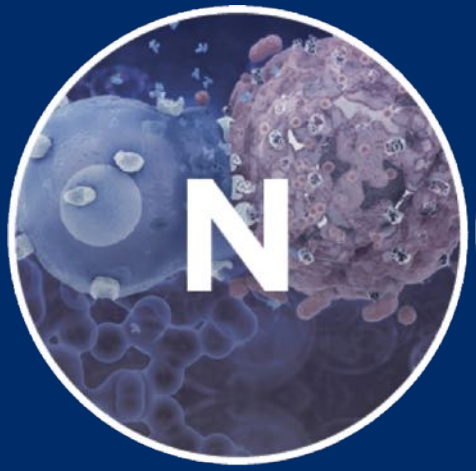
+

Antigen

Adenovirus & Yeast Dendritic Cell Platform

+

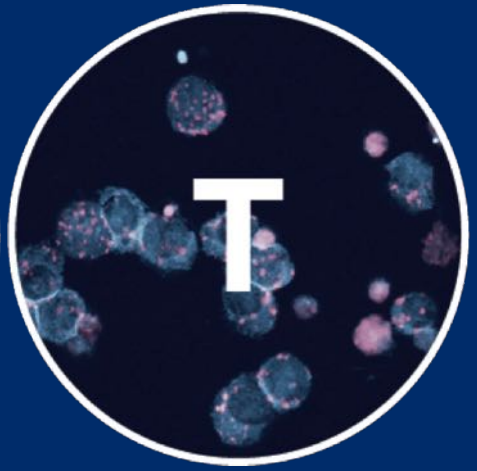
Natural-Killer



Natural Killer Off-The-Shelf NK IL-15 Platform

+

T-Cell



IL-15 Superagonist Fusion Protein Platform

A 21-Day Cycle

NANTWORKS

Key Achievements Since 2017

25 Authorized

25 Authorizations to Initiate Phase I/II in 20 Tumor Types Covering 12 Novel Molecules

Colorectal Cancer, Prostate Cancer, AML/MDS, CEA-Expressing Cancers, Head and Neck Squamous Cell Carcinoma, Merkel Cell Carcinoma, Melanoma, Sarcoma, Metastatic Solid Tumors, Non-Hodgkin Lymphoma, Non-Small Cell Lung Cancer, Ovarian, Pancreatic Cancer, Urothelial Cancer

50 Listed

QUILT (QUantum Integrative Lifelong Trial) Listed to Date (Jan 2018)

Phase I, Phase II, Phase III Trials Listed on **ClinicalTrials.gov** Across 20 Tumor Types

5 First-in Human

FIH Studies in 2017:

QUILT 3.013 Ad-021 (Ad5-HER2 Vaccine) in HER2-Low-Expressing Breast Cancer
QUILT 3.028 haNK in Solid Tumors
QUILT 3.039 NANT Cancer Vaccine with aNK: Pancreatic
QUILT 3.060 NANT Cancer Vaccine with haNK: Pancreatic
QUILT 3.070 NANT Cancer Vaccine with Cryopreserved haNK: Pancreatic

5 Completed Phase I

FIH Safety Demonstrated In 2017:

QUILT 3.013 Ad-021 (Ad5-HER2 Vaccine) in HER2-Low-Expressing Breast Cancer
QUILT 3.028 haNK in Solid Tumors
QUILT 3.039 NANT Cancer Vaccine with aNK: Pancreatic
QUILT 3.060 NANT Cancer Vaccine with haNK: Pancreatic
QUILT 3.070 NANT Cancer Vaccine with Cryopreserved haNK: Pancreatic

7 Planned Phase II/III

Planned Phase II/III Studies to be Initiated 2018:

Metastatic:	Pancreatic, Head & Neck, NSCLC, TNBC, Ewings
First Line:	Pancreatic
Second Line:	Bladder

NANTWORKS

Key Achievements Since 2017

25 Authorized

25 Authorizations to Initiate Phase I/II in 20 Tumor Types Covering 12 Novel Molecules

Colorectal Cancer, Prostate Cancer, AML/MDS, CEA-Expressing Cancers, Head and Neck Squamous Cell Carcinoma, Merkel Cell Carcinoma, Melanoma, Sarcoma, Metastatic Solid Tumors, Non-Hodgkin Lymphoma, Non-Small Cell Lung Cancer, Ovarian, Pancreatic Cancer, Urothelial Cancer

50 Listed

QUILT (QUantum Integrative Lifelong Trial) Listed to Date (Jan 2018)

Phase I, Phase II, Phase III Trials Listed on **ClinicalTrials.gov** Across 20 Tumor Types

5 First-in Human

FIH Studies in 2017:

QUILT 3.013 Ad-021 (Ad5-HER2 Vaccine) in HER2-Low-Expressing Breast Cancer
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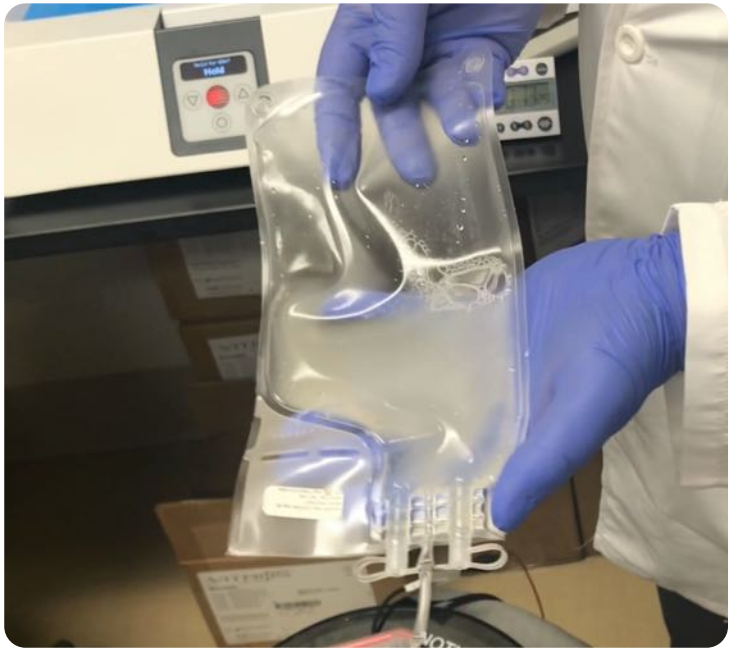
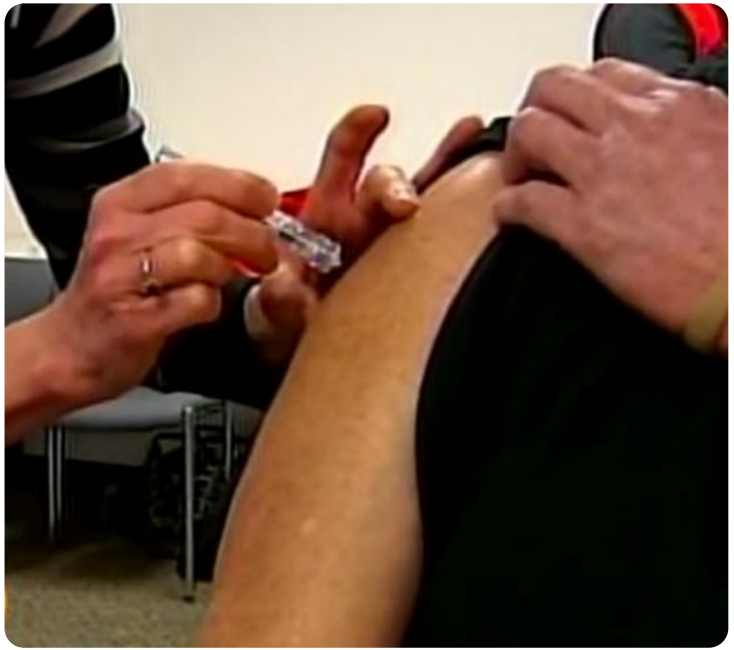
The NANT Cancer Vaccine Treatment



