termsheet

PharmaVentures
Experts in deals and alliances

May 2017 Issue 21

Heads of Terms

Conquering Diagnosis

No matter how good we are at developing new drug therapies we are still highly dependent on the correct diagnosis of a current or impending ailment. In fact, we know that the earlier we can diagnose the disease, the better the treatment outcome. The issue, of course, is that we ourselves can only detect a problem when we present with symptoms, such as pain, fever etc. By the time symptoms become apparent the disease may already have been well established. And it is only at this point that we go to the doctor, who is in effect, a diagnosis practitioner. A doctor will typically use well-established but ancient diagnostic tools such as the stethoscope (invented in 1816), thermometer (first used in medicine in 1612) and the sphygmomanometer to check blood pressure (invented late 1800s). These tools, together with a few prods and questions are often employed to reach a 'diagnosis'. If you are lucky, the doctor may take a urine or blood sample and have it sent off to the lab for 'results'. Even then, it may take several visits before they get an inkling of the problem and finally decides to send you to a specialist clinician. This is quite startling!

In the 21st century it is quite amazing that we have not yet finessed our ability to detect disease early enough to maximize effective treatment outcomes. For people with serious diseases, such as cancer and dementia, diagnosis is particularly difficult. In fact, most people don't know they have cancer until the disease is well established.

An App incorporating Artificial Intelligence (AI) has been touted as a potential solution; performing diagnostics with accuracy and speed superior to that of a doctor's ability. This is not a negative reflection on doctors, but a positive reflection of how fast AI has advanced. This progress, together with an explosion of our understanding of disease biology and incredible advances in non-invasive or minimally invasive diagnostics, will mean that disease can be treated at speed with increased cost effectiveness.

The whole area of diagnostics is about to change significantly and its impact on healthcare could be revolutionary.

Dr Fintan Walton
Chief Executive,
PharmaVentures Ltd.

industry insight

Smarter Drugs
The Convergence of AI and Drug Discovery

Artificial Intelligence Introduction

In 2009, Artificial Intelligence (AI) researchers made the important discovery that NVIDIA GPUs (graphics processing units) are far superior in simulating biological learning than CPUs (central processing units), this along with innovations in chip architecture from both Google (TPU) and Microsoft (FPGA) has led to the rapid explosion of machine learning and AI into a myriad of applications – the life-sciences and healthcare industries included.[1] AI is a truly convergent technology with the potential to disrupt multiple sectors, but rather than one technology it is an umbrella term defined by Bernard Marr as "the broader concept of machines being able to carry out tasks in a way that we would consider smart". The wide ranging disruptive implications of AI are also reflected in an explosion of start-up activity in the space since 2012 (*Figure 1*). Machine learning is a popular development within AI, focused on giving computers access to large data sources and then allowing them to learn and improve. An important sub-area is also neural networks.[2] These are probability weighted networks of algorithms, with in-built feedback loops, that are designed to loosely model the human brain.[3] When these are stacked and overlaid, it is then referred to as deep learning: the fastest growing area of AI research. To avoid excess use of complex terminology, within this piece the term AI will be used and refers to the full spectrum of computational technologies available.

Analysis of 561 AI start-ups founded in Europe

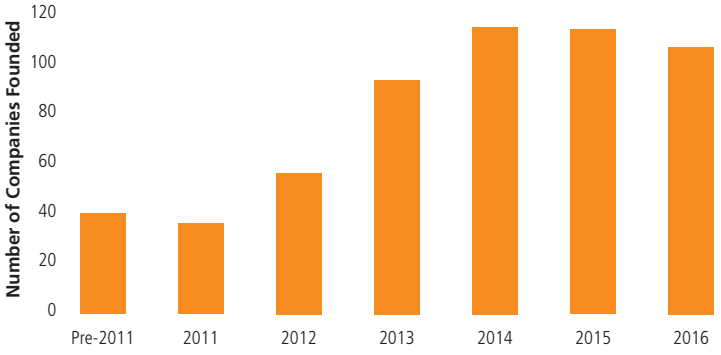

Figure 1

Source: Crowdsourced data published on Tech.eu.[4]

