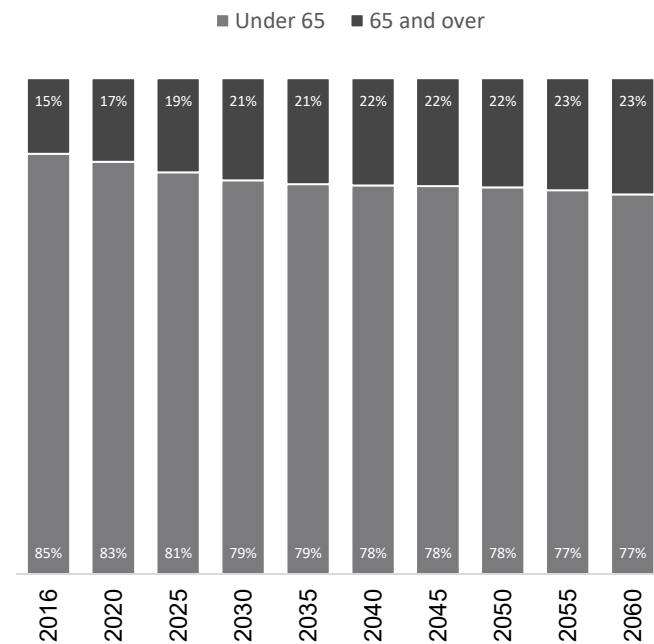Morgan Lewis

ARTIFICIAL INTELLIGENCE IN HEALTHCARE
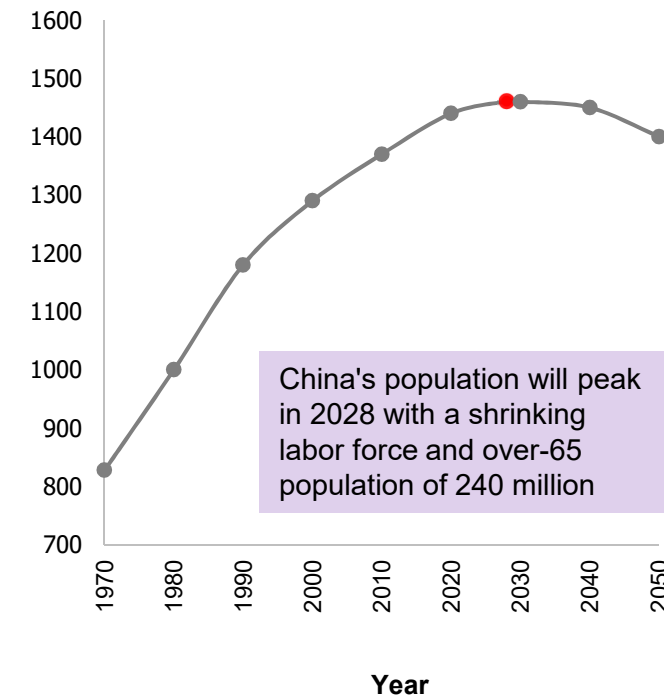
Brett Alan Lovejoy, Ph.D., JD
Morgan, Lewis & Bockius LLP

Healthcare Trends
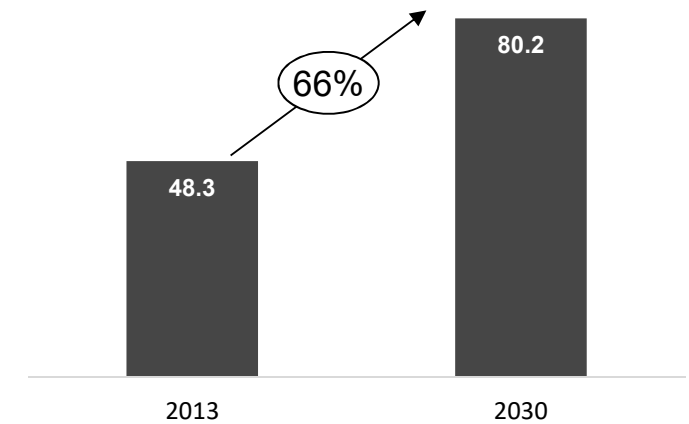
U.S. Population
Population Forecast by Age Group

■ Under 65　■ 65 and over

Year	65 and over	Under 65
2016	15%	85%
2020	17%	83%
2025	19%	81%
2030	21%	79%
2035	21%	79%
2040	22%	78%
2045	22%	78%
2050	22%	78%
2055	23%	77%
2060	23%	77%

Chinese Population
Population Forecast (in M)

China's population will peak in 2028 with a shrinking labor force and over-65 population of 240 million

Year

Global Healthcare Workforce
Estimated Health Worker Demand (in M)

48.3 (2013) → 80.2 (2030), 66%

Morgan Lewis

Healthcare Trends

U.S. Obesity
Prevalence of Overweight and Obesity

■ Overweight, Not Obese ■ Obese

Period	Obese	Overweight, Not Obese
1960-1962	13%	32%
1971-1974	15%	32%
1976-1980	15%	32%
1988-1994	23%	33%
1999-2002	30%	35%
2003-2006	33%	33%
2007-2010	35%	34%
2011-2014	36%	33%
2015-2016	40%	33%
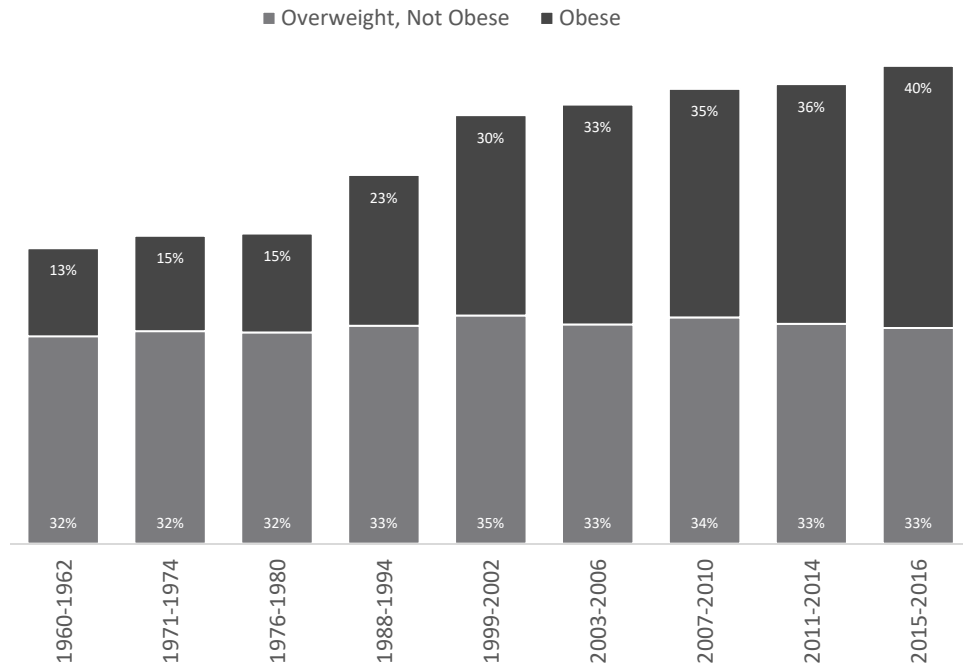
U.S. Healthcare Spending
National Health Expenditure Forecast

$27B → $5,963B

(1960 – 2026)

Morgan Lewis
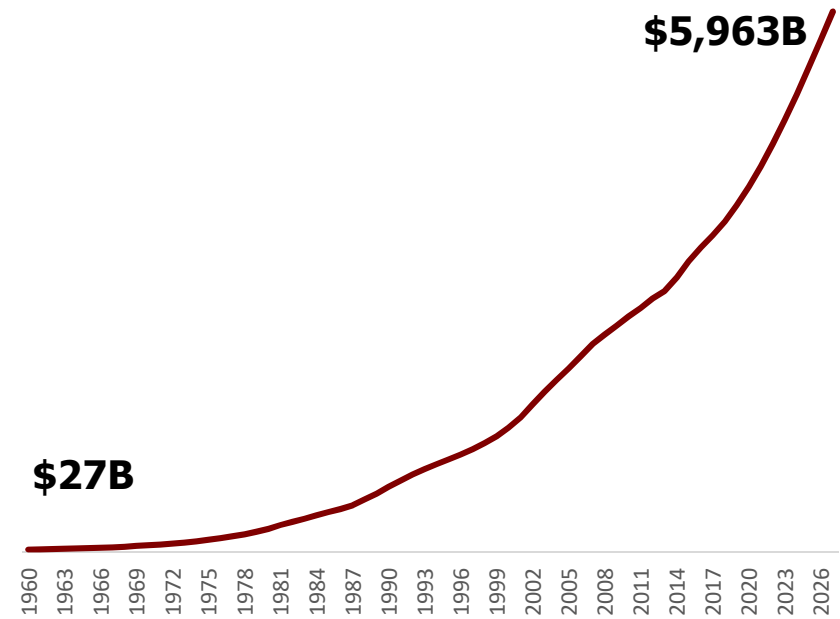
Adoption + Data + Tech → Digital Health Growth

EHR Adoption
U.S. Physician EHR Adoption

87%

21%

2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015
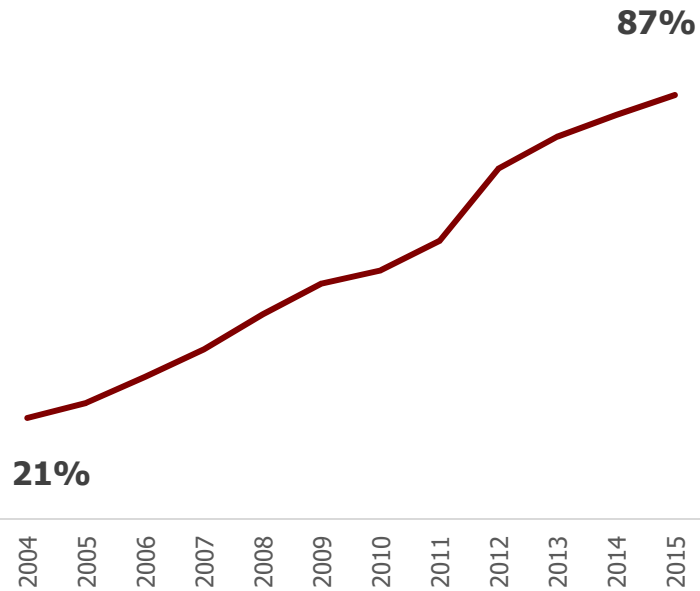
Clinical Trials Growth
No. of Registered Studies

285,416

35,741

2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018
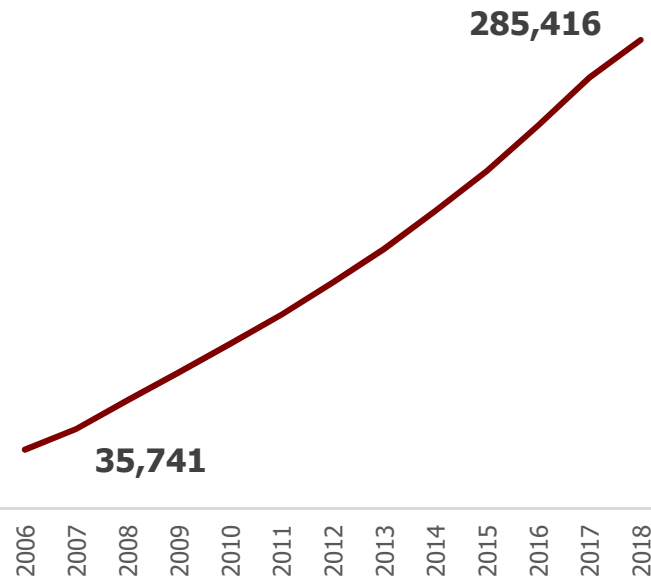
Technological Innovation
Cost to Sequence (p/Genome)