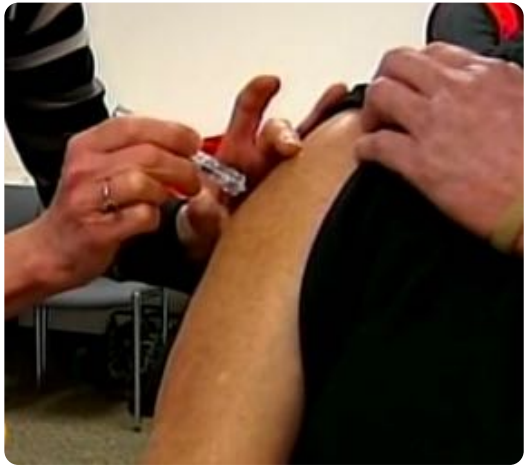
Natural Killer Cell Transfusion



Adenovirus Vaccine and Fusion Protein
Subcutaneous Flu Like Shot

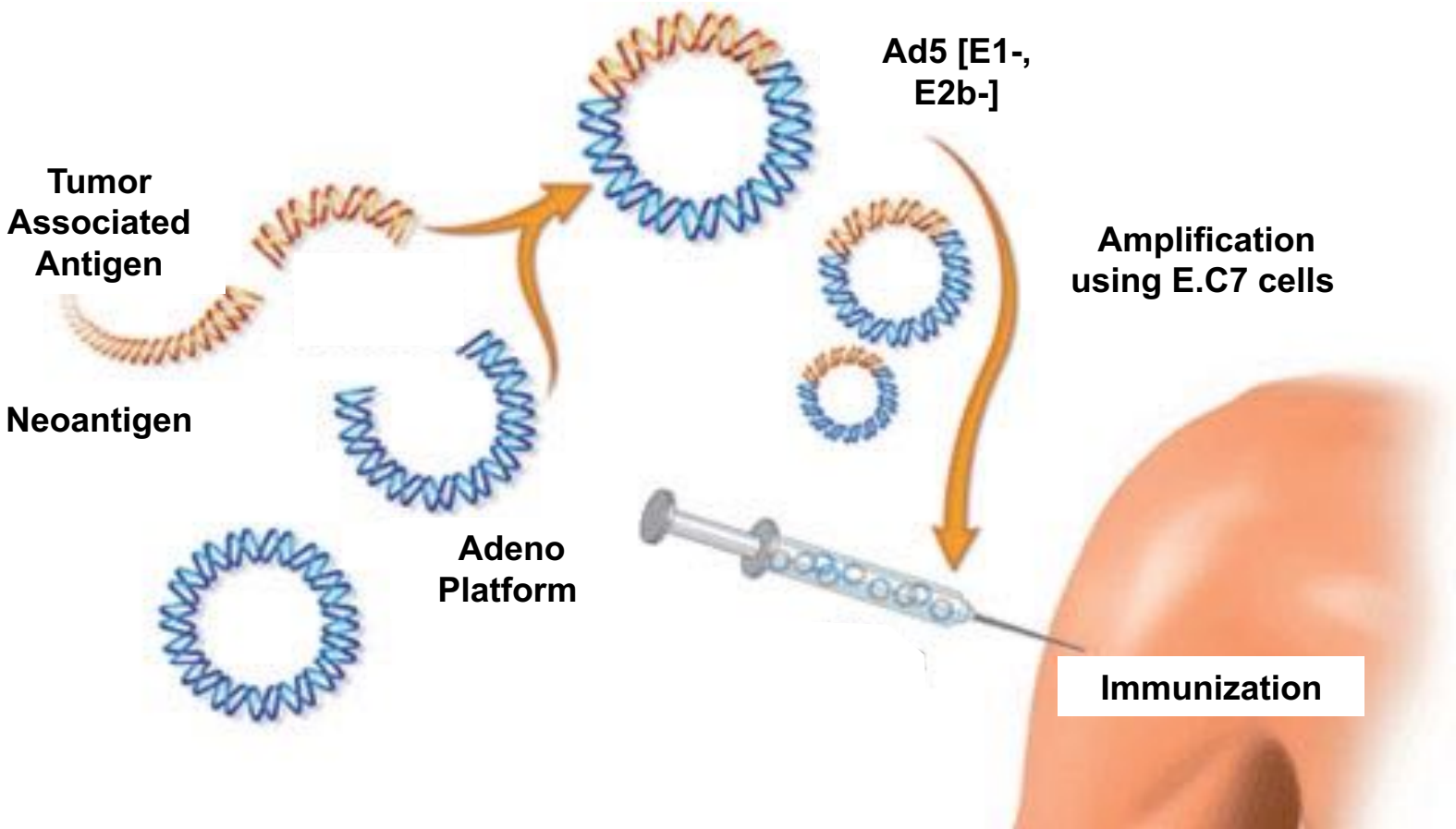
First in Human Study Update (Jan 2018)

Adenovirus / Fusion Protein (IL-15)

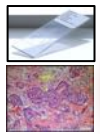


Adenovirus Vaccine Shot
Subcutaneous Flu Like Shot

The NANT Adeno Platform: Product Production and Administration



25 Year Pursuit of the NANT Cancer Vaccine:
Entering the Era of Clinical Genomics & Proteomics to Deliver Neoepitope Immunotherapy for N=1



TUMOR

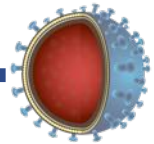
NORMAL

NantAI

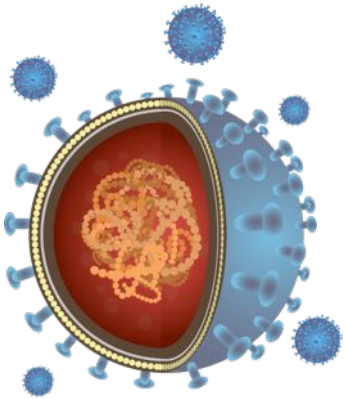
- Augmented Intelligence
- Machine Learning
- Super Computer

- Ad-CEA
- Ad-Her2
- Ad-Brachy
- Ad-MUC1
- Ad-PSA

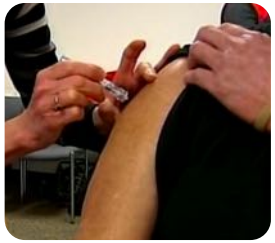
Neoepitope Discovery



Novel Engineered Adenovirus (Common Cold Virus)



Adenovirus Armed with Tumor Associated Antigen & Neoepitope



First in Human Update (Jan 2018)

NANT Cancer Vaccine: Next Generation GPS Guided Cancer Vaccine

CEA Expressing Cancers: **Ad-CEA** + ALT-803 Phase 1/2 Clinical Trial

NCT01127965
QUILT 3.040

STATUS: Currently Enrolling

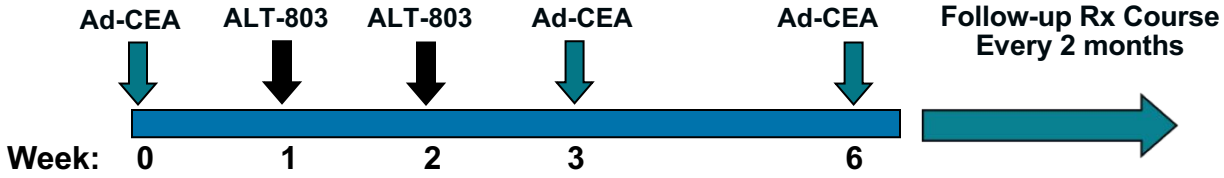
Treatment Sites: Duke University (Mike Morse PI); Medical Oncology Associates, Spokane + plus others

Number of Patients: Phase 1=3, Phase 2= 7 different tumor indications, up to 20 patients each

Patient Profile: CEA expressing tumor, ECOG performance status ≤ 1, life expectancy at least 6 months

Clinical Endpoint: Overall survival, safety, anticancer immunity, genomic/proteomic profile

Clinical Protocol:



	Dose	Number of Patients
Phase 1/2		
Cohort 1	Ad-CEA: 5 x 10^{11} VP ALT-803: 10ug/kg	3
Cohort 2	Ad-CEA: 5 x 10^{11} VP ALT-803: 15ug/kg	3 + 3
Cohorts 3-9	HTD	Up to 140