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1 https://www.wired.com/2014/10/future-of-artificial-intelligence/
2 https://www.forbes.com/sites/bernardmarr/2016/12/06/what-is-the-difference-between-artificial-intelligence-and-machine-learning/#52d3d7bd2742
3 https://deeplearning4j.org
4 http://tech.eu/features/13538/list-artificial-intelligence-ai-startups-europe/

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Smarter Drugs: The Convergence of AI and Drug Discovery

Within the drug discovery process, the application of AI presented here has been segmented into technologies that increase efficiency (such as tools to reduce the literature burden on scientists), tools that develop (and de-risk) therapeutic candidates (thus shortening the drug discovery timeline and cost) and technologies that allow for the identification of new pathways and targets through the use of multifactorial "omics" analysis (thus opening up new areas of biology). Whilst the application of AI to drug discovery is beginning to attract serious attention from investors and industry alike, more established sectors in healthcare AI include: image analysis, wearables, patient data and diagnostics. To date, these aspects of healthcare and life-sciences have constituted the majority of deals and thus significantly outnumber AI start-ups focussed on pure drug discovery.

Investment trends in life-Sciences and healthcare AI

The largest investors into advanced applied AI are currently not traditional pharmaceutical or healthcare companies but more often technology investors looking to pivot into opportunities in healthcare. The largest corporate investors into the wider healthcare AI sector (not just drug discovery) include: GV (formally Google Ventures), Qualcomm Ventures, Tencent, IBM Watson and GE Ventures. Some life-sciences investors that have also invested into this sector include: Celgene, the Roche Venture Fund, Lilly Ventures and Illumina. Other active non-corporate investors include: Kholsa Ventures, Funders Club, Deep Knowledge, Data Collective and Flare Capital Partners.[5]

Financing deal numbers into healthcare AI start-ups

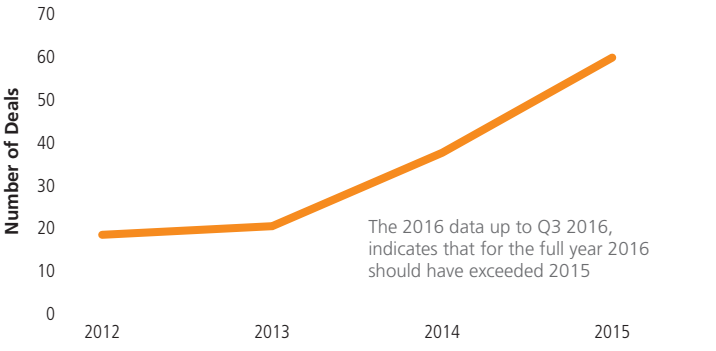

Figure 2 Source: CB Insights

There are also specific funds looking to leverage synergies between the software industry and life-sciences industries. These include DKLS (UK), which focusses on disruptive technologies based around AI and ageing, and the $200M USD Andreessen Horowitz AH Bio fund (US) which predominately invests into software companies looking to disrupt biology.[6] The investor appetite for disruptive healthcare applications of AI is reflected in the deal financing graph (*Figure 2*).

Artificial Intelligence within Drug Discovery

Empowering human scientists to perform at a higher level

With an a new scientific paper published every 30 seconds and 10,000 PubMed updates daily: it is clear that modern research scientists are physically unable to scour and investigate all the relevant literature.[7] Start-up companies, such as Sparrho (London, UK, founded in 2013), are utilising AI to deliver curated and relevant content to scientists; thus reducing problems associated with keyword search strategies. These tools, and others like them, are aimed at improving the efficiency of research scientists.[8]