$95,263,072

$1,121

2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016

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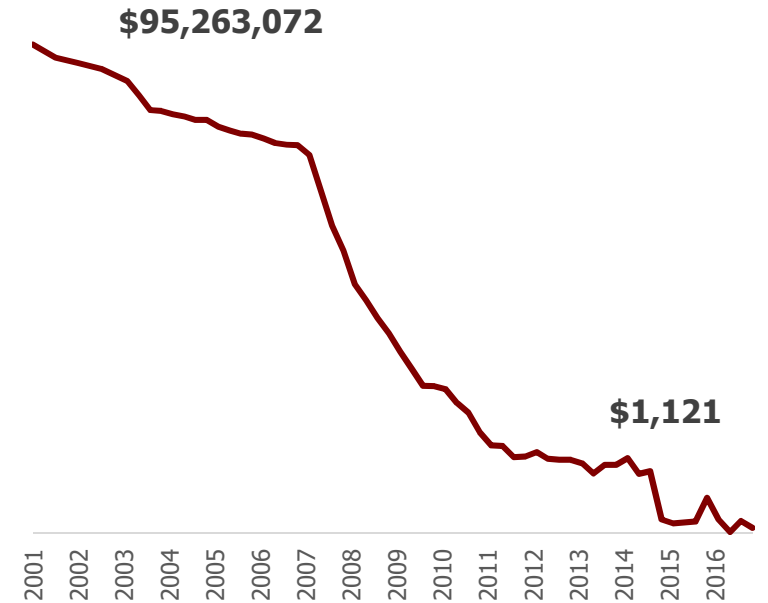
Adoption + Data + Tech → Digital Health Growth

Nebula 30x Whole Genome Sequencing
$299

Nebula 100x Whole Genome Sequencing
$999

Order Summary

30x Whole Genome Sequencing

We decode 100% of your DNA at 30x coverage using next-generation DNA sequencing technology (150bp paired-end reads), reconstruct your genome (using hg38 assembly) and identify all genetic variants. You get full access to all your DNA data including FASTQ, BAM and VCF files (> 100GB) which you can download anytime. **30x Whole Genome Sequencing offers the best value for money and is the best choice for most people.**
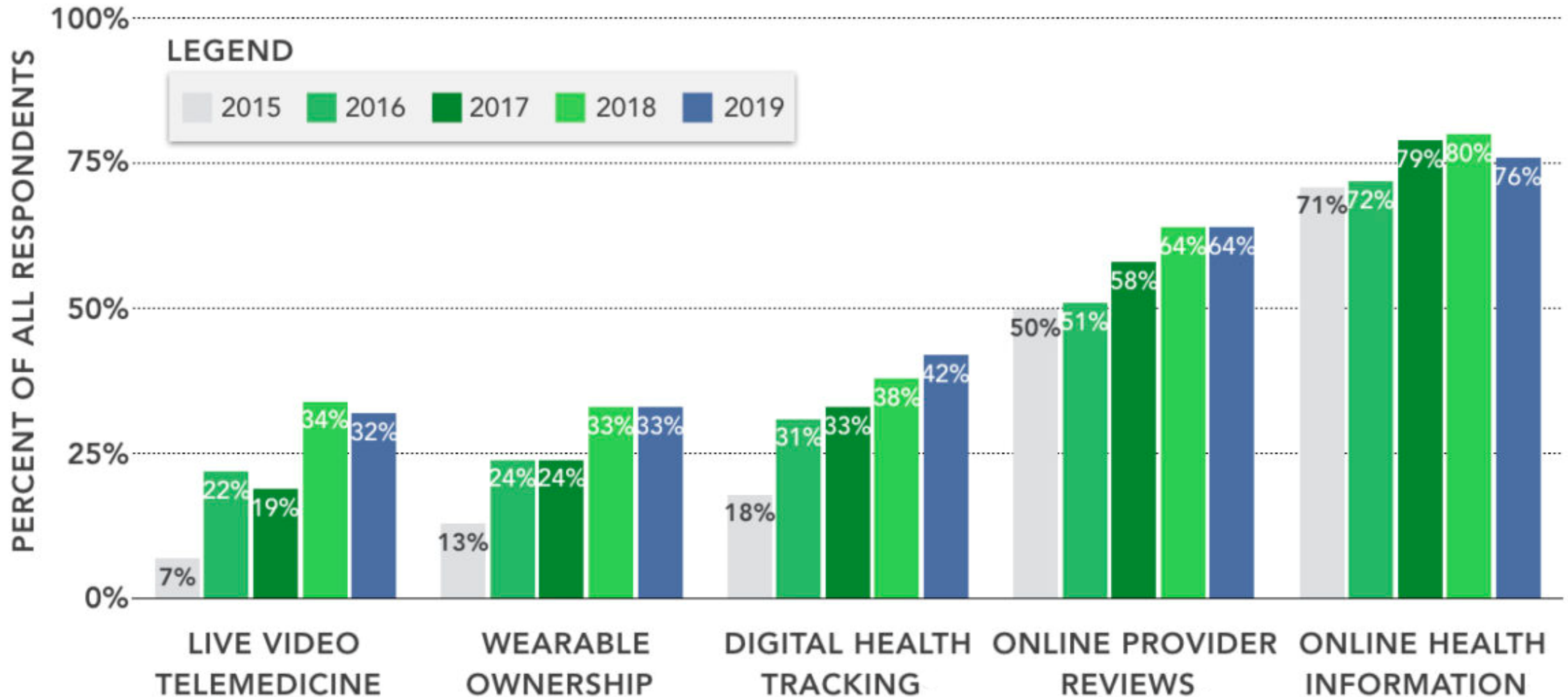
QTY: 1

Was: $1000
Now: $299

Morgan Lewis

Adoption of Digital Health

LEGEND

2015 2016 2017 2018 2019

	LIVE VIDEO TELEMEDICINE	WEARABLE OWNERSHIP	DIGITAL HEALTH TRACKING	ONLINE PROVIDER REVIEWS	ONLINE HEALTH INFORMATION
2015	7%	13%	18%	50%	71%
2016	22%	24%	31%	51%	72%
2017	19%	24%	33%	58%	79%
2018	34%	33%	38%	64%	80%
2019	32%	33%	42%	64%	76%

Sources – 2019 Rock Health Digital Health Consumer Adoption Report

Digital Health AI Funding Reaches New High in 2019

Legend: ■ Value ($M) ● Deal Count

	2018 Q1	2018 Q2	2018 Q3	2018 Q4	2019 Q1	2019 Q2	2019 Q3
Value ($M)	$595.0	$772.0	$749.0	$566.0	$589.0	$926.0	$1,595.0
Deal Count	64	81	63	56	79	79	103

Source – CB Insights Global Healthcare Report Q3 2019
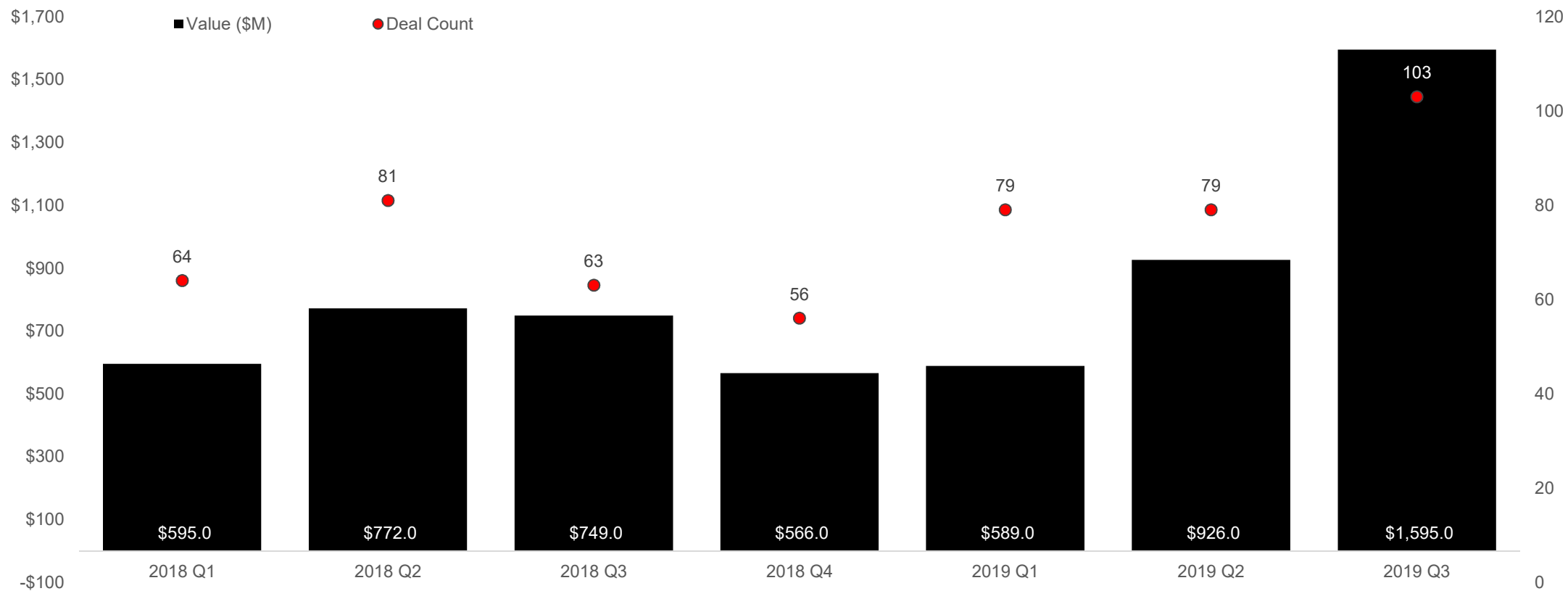
Recent Major Deals

10x GENOMICS®

IPO September '19 (NASDAQ: TXG at $39/share)

Provides next generation sequencing (NGS) kits and tools for analyzing resulting NGS data using artificial intelligence

TEMPUS

Raised $200M in May '19
Uses artificial intelligence to analyze xT data to match cancer patients with targeted therapies

Atomwise

Raised $123M in August '20
Deciphering human disease using an AI-drug discovery portfolio

GRAIL

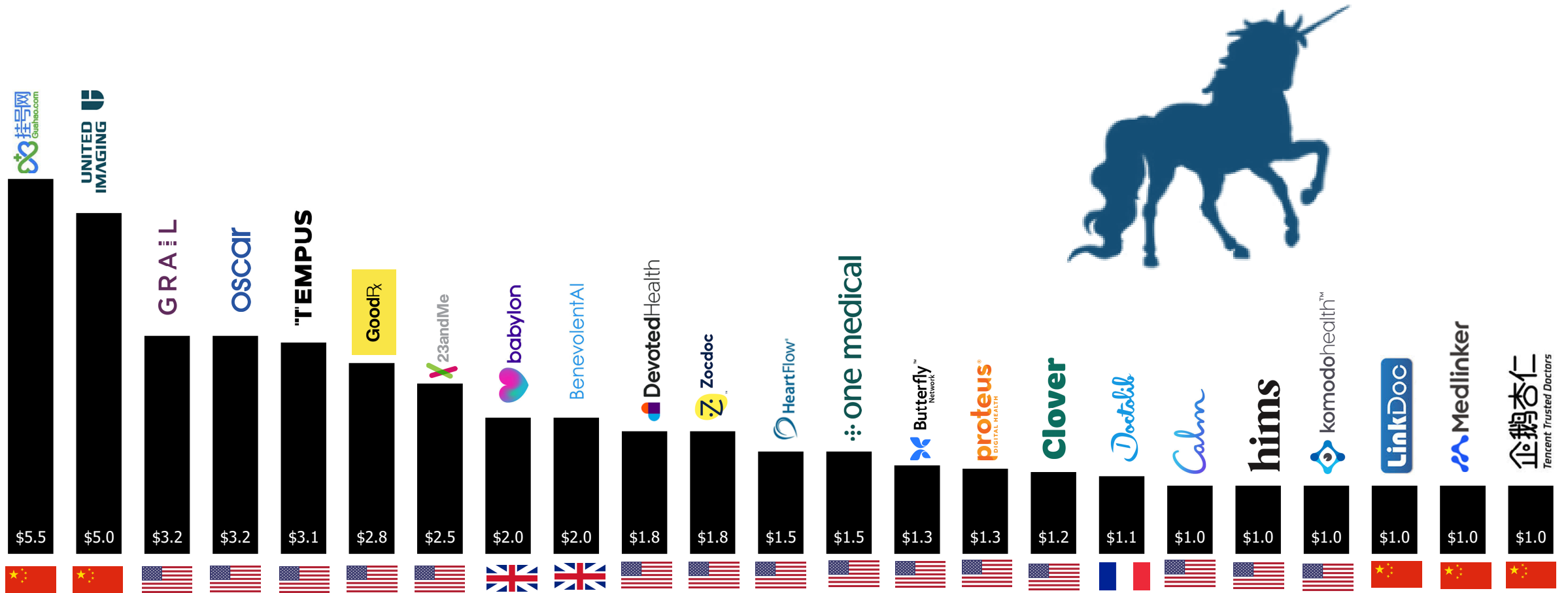**September '20** Earlier stage cancer detection using machine learning, to be acquired by Illumina in 2021 for $8 billion