Phase I Safety Results to Date 3 Patients Completed (Jan 2018): No DLTs

Colorectal Cancer: Phase IIb Randomized Clinical Trial in First Line Patients

NCT03050814
QUILT 2.004

STATUS: Currently Enrolling

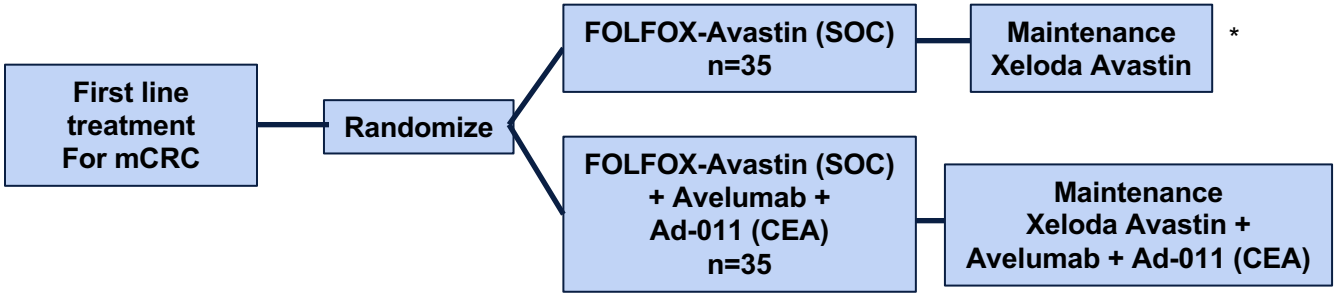
Treatment Site: National Cancer Institute (Julius Strauss, PI)

Number of Patients: 6, Then First Line Randomized 1:1 with 35 patients in each arm

Patient Profile: CRC, ECOG performance status ≤ 1, life expectancy at least 6 months

Clinical Endpoint: Overall survival, safety, anticancer immunity, genomic/proteomic profile

Clinical Protocol:



*Patients on standard of care are allowed to cross-over to Avelumab + Ad-CEA + standard of care at progression of disease

Phase I/II Safety Results to Date 6 Patients (Jan 2018): No DLTs for Vector

mCEA Expressing Cancer: **Ad-CEA/MUC1/Brachyury** Phase 1/2 Trial

NCT03384316
QUILT 3.021

STATUS: FDA document filing

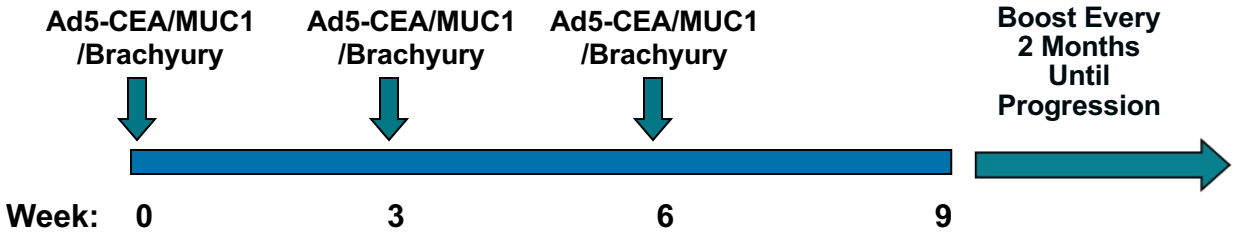
Treatment Sites: National Cancer Institute (Julius Strauss, PI and Jeffrey Schlom) + Others

Number of Patients: 30

Patient Profile: mCEA Expressing Tumor, ECOG performance status ≤ 1, life expectancy at least 6 months

Clinical Endpoint: Overall survival, safety, anticancer immunity, genomic/proteomic profile

Clinical Protocol:



	Dose	Number of Patients
Phase I/II		
Cohort 1	5 x 10^{11} VP of Each Vector	3 +3
Cohort 2	HTD	24

Phase I/II Safety, First Patient Enrollment in Q1 2018

mPSA Expressing Prostate Cancer: **Ad-PSA** Phase 1/2

QUILT 1.002
NCT Pending
IND 17811

STATUS: FDA document filing

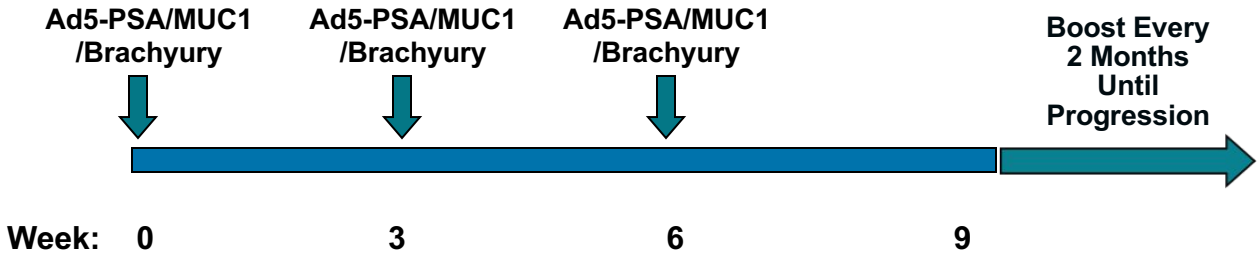
Treatment Sites: National Cancer Institute (James Gulley, MD & Marijo Bilusic, MD) +Others

Number of Patients with Three Doses: 30

Patient Profile: mCRC, ECOG performance status ≤ 1, life expectancy at least 3 months

Clinical Endpoint: Overall survival, safety, anticancer immunity, genomic/proteomic profile

Clinical Protocol:



	Dose	Number of Patients
Phase I/II		
Cohort 1	5 x 10^{11} VP of Each Vector	3 +3
Cohort 2	HTD	24

Phase I/II First Patient Study Q1 2018

Ad-HER2 Expressing Cancer: **Ad-HER2** Phase 1/2 Clinical Trial

NCT02751528
QUILT 3.013

STATUS: Currently Enrolling

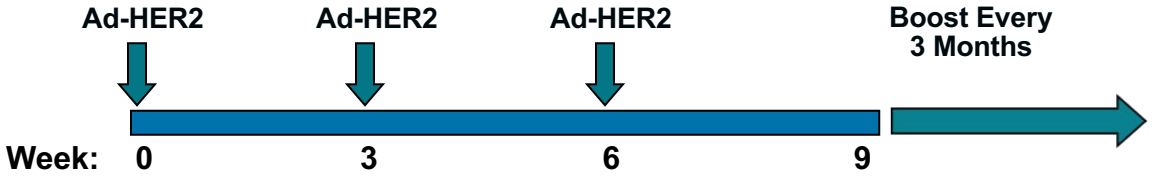
Treatment Sites; Sanford Healthcare, + Medical Oncology Associates, Spokane + Others

Number of Patients: 3 + 3, Then up to 24 additional

Patient Profile: mHER2 Expressing, ECOG performance status ≤ 1, life expectancy at least 6 months

Clinical Endpoint: Overall survival, safety, anticancer immunity, genomic/proteomic profile

Clinical Protocol:



	Dose	Number of Patients
Phase 1/2		
Cohort 1	5 x 10^{10} VP	3
Cohort 2	5 x 10^{11} VP	3
Expansion	HTD	24

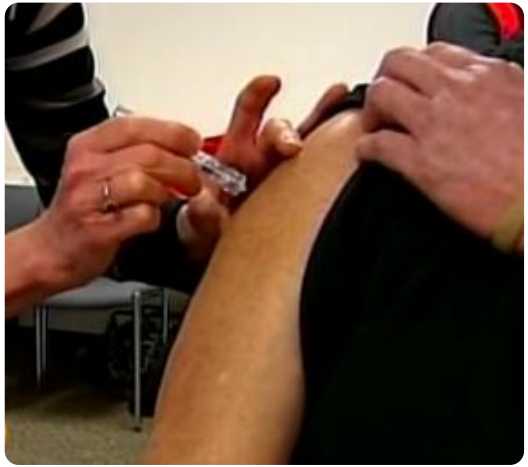
Phase I/II Safety Results to Date 3 Patients (Jan 2018): No DLTs