Artificial Intelligence powered "omics" for new target and biomarker discovery

The application of AI to multifactorial "omics" analysis allows researchers to identify hidden trends and new associations in large unstructured datasets. Areas of interest include the Genome (genes), Transcriptome (RNA etc.), Proteome (proteins), Metabolome (metabolites), Epigenome (epigenetic variations) and the Glycome (glycans/sugars). By utilising data from varying levels of biological understanding (e.g. Genomics and Proteomics), AI algorithms are able to elucidate new pathways or targets for therapeutic programmes. One such company actively involved in this area is, Toronto based, Deep Genomics. Founded in 2015, it has since raised $3.7M USD from investors including True Ventures. Deep Genomics is applying advanced machine learning

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5 https://www.cbinsights.com/blog/artificial-intelligence-startups-healthcare/
6 https://www.forbes.com/sites/alexkonrad/2015/11/18/andreessen-horowitz-launches-biotech-software-fund/#3a76c5ed7968
7 http://www.fiercebiotech.com/cro/benevolentai-forms-licensing-deal-janssen-to-develop-drugs-using-ai
8 http://www.huffingtonpost.co.uk/vivian-chan/from-science-fiction-to-s_b_15493438.html

Issac Jacob promoted to Vice President

PharmaVentures is pleased to announce that Issac Jacob has been promoted to Vice President, reporting to Stephen Waterman, Managing Director.

Fintan Walton, Chief Executive of PharmaVentures said: "I'm delighted to announce Issac Jacob's promotion to Vice President. Issac has extensive experience in investment banking, corporate finance, and provides excellent support to our clients in our M&A and divestment mandates."

Issac has executed healthcare advisory and financing projects exceeding $30bn in North America, Europe and Emerging Markets for blue chip clients, and recently advised IDT Australia Limited (ASX: IDT) in the divestment of their CMAX clinical trials business to the Japanese I'rom Group Co. Limited (TYO:2372).

For over 25 years, PharmaVentures has acted as advisor to over 700 pharmaceutical and biotechnology clients in transactions; covering licensing, mergers, acquisitions, divestments and joint venture activities for companies.

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to elucidate patterns of how genetic variation affects cellular processes. Another interesting case study in the application of AI to the pharmaceutical industry can be found in the US headquartered start-up, Insilico Medicine.[9] Since its foundation in 2014, the company has gone on to raise $10.8M USD in funding from investors including Deep Knowledge Ventures, and has established multiple projects with a range of pharmaceutical and academic partners. Rather than focussing on a single indication, Insilico Medicine has identified the disease apathetic potential of deep learning within life-sciences and as such has established projects across a range of areas including: developmental biology (Embryonic.AI), biomarker discovery (Pharma.AI) and ageing research (Aging.AI 2.0). The company conducts both novel biomarker discovery, drug repurposing and CRO services for the pharmaceutical industry, predominately based upon mining the transcriptome.

Artificial Intelligence for computational drug design and preclinical de-risking

Upon discovery of a novel target (perhaps by AI powered methods), algorithms can be trained to conduct *in silico* high through-put screening assays and advanced computer-aided drug discovery. Whilst computer aided drug discovery is a routine aspect of the process to discover new drugs, the use of AI allows for a rapid acceleration in capabilities – delivering drugs which are more potent and with a lower chance of clinical failure. Atomwise is a San Francisco based start-up company focussed on utilising a deep learning neural network for structure-based drug design and discovery. It has raised $6.35M from grant and seed financing rounds, including an investment from Khosla Ventures. Using its AtomNet™ platform it was able to identify a novel drug candidate for the blocking of Ebola infectivity and has partnerships with both IBM and Merck. NuMedii is also a California based AI start-up that has raised $5.5M USD over 2 rounds, including from Lightspeed Venture Partners and Claremont Creek Ventures. The company aims to discover new drugs and de-risk them by use of a licensed database (comprising of hundreds of millions of human, biological, pharmacological and clinical data points) to train its proprietary big data AI algorithms. With de-risked drug candidates it then looks to out-license these for preclinical testing. Numerate is also a California based start-up, founded in 2008, that has raised over $5.5M USD in funding from investors such as Lilly Ventures and Atlas Ventures. Whilst Numerate has licensed its ApoE4 programme to a stealth biotech, its business model follows that of several others in this sector. That is: develop novel in-house, de-risked, preclinical assets that can then be licensed out to other companies to continue their development. It's technology again utilises a multifactorial machine learning based approach to rapidly screen and virtually develop a lead compound series. The best candidates are then made, tested and the results fed back into the algorithms. Other start-ups active in this area include Globavir (California, $7.5M USD raised, infectious disease, AI driven drug discovery), twoXAR (California, $3.4M USD raised, AI driven drug discovery and repurposing) and Benevolent AI (London, $100M raised, drug discovery and a partnership with Janssen).