GENOMIND®

Raised $22M in October '20
Mental health biotechnology and digital service company bringing innovative solutions to personalized mental healthcare and wellness through genetic testing

Morgan Lewis

Digital Health Unicorns

Company	Value	Country
Guahao.com	$5.5	China
United Imaging	$5.0	China
GRAIL	$3.2	USA
Oscar	$3.2	USA
TEMPUS	$3.1	USA
GoodRx	$2.8	USA
23andMe	$2.5	USA
Babylon	$2.0	UK
BenevolentAI	$2.0	UK
Devoted Health	$1.8	USA
Zocdoc	$1.8	USA
HeartFlow	$1.5	USA
one medical	$1.5	USA
Butterfly Network	$1.3	USA
Proteus Digital Health	$1.3	USA
Clover	$1.2	USA
Doctolib	$1.1	France
Calm	$1.0	USA
hims	$1.0	USA
Komodo Health	$1.0	USA
LinkDoc	$1.0	China
Medlinker	$1.0	China
Tencent Trusted Doctors	$1.0	China

Major AI Categories in Healthcare

- **Medical Imaging and Diagnostics**

    – *"The FDA is greenlighting AI as a medical device."*

- **Advanced Healthcare Biometrics**

    – *"Using neural networks, researchers are starting to study and measure atypical risk factors that were previously difficult to quantify."*

- **Clinical Trial Enrollment**

    – *"One of the biggest bottlenecks in clinical trials is enrolling the right pool of patients. Apple might be able to solve the issue."*

- **Drug Discovery**

    – *"With AI biotech startups emerging, traditional pharma companies are looking to AI SaaS startups for innovative solutions to the long drug discovery cycle."*

Source: CBInsights

Morgan Lewis

AI in Healthcare: U.S.

- 90% of U.S. Hospitals and Insurance companies will implement some type of AI System by 2025
  - **Examples of AI Systems**: Medical image analysis, digital image processing, pattern recognition solutions, machine learning platforms, automated patient guidance and engagement solutions

- Increased adoption of AI will depend on:

- Innovators' ability to decrease cost an improve accuracy of technology such as natural language processing, big data and cognitive technologies

- Trust and acceptance of AI tools from healthcare professionals and patients

Morgan Lewis

Footer (if needed)

CASE STUDIES

SYSTEMS AND METHODS FOR IDENTIFYING
THERMODYNAMICALLY RELEVANT POLYMER CONFORMATIONS

EP Patent No.: 2864917
Filed: June 21, 2013
Granted: October 21, 2020

US Appl No.: 14/409,419
Filed: December 18, 2014
Currently Pending

Also filed in the Australia, Brazil, Canada, China, Hong Kong, India, Japan, South Korea, Mexico, Singapore, and South Africa

- Publicly held biotechnology company based in Vancouver, British Columbia, that develops protein therapeutics for the treatment of cancer as well as for autoimmune and inflammatory diseases using artificial intelligence approaches

SYSTEMS AND METHODS FOR IDENTIFYING THERMODYNAMICALLY RELEVANT POLYMER CONFORMATIONS (continued)

Claims directed to evaluating an effect that a mutation has on a protein, where the mutation is made *in silico* to an atomic structure of the protein.

A subset of residues is selected on a randomized or deterministic basis around the mutation, and the rotamers of this subset of residues is altered.

Repeat the step of randomly selecting a subset of residues and altering their rotamers a number of times to obtain several mutated structures of the protein.

Score the several mutated structures and only keep the thermodynamically most stable ones.

For each residue in the region of the mutation, the rotamers represented by the mutated structures of the protein are clustered.

Group the mutated structures into subgroups based on how often they clustered together (on the residue by residue basis).

Calculate the free energy estimate or configurational entropy for each of the subgroups to identify the effect the mutation has on the protein.

Morgan Lewis

SYSTEMS AND METHODS FOR IDENTIFYING THERMODYNAMICALLY RELEVANT POLYMER CONFORMATIONS (continued)

Claims finally rejected under 35 U.S.C. §101 on December 27, 2018

Final rejection was appealed and an appeal brief was filed October 28, 2019

Patent Board Decision was rendered November 23, 2020

SYSTEMS AND METHODS FOR IDENTIFYING THERMODYNAMICALLY RELEVANT POLYMER CONFORMATIONS (continued)

Alice Corp. v. CLS Bank International, 573 U.S. 208 (2014) a computer-implemented, electronic escrow service for facilitating financial transactions held ineligible under 35 U.S.C. § 101 because it covered abstract ideas ineligible for patent protection.

Mayo v. Prometheus, 566 U.S. 66 (2012) Claims directed to a method of giving a drug to a patient, measuring metabolites of that drug, and with a known threshold for efficacy in mind, deciding whether to increase or decrease the dosage of the drug, were not patent-eligible subject matter.

Morgan Lewis

SYSTEMS AND METHODS FOR IDENTIFYING THERMODYNAMICALLY RELEVANT POLYMER CONFORMATIONS (continued)

The Examiner Argued:

Prong One (2A-1, are the claims directed to a judicial exception?):
- Yes. The claims are directed to a judicially recognized exception that is in the form of a mental process and/or a mathematical concept: obtaining three-dimensional coordinates, mutating a residue in the coordinates, altering rotamer side chains, clustering, grouping into subsets, calculating a free energy estimate.

Prong Two (2A-2, If 2A-1 is affirmative, has the judicial exception been integrated into a practical application?)
- No. There are no positive process limitations recited in the claim for actually using the information produced by the abstract idea outside of the computer.

Step 2B (Do the claims as a whole recite additional limitations such that the claims amount to significantly more than the abstract idea?)
- No. The claims do not improve the computer itself. The limitations as an ordered combination do not amount to a claim as a whole that is significantly more than the abstract idea.

Morgan Lewis

SYSTEMS AND METHODS FOR IDENTIFYING THERMODYNAMICALLY RELEVANT POLYMER CONFORMATIONS (continued)

The Patent Board Adopted Applicant's Arguments and Overturned the Examiner:

An invention is patent-eligible if it claims a "new and useful process, machine, manufacture, or composition of matter." *35 U.S.C. § 101*

However, laws of nature, natural phenomena, and abstract ideas are not patentable (e.g., methods of organizing human activity, fundamental economic practices, mathematical concepts, mental processes). *Alice Corp. v. CLS Bank Int'l, 573 U.S. 208, 216 (2014), and subsequent cases that rely on Alice.*

To determine whether a claim falls into an excluded category, use the Supreme Court's two-part framework. *Alice, and Mayo Collaborative Servs. v. Promethius Labs, Inc. 566 U.S. 66, 75-77 (2012).*

- **(Step 2A, Prong 1)** First, determine what the claims are directed to.
- **(Step 2A, Prong 2)** Second, if the claims are directed to an abstract idea, examine the elements of the claims to determine if contains an inventive concept sufficient to transform the claimed abstract idea into a patent-eligible application.
- **(Step 2B, if directed to abstract idea and no transformation)** Are there specific limitations beyond the judicial exception that are not well-understood, routine or conventional?

Morgan Lewis

SYSTEMS AND METHODS FOR IDENTIFYING THERMODYNAMICALLY RELEVANT POLYMER CONFORMATIONS (continued)

The Patent Board Adopted Applicant's Arguments and Overturned the Examiner:

(Step 2A, Prong 1; Determine what the claims are directed to)

- Directed to an abstract idea.

- The first parts of claim 1 are directed to an abstract idea because they can practically be performed in the human mind, and therefore the claim as a whole recites an abstract idea in the category of mental processes (even though the final parts of the claim including altering side chain rotamer conformations, etc. cannot be mentally performed).

- Contrary to the Examiner's assertions, the final step of determining a free energy estimate does not recite a mathematical concept. A claim does not fall into the mathematical concept exception if it is only based on or involves a mathematical idea. October 2019 Revised Patent Subject Matter Eligibility Guidance at 3.

SYSTEMS AND METHODS FOR IDENTIFYING THERMODYNAMICALLY RELEVANT POLYMER CONFORMATIONS (continued)

Claims directed to evaluating an effect that a mutation has on a protein, where the mutation is made *in silico* to an atomic structure of the protein.

A subset of residues is selected on a randomized or deterministic basis around the mutation, and the rotamers of this subset of residues is altered.

Repeat the step of randomly selecting a subset of residues and altering their rotamers a number of times to obtain several mutated structures of the protein.

Score the several mutated structures and only keep the thermodynamically most stable ones.

For each residue in the region of the mutation, the rotamers represented by the mutated structures of the protein are clustered.

Group the mutated structures into subgroups based on how often they clustered together (on the residue by residue basis).

Calculate the free energy estimate or configurational entropy for each of the subgroups to identify the effect the mutation has on the protein.

Morgan Lewis

SYSTEMS AND METHODS FOR IDENTIFYING THERMODYNAMICALLY RELEVANT POLYMER CONFORMATIONS (continued)

The Patent Board Adopted Applicant's Arguments and Overturned the Examiner:

(Step 2A, Prong 2; examine the elements of the claims to determine if contains an inventive concept sufficient to transform the claimed abstract idea into a patent-eligible application)

- In addition to the mental concepts of obtaining a protein structure and mutating it, the claims recite altering side-chain rotamers, generating sets of clusters, grouping the mutating structures, and determining a free energy estimate
- The specification states that these additional steps combine configurational sampling and structural clustering in novel ways and determines free energies close to the thermodynamic ground state.
- Thus, the claimed method, according to the specification, improves known methods of modeling the effect of mutations on the stability of proteins.
- Thus, the claimed method represents an improvement in the technical field of protein engineering and rational protein design.
- A physical step, such as actually making a mutant protein, is not required in order for the claimed method to constitute a practical application of the recited mental process. *McRO, Inc. v. Bandai Namco Games Amer. Inc.*, 837 F. 3d 1299, 1315 (Fed. Cir. 2016).
- One practical application of the recited claim is to rule out the manufacture of certain mutations that the modeling determines is not stable.