First in Human Study Update (Jan 2018)

Merkel Cell Carcinoma

aNK + IL-15

Natural Killer Cell Transfusion
Freshly Isolated

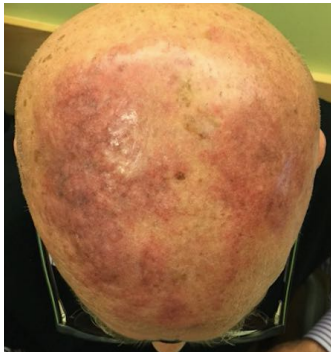


IL-15

Phase I/II: Merkel Cell Carcinoma Who Failed Checkpoints & Previous Chemotherapy

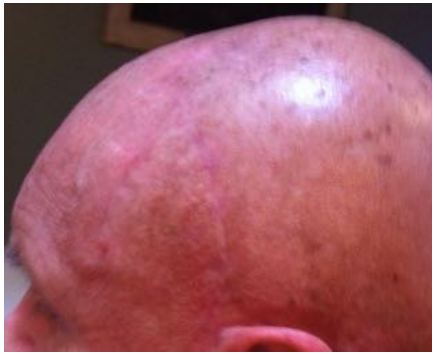
- N=6
- Treatment Single Arm: **aNK Alone** followed by **aNK + IL-15**
- Results to Date:
  - **2 Complete Responses**
  - 1 Partial Response
  - 3 Progressive Disease

Phase I/II: Complete Response in Merkel Cell Carcinoma Who Failed Checkpoints & Previous Chemotherapy



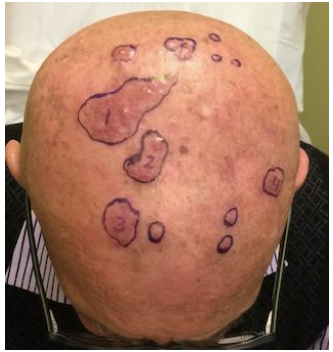
10/2014

First consultation at UW, Seattle



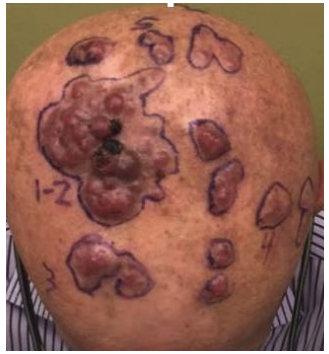
12/2014

After RT plus IFN plus Imiquimod



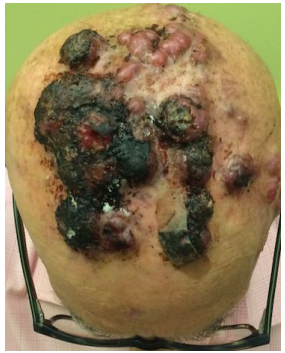
01/2015

Recurrent MCC nodules on scalp in RT fields. Started anti-PD-1 (pembrolizumab) for unresectable MCC



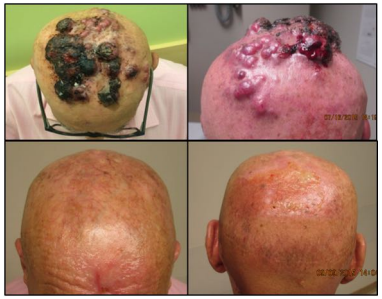
04/2015

anti-PD-1 after 12 weeks of pembrolizumab
Pembrolizumab discontinued due to progressive disease



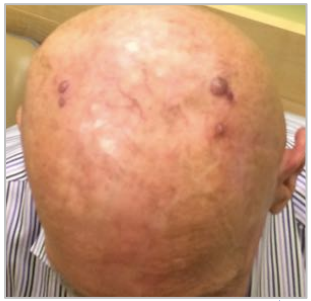
06/2015

Enrolled on a clinical trial of intralesional TLR-4 agonist plus RT



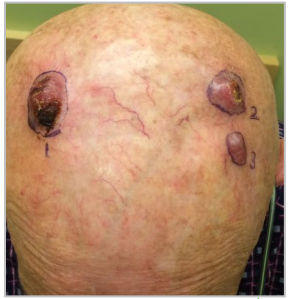
07/2015

Received neutron RT to scalp and B/L neck tumors.



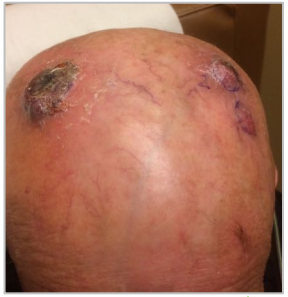
12/2015

Recurrent MCC tumors on scalp.