Future trends in AI that will impact upon the Life-Science Investment landscape

A rapid increase in AI capabilities in Asia could begin to further impact EU/US Life-Sciences

No discussion of the wider impact of AI would be complete without comment on the rapid rise of Chinese competency in AI technologies. China now leads the USA in publications on deep learning and has experienced an exceptional growth rate across the wider AI sector (a projected CAGR of 50% across all applied

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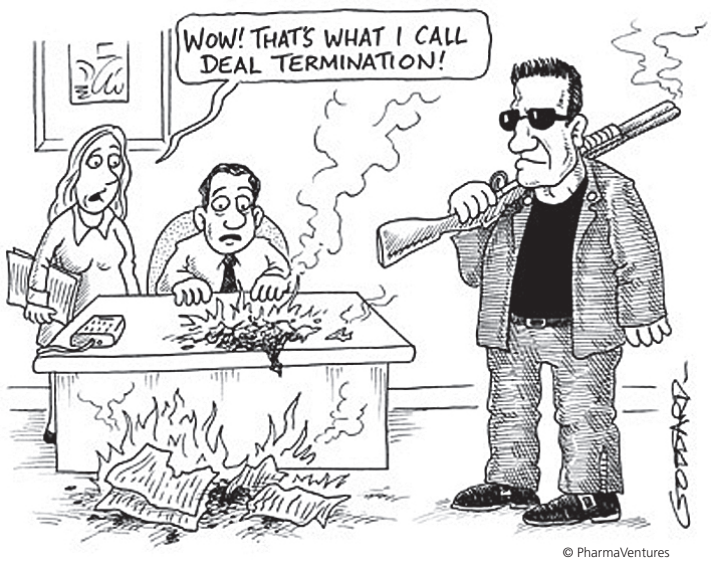
9 https://www.eurekalert.org/pub_releases/2015-12/imi-tfm120815.php

10 http://www.scmp.com/tech/innovation/article/2082217/chinas-artificial-intelligence-sector-danger-becoming-bubble-experts



meet the team

Tamsin Bateman

Tamsin is an Associate at PharmaVentures. She has a background in management consulting and is an experienced analyst. Prior to joining PharmaVentures, Tamsin was an Associate for Scarlatti, a New Zealand-based consultancy focusing on innovation and the primary industries. She has worked on a number of technology development projects, ranging from strategic development plans to investor presentations. Tamsin has also previously worked in technology transfer (UniServices) and medical writing (Adis International).

Tamsin holds a Bachelor of Science (Biomedical Science) and a Master of Bioscience Enterprise (First Class Honours), both from the University of Auckland, New Zealand. Her thesis focused on financial decision making and investments of indigenous trust funds, and she remains passionate about indigenous development.