Morgan Lewis

SYSTEMS AND METHODS FOR OPTIMIZING MANAGEMENT OF PATIENTS WITH MEDICAL DEVICES AND MONITORING COMPLIANCE

- Filed June 1, 2018

- Claims drawn to health care provider monitor compliance
  - First process:
    - Obtain data elements, each from an implanted medical device in a different subject
    - Determine condition of each of the medical device from the data elements
    - Record time-stamped medical codes based on the data elements
  - Second process:
    - For each **epoch in a plurality of epochs**, determine overall compliance for the plurality of subjects by checking to see if a code has been recorded for each subject
  - Third process:
    - Responsive to a compliance request, provide compliance information, provide suggested treatment options, provide list of subjects that appear not to be receiving required standard of care

- Rejected under 35 U.S.C. §101 on February 14, 2019

Morgan Lewis

SYSTEMS AND METHODS FOR OPTIMIZING MANAGEMENT OF PATIENTS WITH MEDICAL DEVICES AND MONITORING COMPLIANCE (continued)

In the February 14, 2019 Office Action, the Examiner Argued:

Prong One (2A-1, are the claims directed to a judicial exception?):
- Yes. The claims are directed to mathematical concepts, mental processes and/or methods of organizing human activity (e.g., "determining whether the first medical codes has been recorded in the medical record" can be a mental process because it can be performed in the human mind).

Prong Two (2A-2, If 2A-1 is affirmative, has the judicial exception been integrated into a practical application?)
- No. The additional claim elements add insignificant extra-solution activity to the abstract ideal They merely link the use of the judicial exception to a particular technological environment or field of use.

Step 2B (Do the claims as a whole recite additional limitations such that the claims amount to significantly more than the abstract idea?)
- No. The additional claim elements amount to no more than recitation of a generic computer or functions that are well understood or routine.

Morgan Lewis

SYSTEMS AND METHODS FOR OPTIMIZING MANAGEMENT OF PATIENTS WITH MEDICAL DEVICES AND MONITORING COMPLIANCE (continued)

Applicant's June 11, 2019 Reply to the February 14, 2019 Office Action

- Amended the claims in view of USPTO's Analysis in June 2018 USPTO Memorandum "Recent Subject Matter Eligibility Decision: *Vanda Pharamaceuticals Inc. v. West-Ward Pharmaceuticals"* (Vanda Memo) to require providing a list of subjects and treatment options based on the compliance information thereby administrating a treatment for the one or more subjects based on their health conditions.

- Vanda Memo – Unlike the claim at issue in *Mayo*, the claims here require a treating doctor to administer iloperidone. As a result, the Federal Circuit held the claims in Vanda patent eligible under the first step of the Alice/Mayo framework (step 2A) because the claims are directed to a method of using iloperidone to treat schizophrenia rather than being directed to a judicial exception.

SYSTEMS AND METHODS FOR OPTIMIZING MANAGEMENT OF PATIENTS WITH MEDICAL DEVICES AND MONITORING COMPLIANCE (continued)

June 25, 2019 Final Rejection (35 U.S.C. §101 rejection maintained)
- Applicant's "providing a list of subjects and treatment options based on the compliance information thereby administrating a treatment for the one or more subjects" do not amount to an actual administration of a therapy after data analysis.
- Claims are not solving a technical problem but rather are attempting to solve problems rooted in a business process (managing compliance and treatment of subjects).

September 24, 2019 Response
- Removed treatment option
- Made the device more specific "cardiac implantable electronic device"
- **Argued under Step 2A, Prong Two (2A-2, has the judicial exception been integrated into a practical application?) that it improves the field of cardiac health monitoring.**
- Applicant's argued that the claimed invention uses an ordered combination of specific rules to determine the compliance of a plurality of cardiac implantable electronic medical devices and to provide suggested treatment options for subjects based on the compliance information.

Morgan Lewis

SYSTEMS AND METHODS FOR OPTIMIZING MANAGEMENT OF PATIENTS WITH MEDICAL DEVICES AND MONITORING COMPLIANCE (continued)

October 21, 2019 Rejection
- The 35 U.S.C. §101 rejection was maintained
- The claims recite several limitations that can be reasonably performed in the human mind and also recite methods of organizing human activity.

February 19, 2020 Response

(i) measuring ~~obtaining~~ the respective data element in the plurality of data elements from a wireless signal transmitted by the corresponding cardiac implantable electronic medical device ~~connected to~~ implanted within a corresponding subject in a first plurality of subjects, wherein the respective data element comprises (a) a medical device identifier and (b) a condition of the cardiac implantable electronic medical device or a medical device measurement.

- February 19, 2020 Examiner interview, the Examiner indicated that the proposed claim amendment would be sufficient to establish claim is not directed to an abstract idea because the wireless signal cannot be received by the human mind.

Morgan Lewis

SYSTEMS AND METHODS FOR OPTIMIZING MANAGEMENT OF PATIENTS WITH MEDICAL DEVICES AND MONITORING COMPLIANCE (continued)

March 5, 2020 Final Rejection (35 U.S.C. §101 rejection maintained)
- Applicant's "providing a list of subjects and treatment options based on the compliance information thereby administrating a treatment for the one or more subjects" can be a mental process because this limitation can be performed in the human mind and is a method of organizing human activity.
- The active of wirelessly measuring in merely extra-solution activity used t provide a list of subjects and suggested treatments.

June 20, 2020 Interview
- Examiners: Applicant needs to amend the claims to emphasize how the data analysis is used to alter the operation of the implanted device or the computer itself
- Applicants: Proposed to amend claims to specify that the claimed data analysis is used to adaptively change the length of the epoch period (poor compliance, shorter epoch).

September 3, 2020 Case allowed

Morgan Lewis

SYSTEMS AND METHODS FOR FACILITATING PATIENT SELF-SELECTION

Filed January 22, 2018

Claims directed to a method of lowering cholesterol with an over the counter statin:
- Subject takes a survey and is asked sex, age, total cholesterol level, pregnant, etc.
- Survey results run against a first set of filters
- If subject fails any filter in the first set of filters (e.g., pregnancy) than subject is not authorized
- Survey results run against a second set of filters
- If subject fails any filter in the second set of filters (e.g., total cholesterol) than subject is authorized provided that they acknowledge that they have discussed the risk factor with their physician
- Includes final step of proceeding with fulfilment process if the first and second set of filters have been satisfied

May 30, 2018 Office Action
- Claims rejected under 35 U.S.C. §101

SYSTEMS AND METHODS FOR FACILITATING PATIENT SELF-SELECTION (CONT.)

In the May 30, 2018 Office Action, the Examiner Argued:

Prong One (2A-1, are the claims directed to a judicial exception?):
- Yes. The claims are directed to obtaining an information set from a human, running the information set against a plurality of filters. The identified abstract idea is analogized to collection information, analyzing it, and displaying certain results.

Prong Two (2A-2, If 2A-1 is affirmative, has the judicial exception been integrated into a practical application?)
- No. The additional verbiage and limitations recited in the claims all describe the abstract idea or do not amount to significantly more.

Step 2B (Do the claims as a whole recite additional limitations such that the claims amount to significantly more than the abstract idea?)
- No. Essentially, the Applicant is attempting to claim the mental process a physician would perform when deciding whether a statin should be provide to a patient.

Applicant's November 30, 2018 Reply to the May 30, 2018 Office Action
- Amended the claims in view of USPTO's Analysis in June 2018 USPTO Memorandum "Recent Subject Matter Eligibility Decision: *Vanda Pharamaceuticals Inc. v. West-Ward Pharmaceuticals" (Vanda Memo)* to require "administering, upon authorization of the provision (of the statin)"

February 6, 2019 Notice of Allowance
- With respect to 35 U.S.C. §101 "The claims recite a method for lowering cholesterol in a human with an over the counter drug by comparing patient survey information to statin safety information and obtaining confirmation of receiving and reading drug information and subsequently administering the statin pharmaceutical composition to a human."

- Therefore, Prong Two (2A-2, If 2A-1 is affirmative, has the judicial exception been integrated into a practical application?), the claims include an additional element that applies or used a judicial exception to effect a particular treatment and so the claims are not "directed to" the judicial exception

Morgan Lewis

NOVO NORDISK European Patent No. 3479267

REGIMEN ADHERENCE MEASURE FOR INSULIN TREATMENT BASED ON GLUCOSE MEASUREMENTS AND INSULIN PEN DATA

Filed: June 22, 2017

Claims directed to a method of adjusting a standing insulin regimen for a subject:
- Obtain a first dataset comprising autonomous time-stamped glucose measurements
- Obtain a second dataset from an insulin pen used to apply the insulin, that included timestamped injection events (including amount injected)
- Identifying fasting events using the first dataset
- Characterizing each fasting event as basal regimen adherent (when the second data set includes one or more records that establish, on a temporal and quantitative basis, adherence with the standing basal insulin dosage regimen during the respective fasting event) or not adherent
- adjusting amounts of insulin medicament dosage in the basal insulin medicament dosage regimen for the subject based upon glucose measurements in the first data set that are contemporaneous with the fasting events that are deemed basal regimen adherent and by excluding glucose measurements in the first data set that are contemporaneous with fasting events that are deemed basal regimen nonadherent

Morgan Lewis

International Search Report – the problems to be solved by the present invention may be regarded as:

- How to systematically allow tracking and recording of adherence to a basal insulin regimen based on automatically generated event-dependent reference points in time

- How to flexibly adjust regimen dosage base on a correlation between medication injection events and metabolic (fasting) events of a patient

- How to adjust a standing regimen dosage by additionally discarding/excluding non-compliant adherence data from consideration

Morgan Lewis
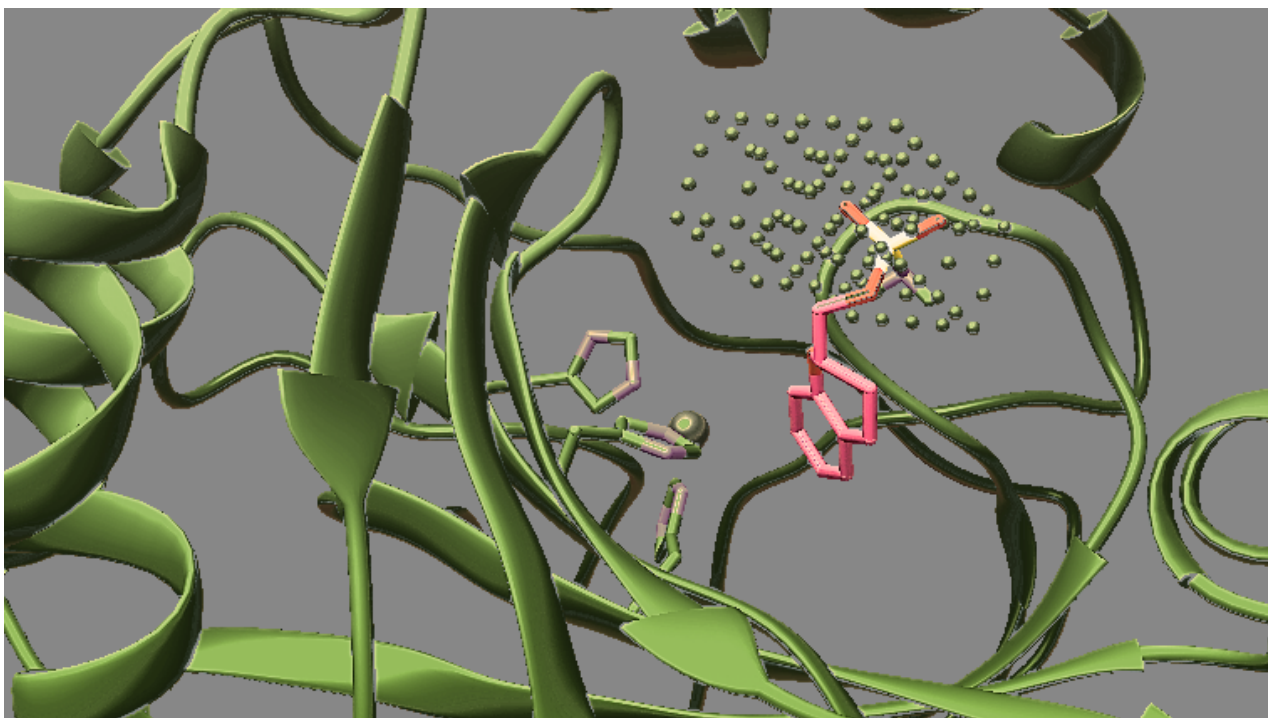
- Founded in 2012
- Based in San Francisco, CA
- ~50 employees
- Annual revenue: USD $2M
- Patented use of deep neural networks for structure-based drug design
- CEO: Abraham Heifets, Ph.D.
  - Formerly at the University of Toronto
  - Created SCRIPDB database and LigAlign protein analysis tool
- 17 investors (ex: B Capital Group, Monsanto Growth Ventures, Y Combinator, Khosla Ventures, DFJ)
- 200 academic collaborations (e.g., Dana Farber Cancer Institute, Tulane, and Duke University)

Morgan Lewis

(12) **United States Patent**
Heifets et al.