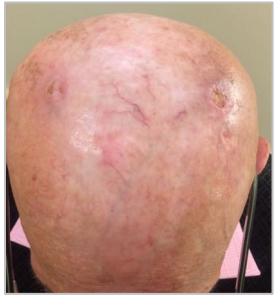
03/14/2016

Enrolled on aNK trial
Baseline Day 01
First Infusion on 03/15/2016



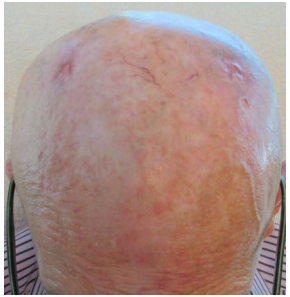
03/30/2016

Day 14



06/21/2016

Day 99
No New Lesions
Since 03/14/2016

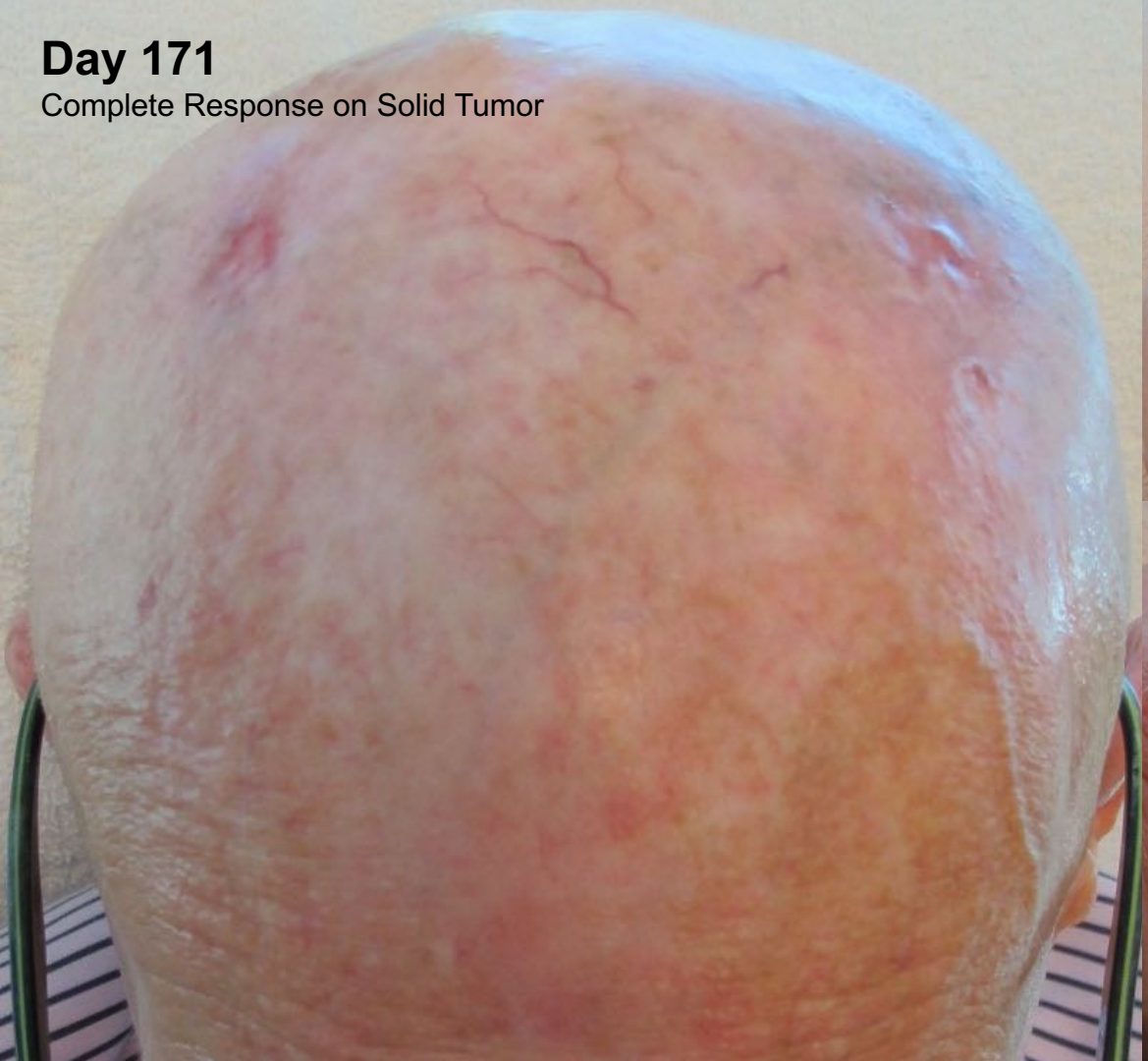


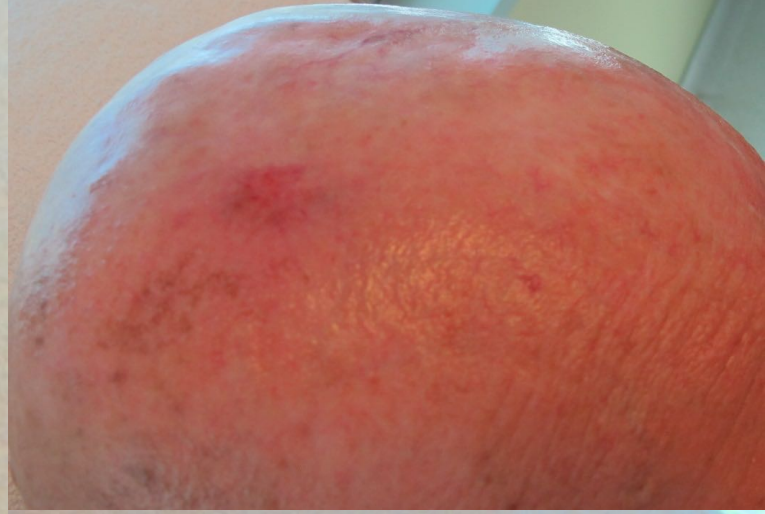
09/01/2016

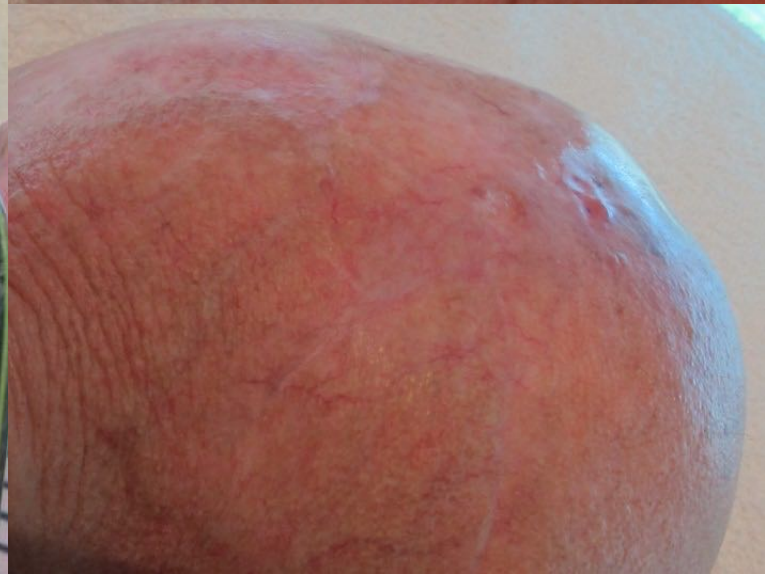
Day 171
No New Lesions
Since 03/14/2016

Day 171

Complete Response on Solid Tumor



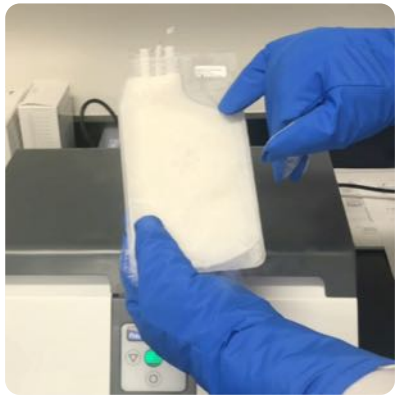




First in Human Study Update (Jan 2018)

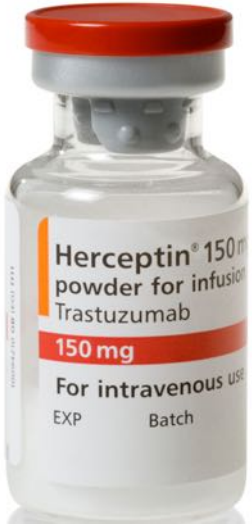
Natural Killer (NantKwest)
haNK off-the-shelf in Solid Tumors

Natural Killer Cell Transfusion
Freshly Isolated



Natural Killer Cell Transfusion
Cryopreserved & Thawed at Bedside

Potential to Enhance Antibody Based Killing with haNK



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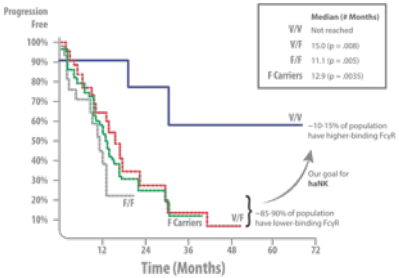
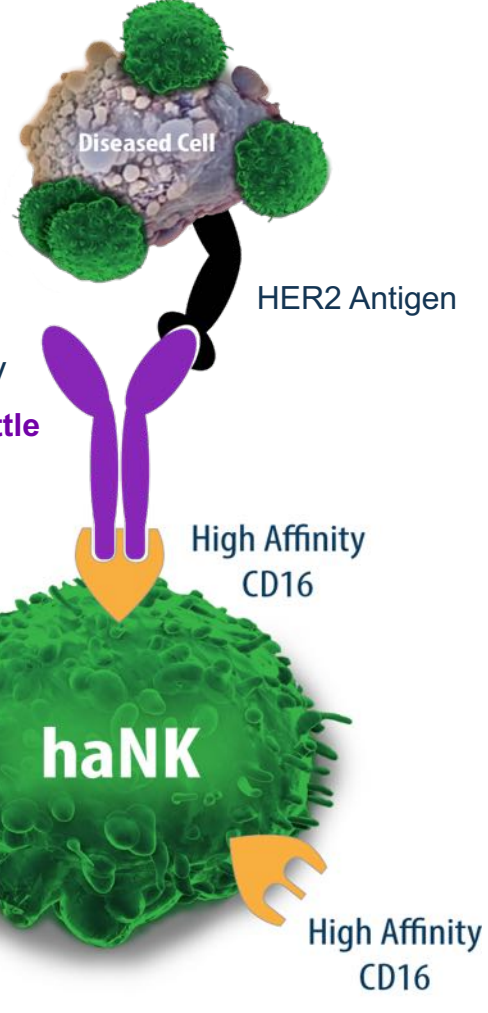