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areas of AI through to 2020). This explosion within the wider Chinese AI sector has led some to speculate on the formation of a bubble as salaries and valuations both rocket.[10] But Chinese AI expansion isn't just confined to Asia with companies such as ICarbonX looking internationally for new technologies or datasets. Founded in October 2015, ICarbonX is a Shenzhen based healthcare company (and the first Yuan biotech unicorn) that combines multi-omics data with behavioural, environmental and psychological data to provide AI driven personalised healthcare solutions. In the 18 months since its foundation it has raised over 1.3Bn RMB in funding from Tencent holdings, Zhongyuan Union Cell & Gene Eng., and China Bridge capital. It is now conducting its own international investments into companies such as AOBIOME (Microbiome, MA/USA, $30M USD, Series-C, 2017), Imagu Vision Technologies (Image Processing, Tel Aviv, acquisition, 2016) and PatientsLikeMe (US patient network, MA/USA, $100M USD, 2017). Other large Chinese companies, such as search giant Baidu, are also investing heavily into internal AI as well as exploring applications in life-sciences - as such more cross-sector/cross border AI deals into healthcare and life-sciences should be expected in the future.[11]

The funders of innovation are themselves prone to disruption by AI

For an industry that funds innovation, the venture capital industry has also remained remarkably resilient to disruption by advanced technologies. Whilst innovative funds such as Deep Knowledge Ventures have incorporated AI into their investment evaluation process, the majority of funds are still operated in a traditional manner; utilising human capital to conduct deal sourcing, due diligence and deal evaluation.[12] As both the capability and applications of AI continues to develop, one may expect more funds beginning to rely on advanced AI (sourcing data inputs from a range of sources) instead of investment professionals, thus reflecting rapid changes that are afoot in other aspects of the finance sector (e.g. the JP Morgan COIN programme or the Japanese Goldman Sachs' global big data investment strategy instrument).

Conclusions

With the explosion of funding into AI sector in the past 5 years, as well as an increasingly competitive market in areas such as image analysis – one may start to see more (non-pharmaceutical) companies applying their technologies to the relative virgin ground of drug discovery. In addition, increasing adoption and integration of wearable technologies into both life-style health management programmes and clinical trials will provide increasingly granular data sources for advanced analytics and machine learning applications. There are also breaking advances in areas such as quantum computing, robotics and blockchain that may in the future begin to impact sectors with a lower barrier to entry – the inevitable consequence being that these technologies will slowly converge into drug discovery.[13,14]

11 https://www.forbes.com/sites/jlim/2015/12/28/baidu-teams-up-with-medical-researchers-to-fight-cancer/#29dddfd0447a

12 http://www.huffingtonpost.co.uk/2014/05/15/artificial-intelligence-board-directors_n_5329370.html

13 https://www.eurekalert.org/pub_releases/2016-11/imi-bta111716.php

14 http://www.bio-itworld.com/2016/5/4/how-blockchain-is-helping-genomics-research.aspx

About the author(s)

Peter Crane is a PhD student from Oxford University, where he specialised in carbohydrate chemistry, synthetic biology and glycobiology. In addition, he spent stints in industrial small molecule and biologic research, conducted over 1 year of venture sourcing and due diligence for an international pharmaceutical company, and ran several entrepreneurial initiatives across the globe. Whilst awaiting his viva examination, he now is launching life-science companies, working with several Chinese ventures on international projects and also serves as a global director for the Innovation Forum.

The Innovation Forum is a global, not-for-profit, interdisciplinary network of over 10,000 researchers, industry leaders and entrepreneurs. It aims to connect academia, industry and policy makers to accelerate technology development. The Innovation Forum, Oxford team, is currently concluding a 15-part lecture series on technology comercilisation and will be holding a global innovation conference in Oxford (December 2017).

The author credits Dr Mira Kassouf for help researching and proof reading this document.

For more information, please visit: www.inno-forum.org

conference update

Biotrinity
8-10 May, London

Anglonordic Biotech Conference
30 May, London

BIO International Convention
19-22 June, San Diego

On Helix
13 July 2017, Cambridge

To meet with PharmaVentures' experts at any of these conferences, please contact
Ellie Shatford: ellie@pharmaventures.com

Or

To arrange an interview with PharmaTelevision, please contact
Matt Royan: matt@pharmaventures.com