(10) Patent No.: **US 10,002,312 B2**
(45) Date of Patent: *Jun. 19, 2018
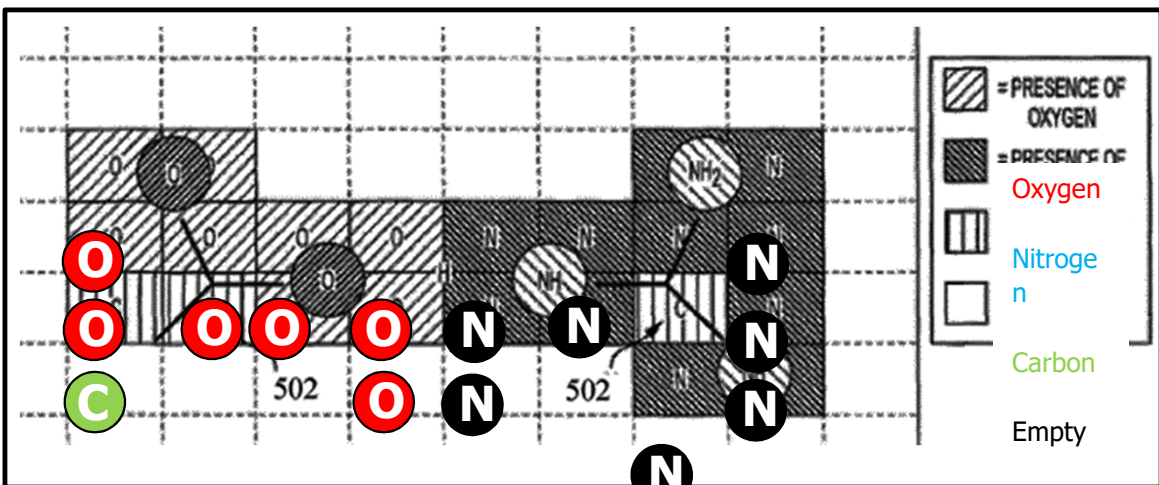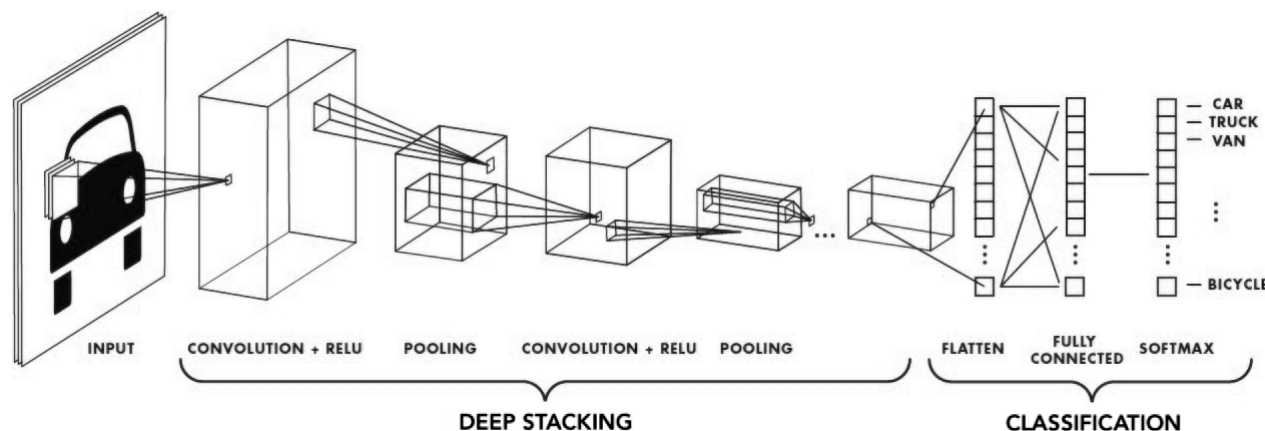
(54) **SYSTEMS AND METHODS FOR APPLYING A CONVOLUTIONAL NETWORK TO SPATIAL DATA**

(71) Applicant: **Atomwise Inc.**, San Francisco, CA (US)

(72) Inventors: **Abraham Samuel Heifets**, San Francisco, CA (US); **Izhar Wallach**, Tel-Mond (IL); **Michael Dzamba**, San Francisco, CA (US)

(73) Assignee: **Atomwise Inc.**, San Francisco, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 186 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **15/187,018**

(22) Filed: **Jun. 20, 2016**

(65) **Prior Publication Data**
US 2016/0300127 A1   Oct. 13, 2016

Related U.S. Application Data

(63) Continuation of application No. 15/050,983, filed on Feb. 23, 2016, now Pat. No. 9,373,059, which is a (Continued)

(51) **Int. Cl.**
G06K 9/62   (2006.01)
G06K 9/66   (2006.01)
(Continued)

(52) **U.S. Cl.**
CPC **G06K 9/66** (2013.01); **G06F 19/16** (2013.01); **G06F 19/18** (2013.01); **G06F 19/24** (2013.01);
(Continued)

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

(56) **References Cited**

U.S. PATENT DOCUMENTS

9,190,053 B2   11/2015 Penn et al.
9,202,144 B2   12/2015 Wang et al.
(Continued)

FOREIGN PATENT DOCUMENTS

WO   WO 2015/168774 A1   11/2015

OTHER PUBLICATIONS

Chae, Myong-Ho, et al. "Predicting protein complex geometries with a neural network." Proteins: Structure, Function, and Bioinformatics 78.4 (2010): 1026-1039. 14 pages.*
(Continued)

Primary Examiner — Ryan P Potts
(74) *Attorney, Agent, or Firm* — Morgan, Lewis & Bockius LLP

(57) **ABSTRACT**

Systems and methods for test object classification are provided in which the test object is docked with a target object in a plurality of different poses to form voxel maps. The maps are vectorized and fed into a convolutional neural network comprising an input layer, a plurality of individually weighted convolutional layers, and an output scorer. The convolutional layers include initial and final layers. Responsive to vectorized input, the input layer feeds values into the initial convolutional layer. Each respective convolutional layer, other than the final convolutional layer, feeds intermediate values as a function of the weights and input values of the respective layer into another of the convolutional layers. The final convolutional layer feeds values into one or more fully connected layers as a function of the final layer weights and input values. The one or more full
(Continued)

1. A computer system for characterization of a test object using spatial data, the computer system comprising:

at least one processor: and
memory addressable by the at least one processor, the memory storing at least one program for execution by the at least one processor, the at least program comprising instructions for:
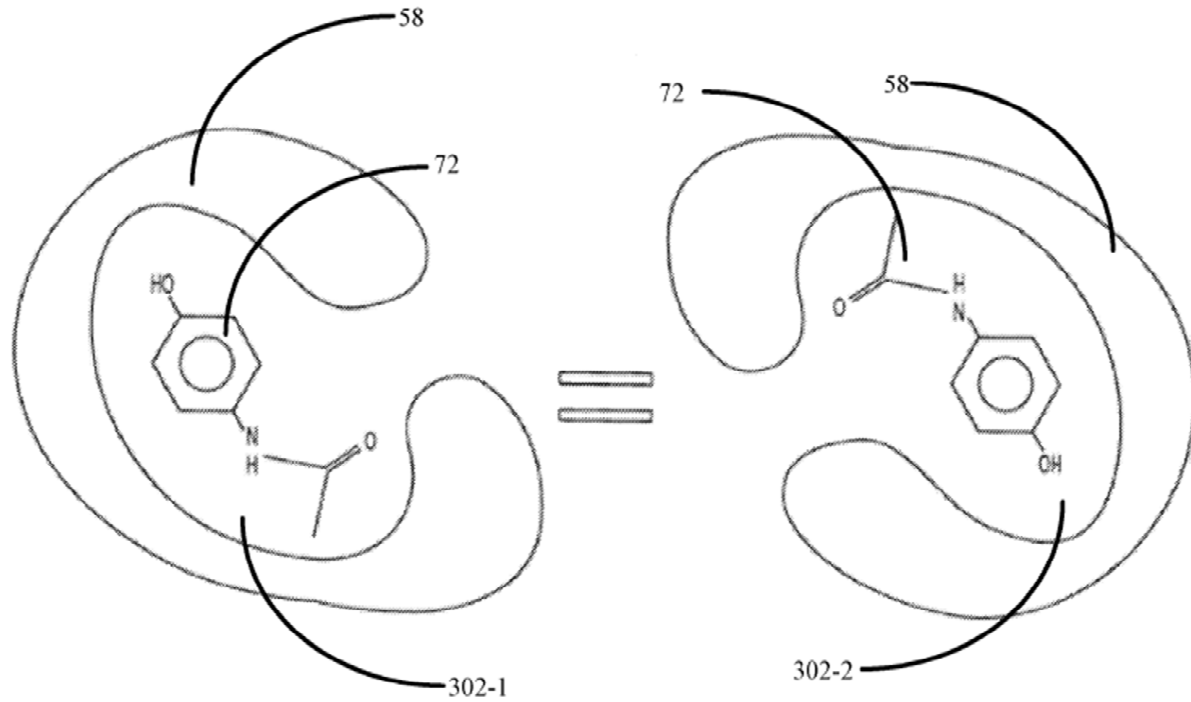
[...]