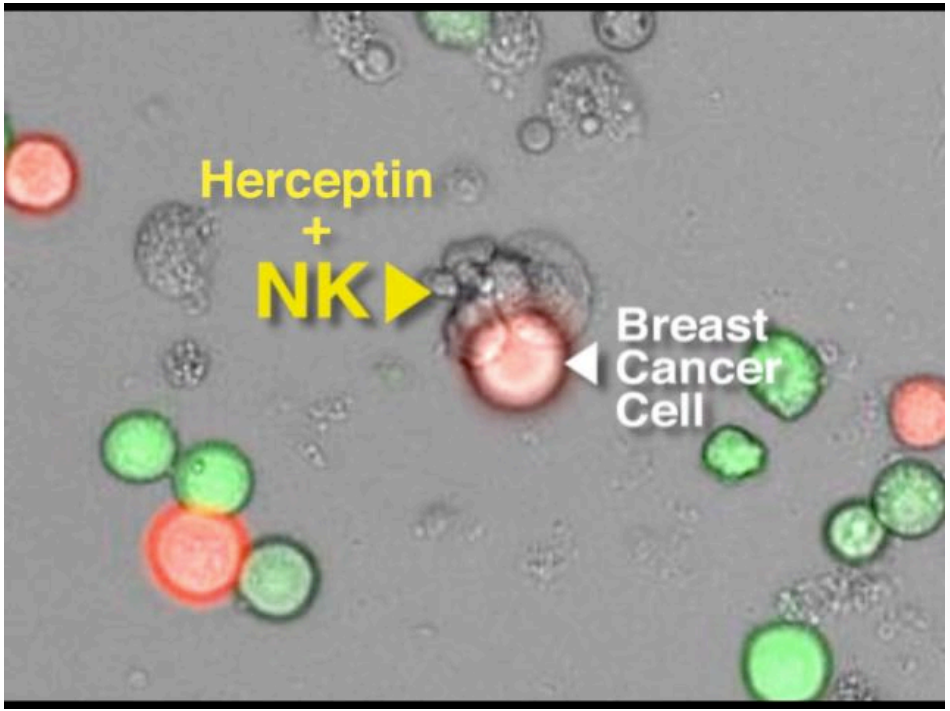
ADCC

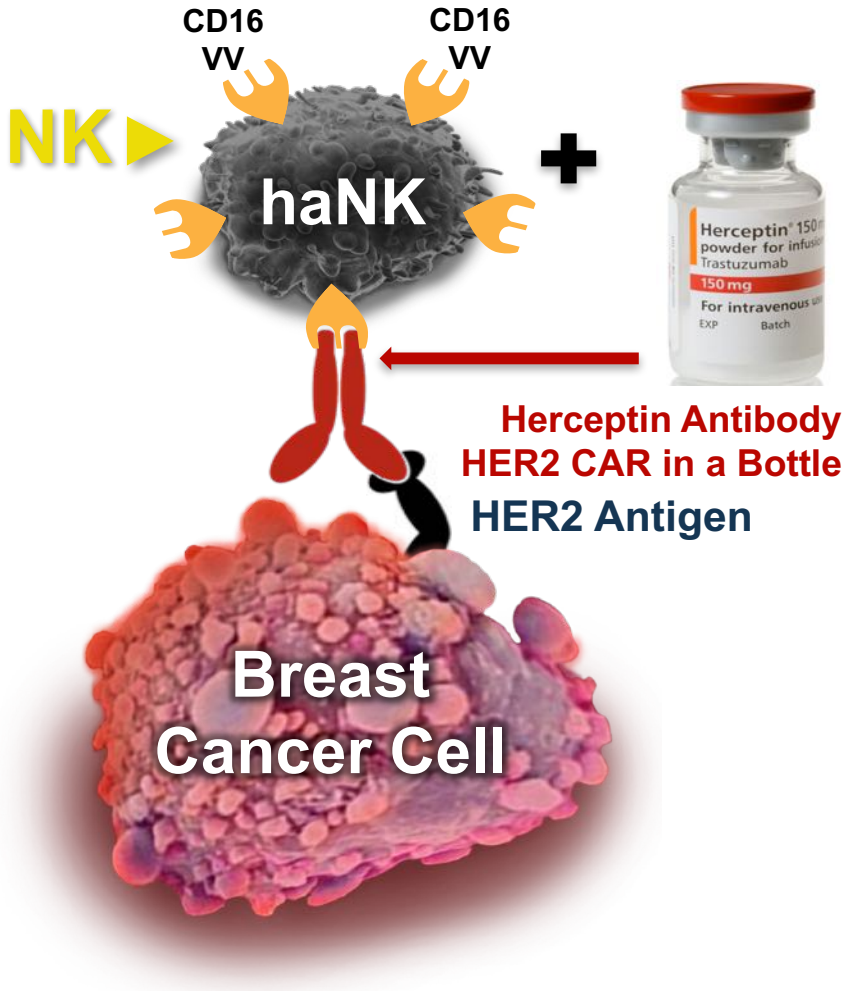
Herceptin Antibody

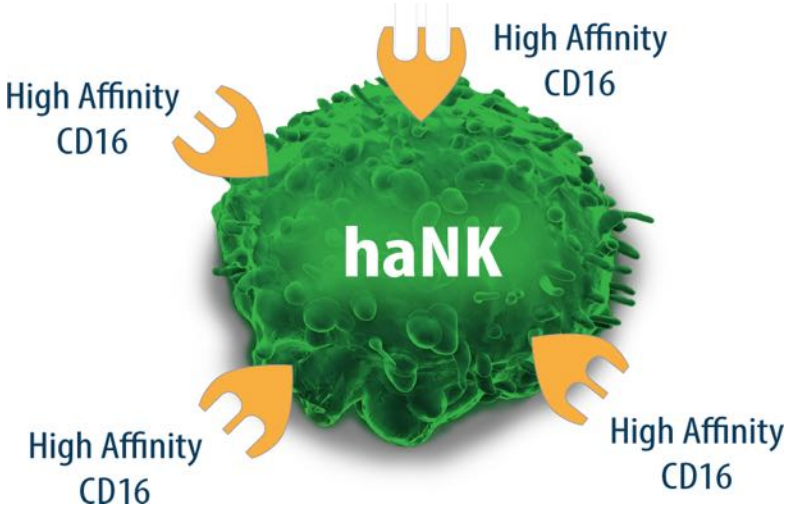
HER2 CAR in a Bottle



Potential to Enhance Antibody Based Killing with haNK

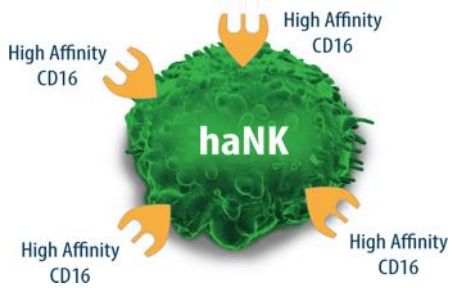






haNK has the potential to be the backbone of ADCC induced cell death in combination with **mAbs**

The haNK First in Human (FIH) Trial of Off-The-Shelf Freshly Isolated haNK

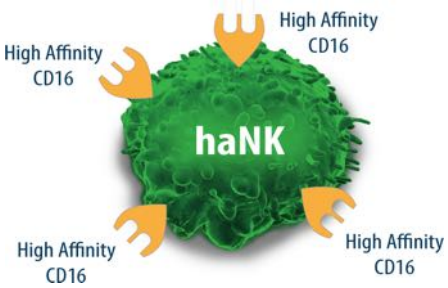


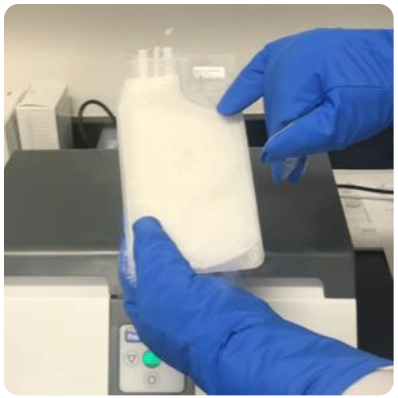
Natural Killer Cell Transfusion
Freshly Isolated
2 Billion Cells Per Bag

All Patients Received 2 Billion Fresh haNK Cells Per Dose

- N = 3
- Patient #1: Adenoid cystic carcinoma – received weekly x 3 doses
- Patient #2: Head and Neck Squamous Cell Carcinoma – received weekly x 4 doses
- Patient #3: Colorectal Carcinoma – received weekly x 4 doses
- **Results: No DLTs, Single Agent, Freshly Isolated haNK**