(D) inputting [a] plurality of vectors to a network architecture that includes an input layer for sequentially receiving the plurality of vectors, a plurality of convolutional layers, and a scorer
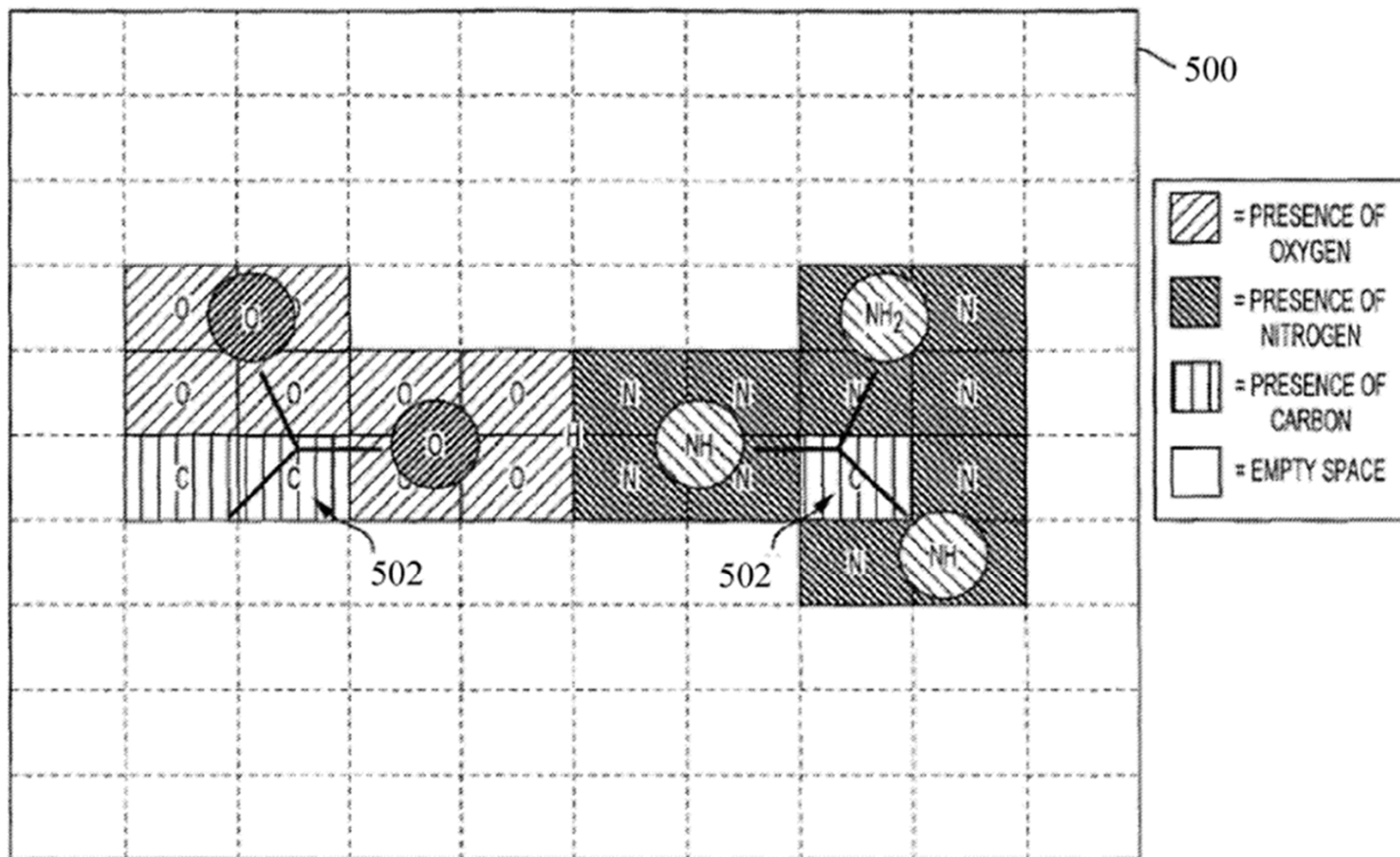
[...]

(F) using the plurality of scores to characterize [a] test object

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- Sample a test compound after it has been docked to the macromolecular target by encoding, as a plurality of vectors, a three-dimensional matrix representation of the test compound docked to the macromolecular target.

10,002,312 - continued

- Feed the plurality of vectors, which collectively represent the test compound after it has been docked to the macromolecular target, into the same form of convolutional neural network that classically has been trained to recognize objects, such as cars in images, or perform facial recognition.
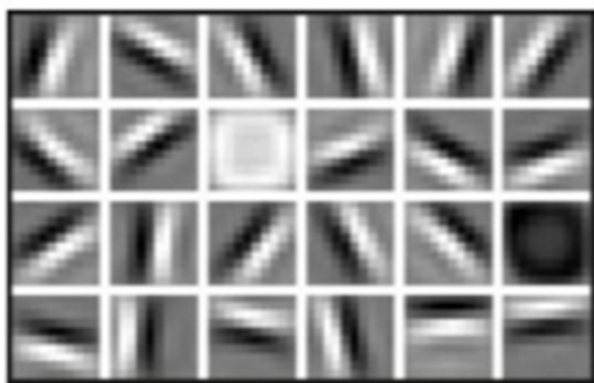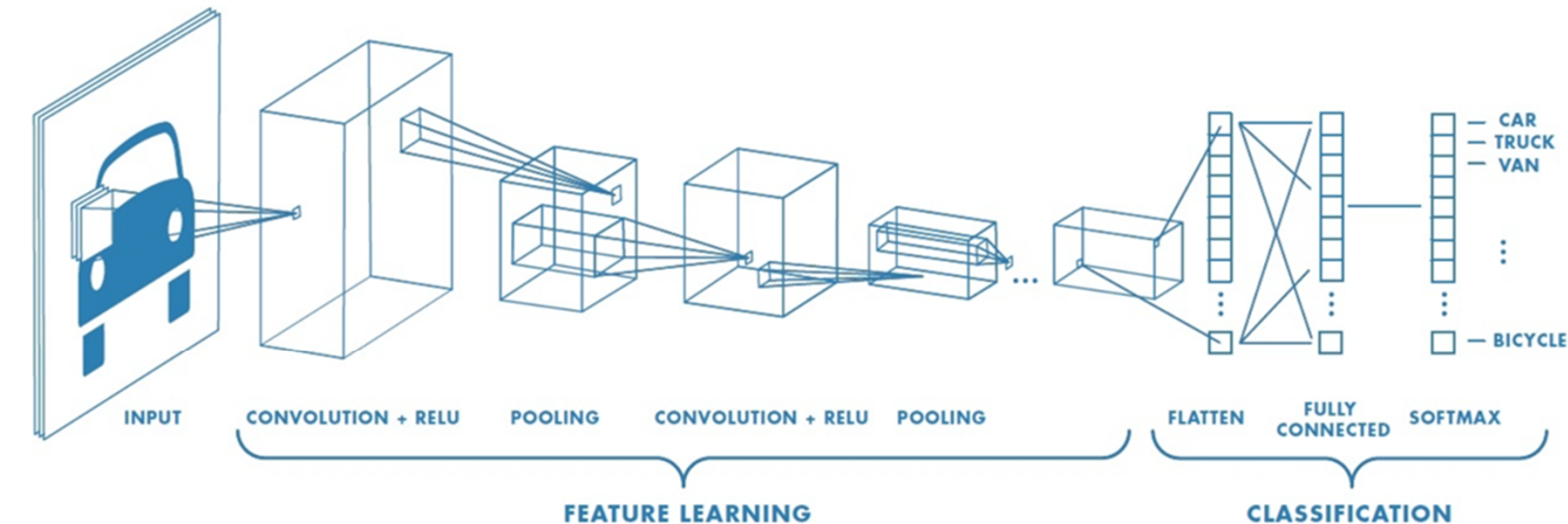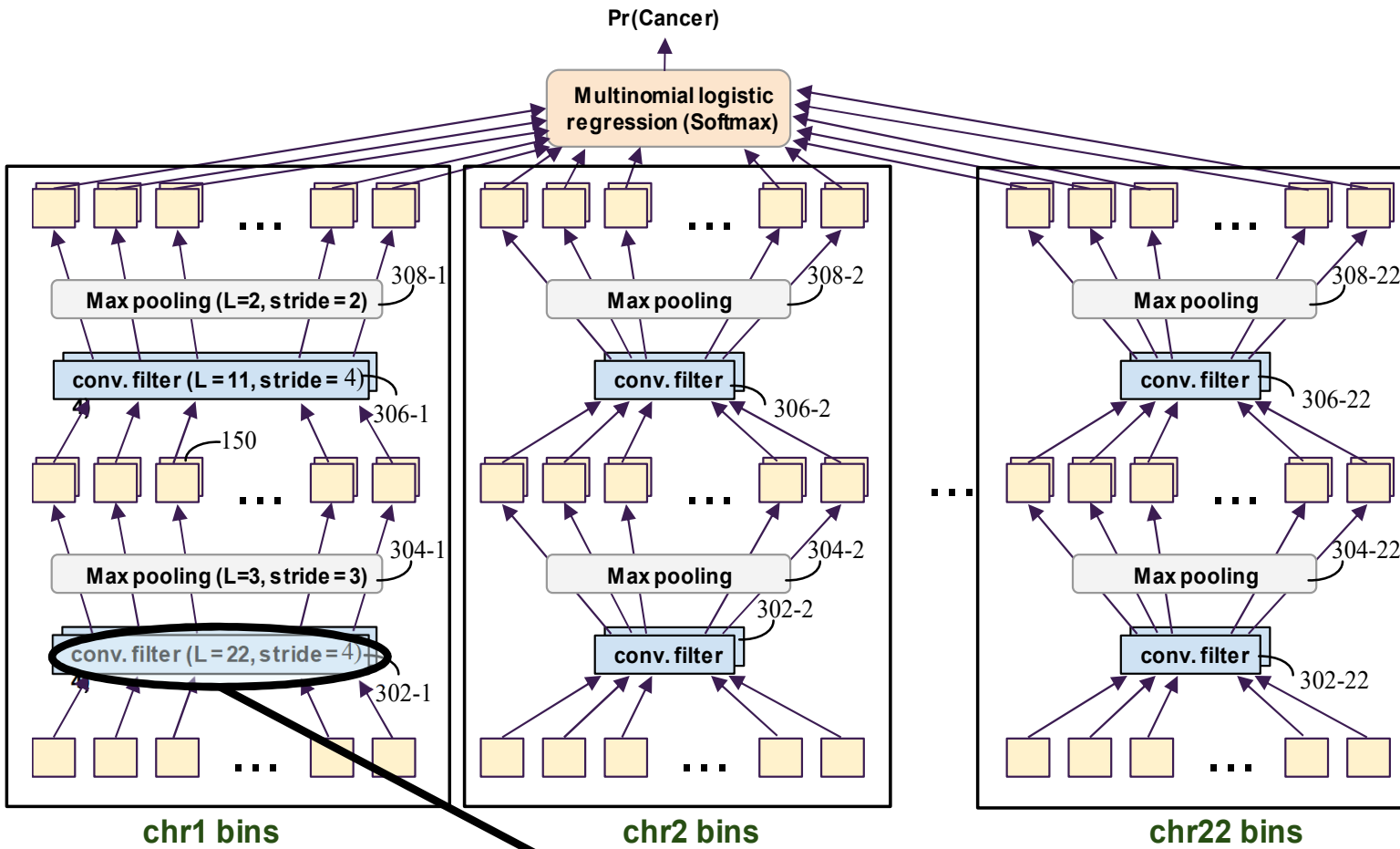

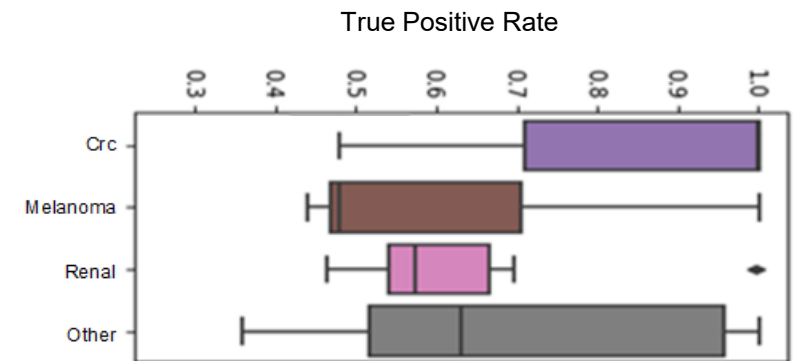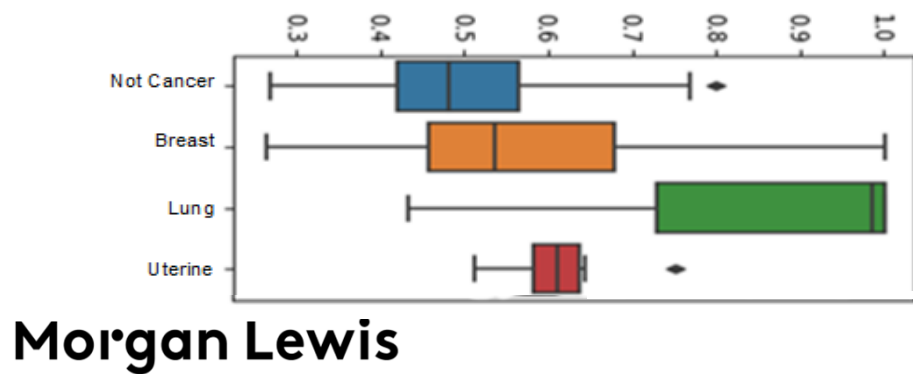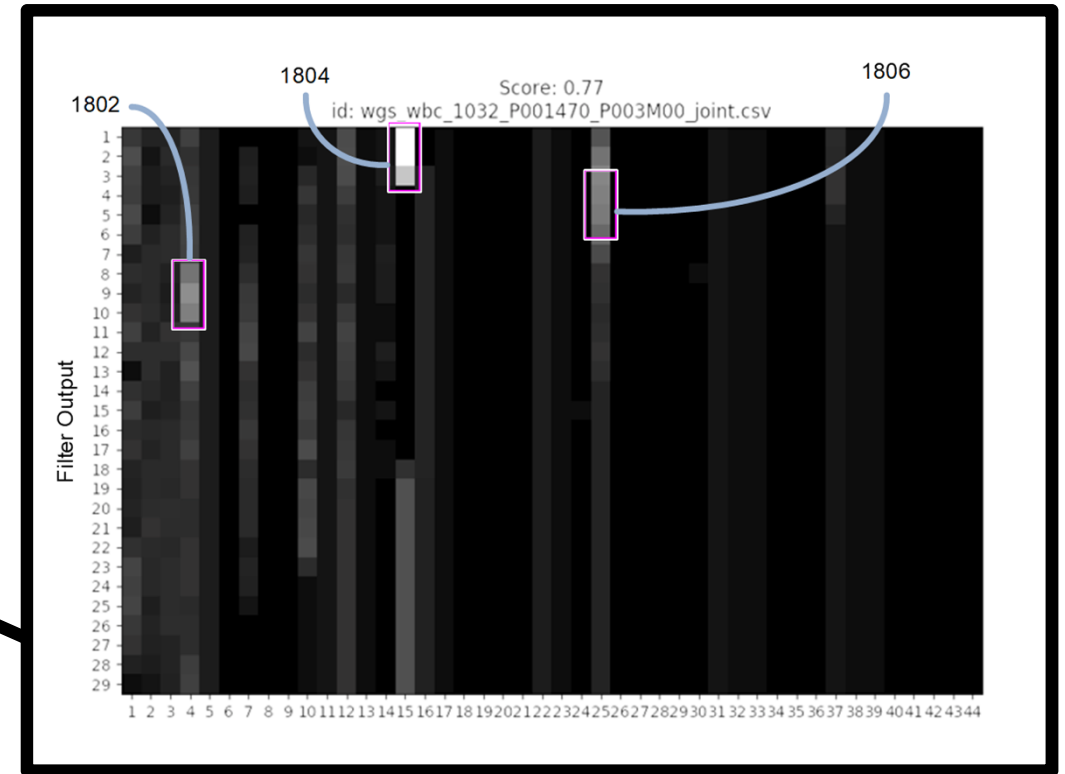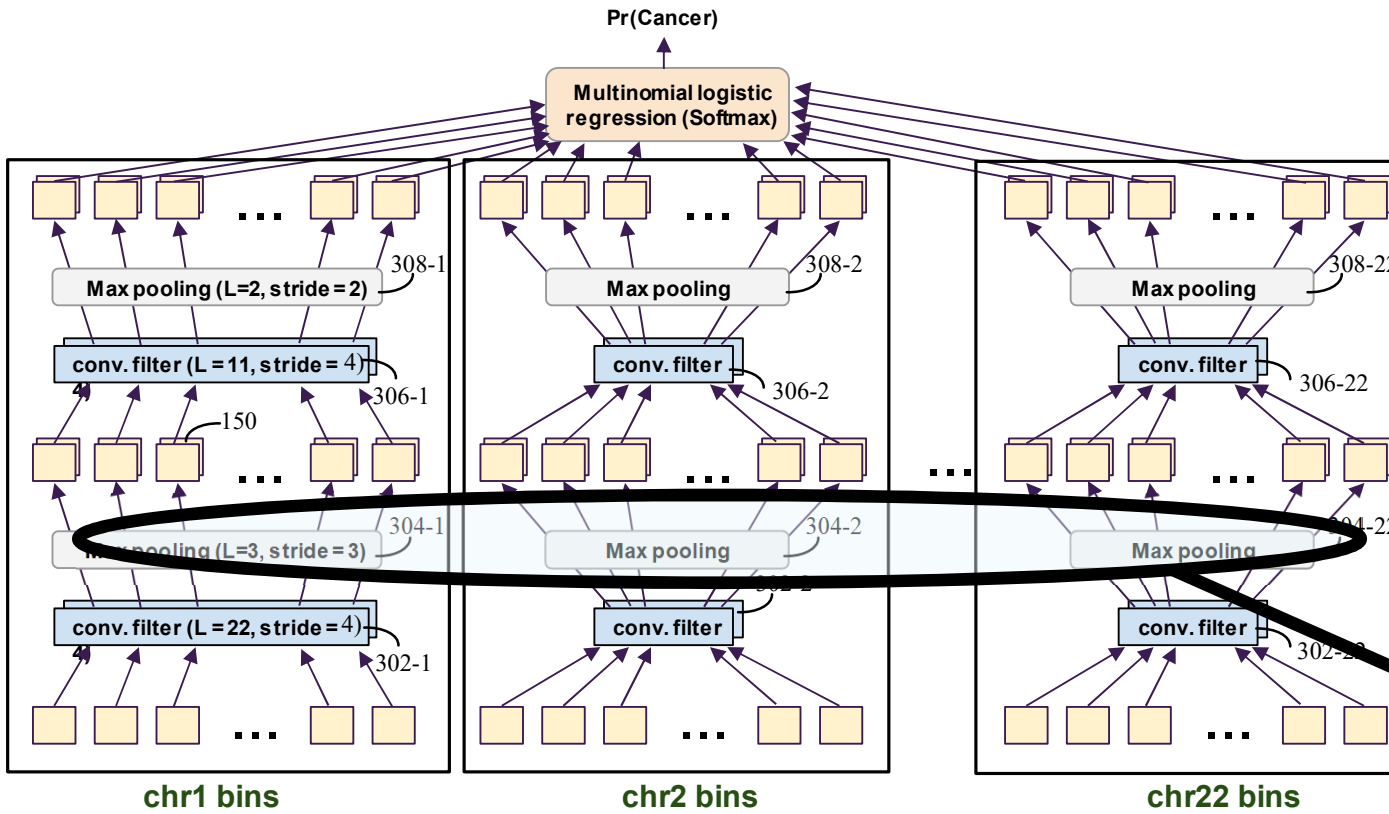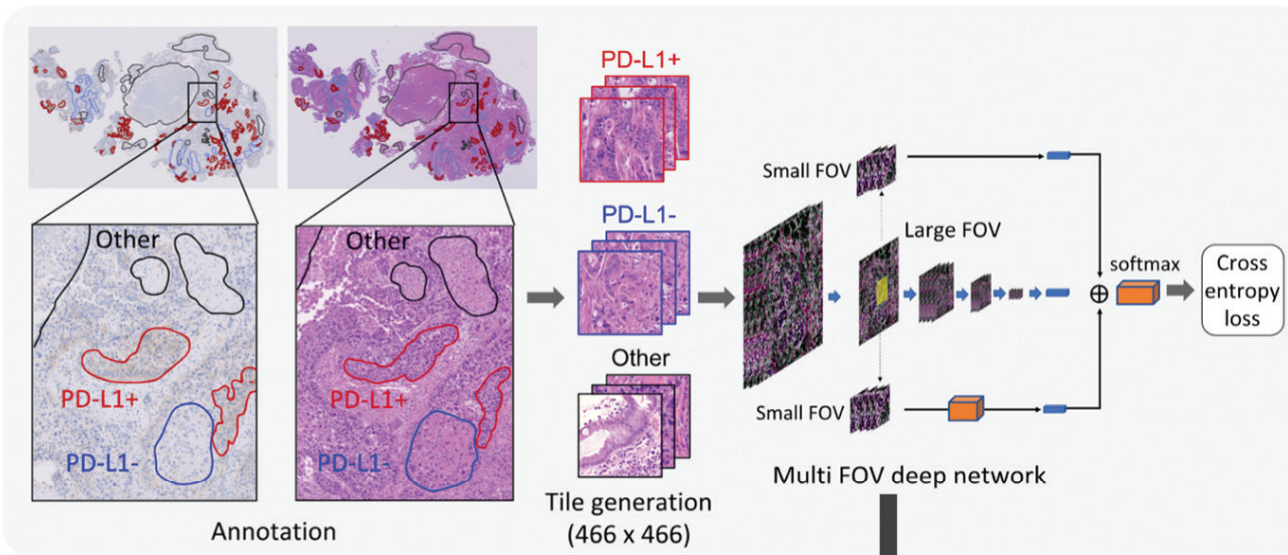First Layer Representation   Second Layer Representation   Third Layer Representation

- Founded in 2015
- Based in Palo Alto, CA
- ~500 employees
- Valuation: USD $8B
- Privately held spin out of Illumina
- Focus on use of early cancer detection and tissue of origin determination using patent pending artificial intelligence analysis of cell-free nucleic acid from liquid biopsies
- CEO: Hans Bishop
  - 30+ years experience in biotech
  - Executive Chair of Sana Board and Director at Celgene and Agilent Technologies
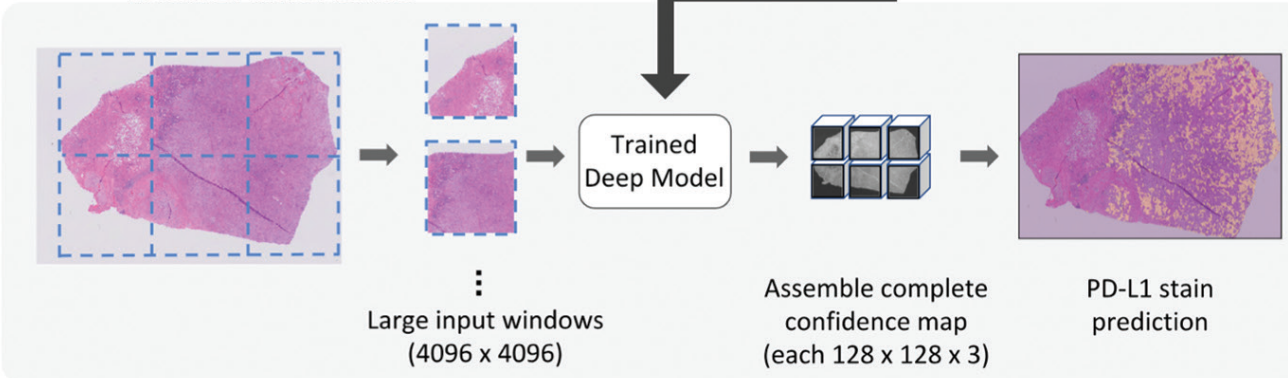 - Former CEO of Juno Therapeutics

Pr(Cancer)

Multinomial logistic regression (Softmax)

Max pooling (L=2, stride=2) — 308-1
Max pooling — 308-2
Max pooling — 308-22

conv. filter (L=11, stride=4) — 306-1
conv. filter — 306-2
conv. filter — 306-22

150

Max pooling (L=3, stride=3) — 304-1
Max pooling — 304-2
Max pooling — 304-22

conv. filter (L=22, stride=4) — 302-1
conv. filter — 302-2
conv. filter — 302-22

chr1 bins   **chr2 bins**   **chr22 bins**

Score: 0.77
id: wgs_wbc_1032_P001470_P003M00_joint.csv

1802   1804   1806

Filter Output

True Positive Rate

Not Cancer
Breast
Lung
Uterine

Crc
Melanoma
Renal
Other

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- Founded in 2015
- Based in Chicago, IL
- ~900 employees
- Valuation: USD $3B
- Developed xT platform that includes (i) analytics of patient's structured clinical data, (ii) molecular data from tumor/normal matched DNA sequencing, (iii) whole-transcriptome RNA sequencing and (iv) immunological biomarker measurements
- Used artificial intelligence to analyze xT data to match cancer patients with targeted therapies
- CEO: Eric Lefkofsky
  - American billionaire businessman
  - Founder of Tempus and Groupon
  - Managing director of Lightbank
- Has raised USD $520 million in venture capital (*e.g.*, Franklin Templeton, New Enterprise Associates)

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(54) **SEQUENCE ASSEMBLY AND CONSENSUS SEQUENCE DETERMINATION**

(75) Inventor: **Mark Chaisson**, San Francisco, CA (US)

(73) Assignee: **Pacific Biosciences of California, Inc.**, Menlo Park, CA (US)

Primary Examiner — John S Brusca
(74) Attorney, Agent, or Firm — Morgan, Lewis & Bockius LLP

ALGORITHMS

PRODUCTS
PACBIO RS II ›
Workflow ›
CONSUMABLES ›
SMRT Cells ›
Reagents ›
Disposables ›
SOFTWARE ›
Instrument ›
Analysis ›
Algorithms
SMRT TECHNOLOGY ›
SMRT Sequencing
Advantage ›

PacBio offers a full sui... ...ata. Bundled together in the SMRT ... of applications including:

- De novo assembly
- Genome finishing and scaffolding
- DNA base modification detection
- Bacterial methylome and motif analysis
- Minor variant detection
- Compound mutations and phasing of distant SNPs
- Highly accurate consensus calling with variant detection

Download the **PacBio Software and Analysis Brochure**.