The haNK First in Human (FIH) Trial of Off-The-Shelf Cryopreserved haNK





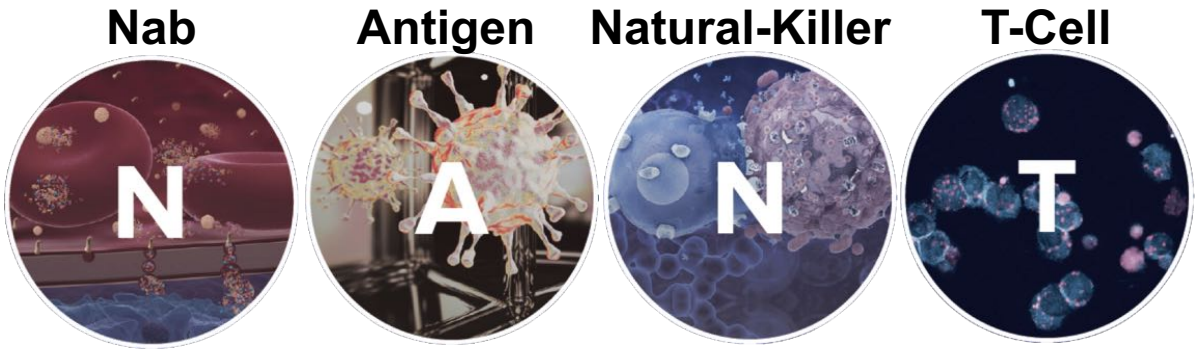
Natural Killer Cell Transfusion
Cryopreserved & Thawed at Bedside
2 Billion Cells Per Bag

First in Human Off-The-Shelf FIH Cryopreserved haNK

- N=6
- 2 Billion Cells of Cryopreserved haNK Cells Per Dose
- 24 Doses Administered to Date (Jan 2018)
- **Results: No DLTs**

First in Human Receiving NANT Pancreatic Cancer Vaccine with Cryopreserved haNK in Combination with NANT Bio Molecules 2nd and 3rd Line Who Failed Standard Chemo

Natural Killer Cell Transfusion
Cryopreserved & Thawed at Bedside
2 Billion Cells Per Bag



Immune Suppressor & ICD Signal Inducer Platform

Adenovirus & Yeast Dendritic Cell Platform

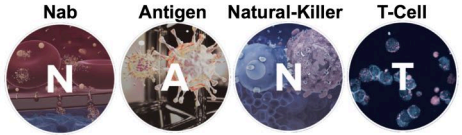
Natural Killer Off-The-Shelf NK IL-15 Platform

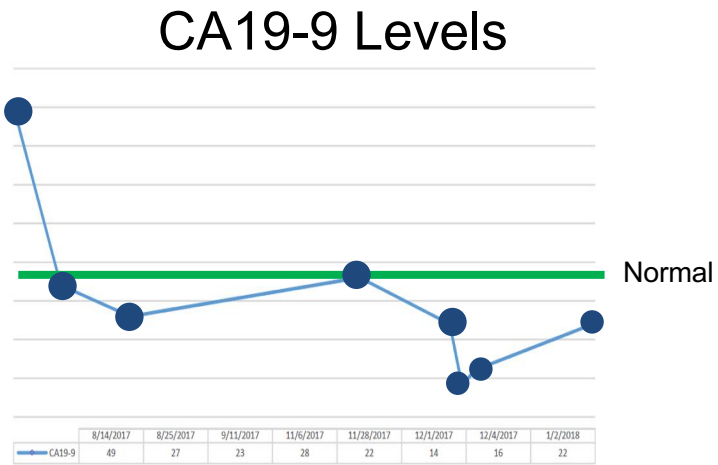
IL-15 Superagonist Fusion Protein Platform

Patient #1: First in Human NANT Pancreatic Cancer Vaccine 2nd and 3rd Line Who Failed Standard Chemo

- 35 Year Old Male with metastasis to liver and lung failed first line and second line chemotherapy
- First dosing of NCV on August 14, 2017
- Received 9 cycles to date (initially with aNK and evolved to cryopreserved haNKs)
- CA-19-9 Normalized from a high of 49 to 22
- Patient pain free
- Weight gain of 12 lbs.
- CT Scan 20% reduction of tumor mass
- No DLTs over 9 cycles to date
- **Stable disease with normalization of CA-19-9, weight gain, pain-free and tumor reduction for 5 months to date (Jan 2018)**
- **NANT Pancreatic Cancer Vaccine ongoing**

Natural Killer Cell Transfusion
Cryopreserved & Thawed at Bedside
2 Billion Cells Per Bag



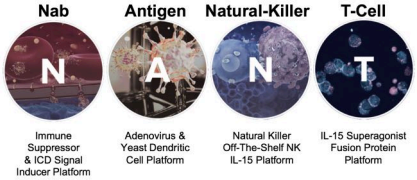


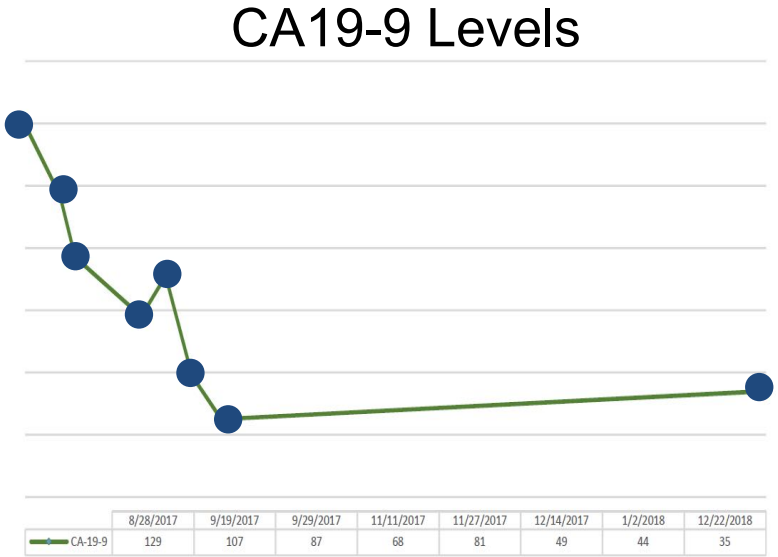
QUILT 3.060 & 3.039

Patient #2: First in Human NANT Pancreatic Cancer Vaccine 2nd and 3rd Line Who Failed Standard Chemo

- 50 Year old female with mets to liver and lung failed first line and second line chemotherapy
- Cachetic with active weight loss at time of initiation of trial and on high dose methadone pain medications BID
- First dosing of NCV on Sept 4, 2017
- Received 8 cycles to date (initially with aNK and evolved to cryopreserved haNKs)
- CA-19-9 Dropped >50% from a high of 129 to 35
- Pain completely resolved and patient on methadone free from cycle 2
- Weight gain, 12 lbs.
- No DLTs over 8 cycles to date
- **Stable disease for 4.5 months with reduction of CA-19-9, weight gain and pain free 4.5 months to date (Jan 2018)**
- **NANT Pancreatic Cancer Vaccine ongoing**

Natural Killer Cell Transfusion
Cryopreserved & Thawed at Bedside
2 Billion Cells Per Bag