Here are some of the software algorithms included in SMRT Analysis.

HGAP
The Hierarchical Genome Assembly Process (HGAP) generates high quality (>99.999% accurate) de novo assemblies using a single PacBio library prep. HGAP consists of pre-assembly, de novo assembly with Celera Assembler, and assembly polishing with Quiver.

BLASR
BLASR (Basic Local Alignment with Successive Refinement) rapidly maps reads to genomes by finding the highest scoring local alignment or set of local alignments between the read and the genome. Optimized for PacBio's extraordinarily long reads and taking advantage of rich quality values, BLASR maps reads rapidly with high accuracy.

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- Founded in 2004
- Based in Menlo Park, California
- ~440 employees
- Applies patented artificial intelligence techniques to analyzing sequence read data
- Presently in contract to be acquired by Illumina for $1.2B
- 2018 Revenue: $78.6M
- CEO: Michael Hunkapiller, Ph.D.
  - 30 year career at Applied Biosystems (acquired by Thermo Fisher Scientific Inc.)

What is claimed is:

1. A method of aligning a sequence read r to a reference sequence g using a minimum match length of k nucleotides, comprising:

a) obtaining the sequence read r of a target nucleic acid by performing a single molecule sequencing assay, wherein the sequence read r has an insertion-deletion error rate of over 5%;

- Founded in 2012
- Based in Pleasanton, California
- ~425 employees
- IPO September 2019 (NASDAQ: TXG at $39/share)
- Now at $51-$56/share (market cap $5B)
- Expected 2019 revenue: $240M
- Provides next generation sequencing (NGS) kits and tools for analyzing resulting NGS data using artificial intelligence
- CEO: Serge Saxonov
  - Founding architect and director of R&D at 23andMe

(12) **United States Patent**
Wong et al.

(10) **Patent No.:** US 10,347,365 B2
(45) **Date of Patent:** Jul. 9, 2019

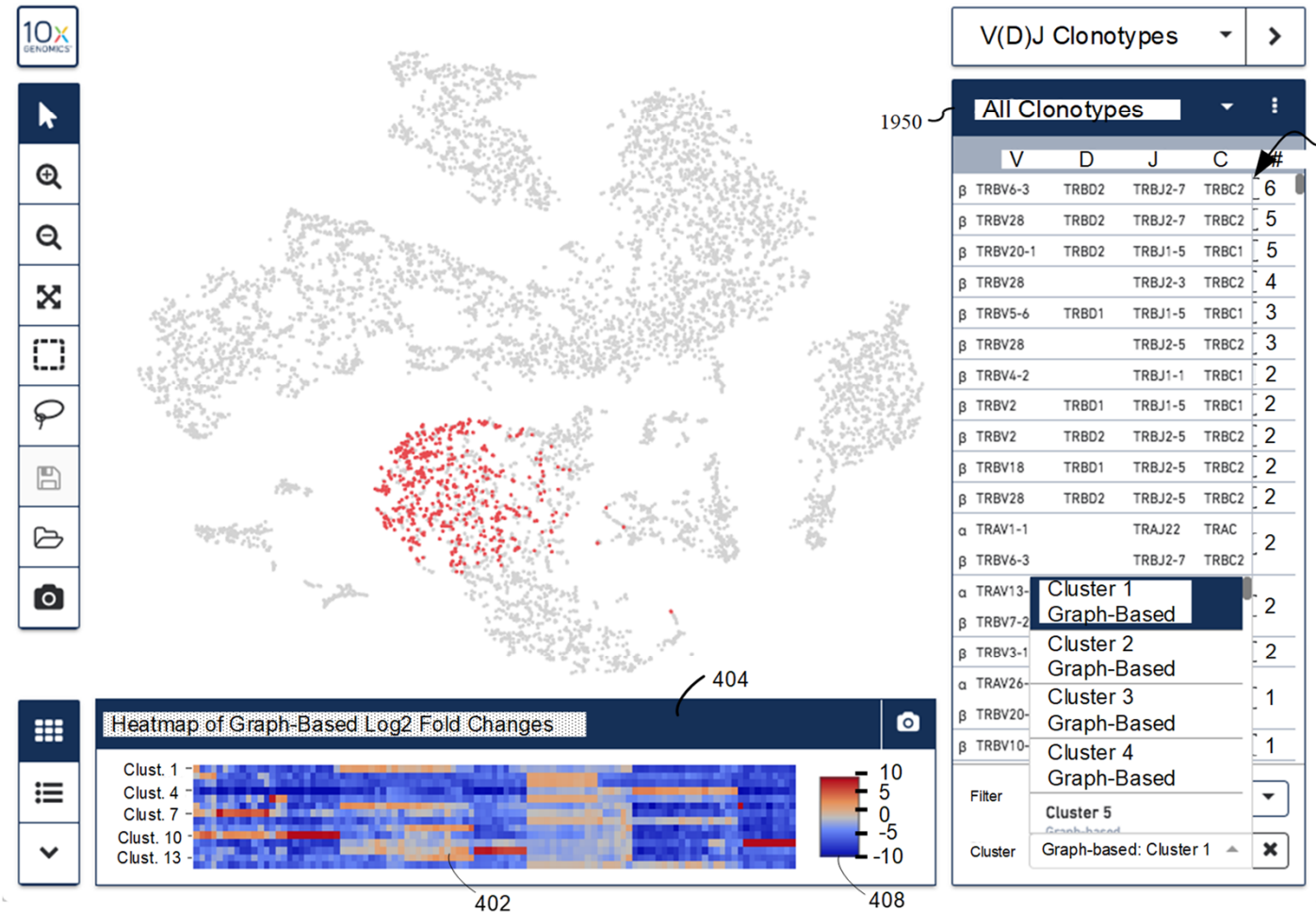(54) SYSTEMS AND METHODS FOR VISUALIZING A PATTERN IN A DATASET

(71) Applicant: **10X Genomics, Inc.**, Pleasanton, CA (US)

(73) Assignee: **10X GENOMICS, INC.**, Pleasanton, CA (US)

(21) Appl. No.: **15/891,607**

(22) Filed: **Feb. 8, 2018**

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

(74) *Attorney, Agent, or Firm* — Morgan, Lewis & Bockius LLP

- Founded in 2013
- Based in Salt Lake City, Utah
- ~165 employees
- Applies patented artificial intelligence techniques to morphological profiles derived by cell painting to identify and develop drugs for over 30 diseases
- **CEO**: Chris Gibson, Ph.D.
    2013 Ph.D. graduate of University of Utah
- **Total VC investment to date:** USD $200M
- **Notable 2019 events:**
    - *"Recursion Pharmaceuticals, which uses automated, experimental biology with artificial intelligence to reveal new drug targets and develop drug candidates, raised $121 million (led by investment fund Baillie Gifford) in a Series C round to further develop its in-house pipeline of small molecules and the technology."*
    - *"…new therapeutic candidates identified for over a half a dozen diseases within its AI-driven collaboration with Takeda Pharmaceuticals, started in 2017. This year Takeda has exercised its option for drug candidates in two rare diseases, and the companies extended collaboration*

(12) **United States Patent**
Victors et al.

(10) **Patent No.:** US 10,281,456 B1
(45) **Date of Patent:** *May 7, 2019

(54) SYSTEMS AND METHODS FOR DISCRIMINATING EFFECTS ON TARGETS

(71) Applicant: **Recursion Pharmaceuticals, Inc.,** Salt Lake City, UT (US)

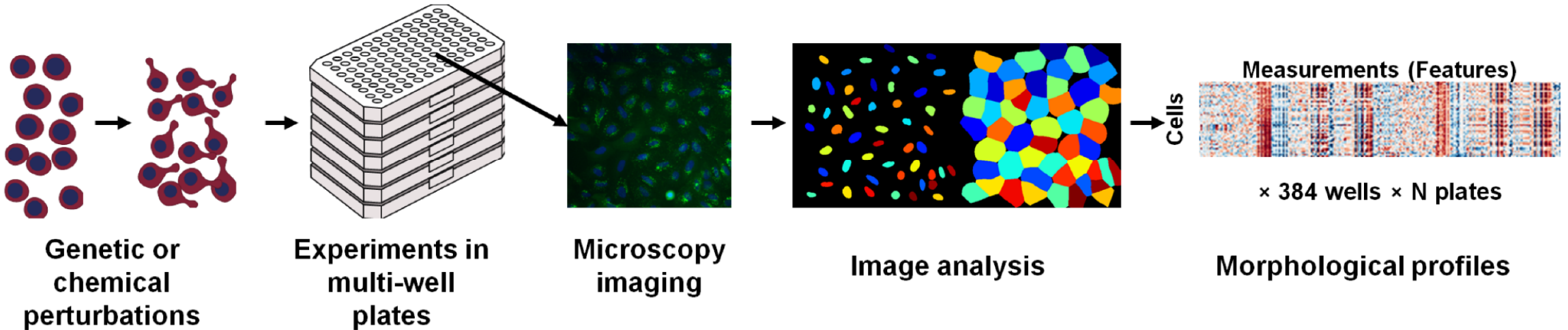(21) Appl. No.: **15/995,835**

(22) Filed: **Jun. 1, 2018**

Buenrostro et al., 2013, "Transposition of native chromatin for fast and sensitive epigenomic profiling of open chromatin, DNA-binding proteins and nucleosome position," Nature Methods 10, 1213-1218.

Primary Examiner — Russell S Negin
(74) Attorney, Agent, or Firm — Morgan, Lewis & Bockius LLP

Genetic or chemical perturbations → **Experiments in multi-well plates** → **Microscopy imaging** → **Image analysis** → **Morphological profiles**

Measurements (Features)
Cells
× 384 wells × N plates

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Brett Lovejoy, Partner

Morgan, Lewis & Bockius LLP
One Market, Spear Street Tower | San Francisco, CA 94105
Direct: +1.415.442.1211 | Main: +1.415.442.1000 | Fax: +1.415.442.1001
brett.lovejoy@morganlewis.com | www.morganlewis.com
Assistant: Julie K. Costello | +1.415.442.1610 | julie.costello@morganlewis.com

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