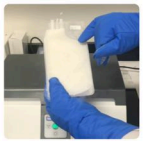




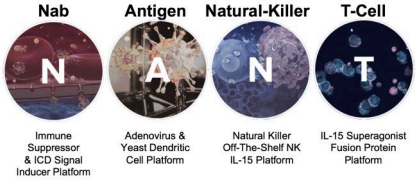
QUILT 3.060 & 3.039

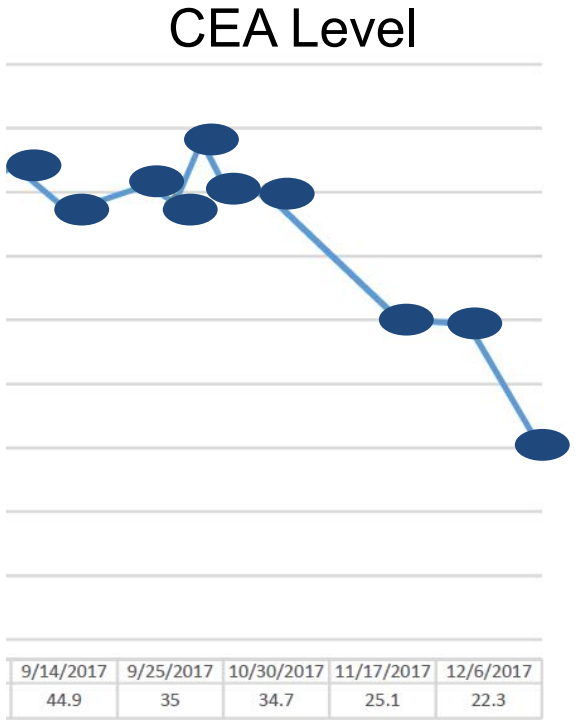
Patient #3: First in Human NANT Pancreatic Cancer Vaccine 2nd and 3rd Line Who Failed Standard Chemo

- 63 Year old male with mets to liver failed first line and second line chemotherapy
- First dosing of NCV on October 2, 2017
- Received 4 cycles to date (initially with aNK and evolved to cryopreserved haNKs)
- CEA dropped ~50% from a high of 45 to 22
- No DLTs over 4 cycles to date
- **Stable disease for 4 months with reduction of CEA and pain free to date (Jan 2018)**
- **NANT Pancreatic Cancer Vaccine ongoing**



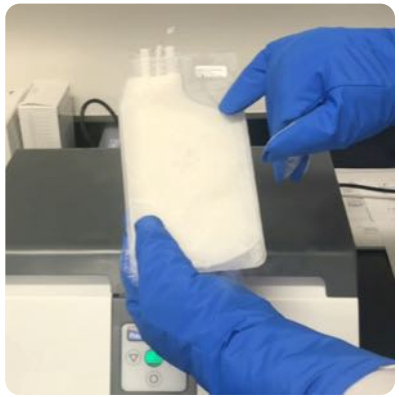
Natural Killer Cell Transfusion
Cryopreserved & Thawed at Bedside
2 Billion Cells Per Bag





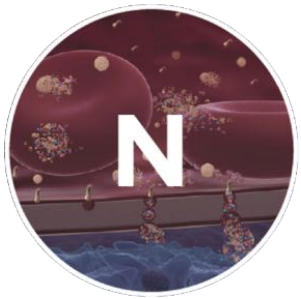
QUILT 3.060 & 3.039

First Six (6) Patients Receiving NANT Pancreatic Cancer Vaccine with Cryopreserved haNK in Combination with NANT Bio Molecules 2nd and 3rd Line Who Failed Standard Chemo



Natural Killer Cell Transfusion
Cryopreserved & Thawed at Bedside
2 Billion Cells Per Bag

Nab

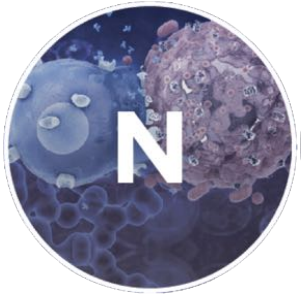


Immune
Suppressor
& ICD Signal
Inducer Platform

Antigen

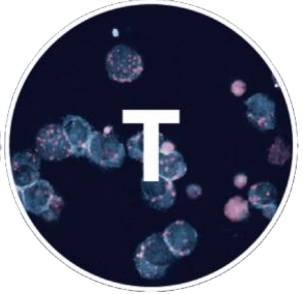
Adenovirus &
Yeast Dendritic
Cell Platform

Natural-Killer



Natural Killer
Off-The-Shelf NK
IL-15 Platform

T-Cell



IL-15 Superagonist
Fusion Protein
Platform

Results: No Dose Limiting Toxicities (DLTs) To Date
Over 50 Doses Administered To Date
Phase I Completed (2017)
Phase II Initiated (Q1 2018)

NANTWORKS

Key Achievements Since 2017

25 Authorized

25 Authorizations to Initiate Phase I/II in 20 Tumor Types Covering 12 Novel Molecules

Colorectal Cancer, Prostate Cancer, AML/MDS, CEA-Expressing Cancers, Head and Neck Squamous Cell Carcinoma, Merkel Cell Carcinoma, Melanoma, Sarcoma, Metastatic Solid Tumors, Non-Hodgkin Lymphoma, Non-Small Cell Lung Cancer, Ovarian, Pancreatic Cancer, Urothelial Cancer

50 Listed

QUILT (QUantum Integrative Lifelong Trial) Listed to Date (Jan 2018)

Phase I, Phase II, Phase III Trials Listed on **ClinicalTrials.gov** Across 20 Tumor Types

5 First-in Human

FIH Studies in 2017:

QUILT 3.013 Ad-021 (Ad5-HER2 Vaccine) in HER2-Low-Expressing Breast Cancer
QUILT 3.028 haNK in Solid Tumors
QUILT 3.039 NANT Cancer Vaccine with aNK: Pancreatic
QUILT 3.060 NANT Cancer Vaccine with haNK: Pancreatic
QUILT 3.070 NANT Cancer Vaccine with Cryopreserved haNK: Pancreatic

5 Completed Phase I

FIH Safety Demonstrated In 2017:

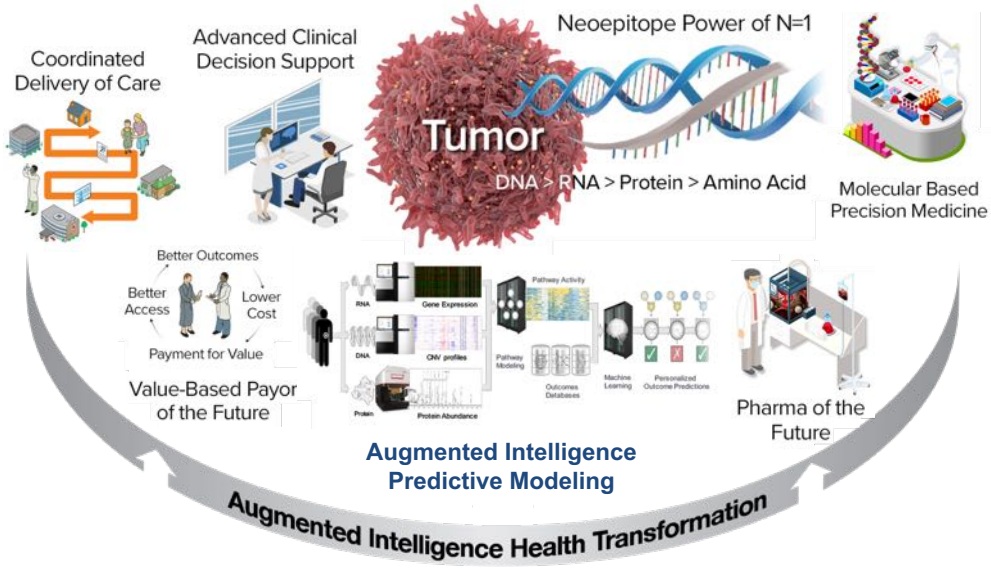
QUILT 3.013 Ad-021 (Ad5-HER2 Vaccine) in HER2-Low-Expressing Breast Cancer
QUILT 3.028 haNK in Solid Tumors
QUILT 3.039 NANT Cancer Vaccine with aNK: Pancreatic
QUILT 3.060 NANT Cancer Vaccine with haNK: Pancreatic
QUILT 3.070 NANT Cancer Vaccine with Cryopreserved haNK: Pancreatic

7 Planned Phase II/III

Planned Phase II/III Studies to be Initiated 2018:

Metastatic:	Pancreatic, Head & Neck, NSCLC, TNBC, Ewings
First Line:	Pancreatic
Second Line:	Bladder

Unraveling the Mysteries of Cancer: The Power of N=1
Neoepitope Driven Immunotherapy



“Here’s my DNA Sequence”


NANTWORKS
Thank You
info@nantworks.com