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PetMedix – bringing antibody innovation to animal health

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Abstract: PetMedix™ is a Cambridge, UK based research and development stage biopharmaceutical company developing antibody-based therapeutics for companion animals. The growing team have over 30 years' experience building platforms that can develop species-specific therapeutic antibodies.

Driven by the core value of improving the health and welfare of animals, PetMedix™ is taking the cutting edge of human medicine and using it to develop innovative new veterinary treatments against a wide range of clinical indications for dogs and for cats.

Keywords: Companion Animal, Antibodies, mAbs, canine, feline

1. The success story

Antibody therapeutics have transformed human medicine over the last 30 years, with more than 90 receiving regulatory approval in this time and making up 7 of the top 10 bestselling human therapies. Their success partly derives from their physical nature. At one end of the antibody you have the variable regions that are capable of very tightly and specifically binding to the target of interest, and at the other you have the constant region which can act as a potent signal to the immune system, or be utterly silent, depending on the desired effector function. As a natural part of our immune systems, these proteins are very safe and adverse effects related to these therapies are generally mild and either related to the administration or the specific target biology being modulated.

Given that they are natural proteins, it is important that antibodies are a correct species match for their patient, in much the same way that blood and organ donations must be well-matched. Without this matching, the immune system of the patient will recognise the antibody as foreign, destroy it, and abrogate its effects. Virtually all of the antibodies on the market today started with a mouse antibody, and over the last three decades we have worked through different technologies to make this mouse antibody more and more human. The current gold standard

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approach is to modify the mouse itself, instead of the antibodies it produces. Advances in genome engineering have made it possible to replace the immune system of the mouse, or more specifically its immunoglobulin genes, with those from a human. There have been a number of iterations of this approach, with the most advanced being a complete in situ replacement of the genes. This is the basis of the platforms used by American company Regeneron, as well as the Cambridge, UK-based company, Kymab.

Our pets are getting sick with exactly the same diseases we are, and the parallels are often so close that dogs and cats with naturally occurring disease are often used as models in human medical research and drug discovery. There are many small molecule drugs that are successfully used in animal health as well as human health, and that forms the basis of many of the veterinary medicines available. However, it's not possible to give a human antibody therapy to a dog or cat, and so antibodies haven't been able to positively benefit animal health the way that they have for human health. PetMedix is looking to change that.

PetMedix shares a scientific founder and CSO with Kymab, and in fact is in the building next to them on the Babraham Research campus. We are using the same cutting-edge transgenic technology as Kymab, albeit with mice engineered to express dog or cat antibodies instead of human ones. We are using these platforms for drug discovery, and plan to develop a broad pipeline of therapeutic antibodies in order to help transform veterinary medicine.

2. How did it start

The story of PetMedix starts with our scientific founder, Professor Allan Bradley FRS. During his PhD at the University of Cambridge, he worked on murine embryonic stem cells, a development that would lead to his PhD supervisor, Martin Evans, receiving the Nobel prize in 2007. After some time in Cambridge, Allan went to Baylor College of Medicine where he helped establish their mouse genomics programme. Whilst there, he became a founding adviser to a company called GenPharm, which later became Medarex. This company, which was bought by BMS in 2009, was one of the first to develop a transgenic mouse for the development of human therapeutic antibodies. In 2000 he returned to the UK to become the second director of the Wellcome Trust Sanger Institute, and work began in his lab there to develop a mouse with a completely humanised immunoglobulin repertoire.

The work was fruitful, and in 2010 Kymab was founded to commercialise this project and begin developing human therapeutic antibodies. Kymab has been very successful, raising over $220M to date and developing a rich pipeline, the lead asset of which had a positive phase 2a readout in August 2020. A few years into the Kymab project, Allan recognised that the technology that had been developed in his lab and taken forward by Kymab could be readily applied to other species and so advertised a PhD project to explore this possibility. Jolyon Martin joined Allan's lab in 2014 as a PhD student and work began to develop a mouse transgenic for canine antibody genes, alongside a more fundamental look into canine antibody genetics and expression.

Upon completion of Jolyon's PhD in late 2017, there was an early version of just such a mouse and so Allan and Jolyon agreed to found a company to commercialise the work. In order to do so, Dr Tom Weaver, founding CEO of a number of life sciences companies including most-

recently Congenica, was brought in as the third co-founder to lead the new company. Tom, Allan, and Jolyon then spent the next year putting together a business plan and raising capital, whilst the scientific work continued within Allan's lab. In February 2019 PetMedix raised an £8M series A from New York VC Digitalis and London-based Parkwalk Advisors, and the company began in earnest – moving out of Allan's lab and hiring its core team.

Figure 1. Dr Jolyon Martin - head of business development and the author of this paper (left) and Dr Thomas Weaver – CEO of PetMedix (right)

3. Why is it needed?

Pets are currently suffering, and in many cases dying, from conditions that are being successfully treated in people with therapeutic antibodies. For example, dogs in the USA are diagnosed with cancer at more than ten times the rate that humans are (5,300/100,000 dogs vs 500/100,000 people)[1]. However, veterinary oncologists generally only have surgery, radiation, or conventional chemotherapy to rely on and so canine cancer patients can often have worse outcomes than their human counterparts. Furthermore, owner perspectives on chemotherapy can be very negative, with 58% of surveyed owners saying they would not subject their dog to chemotherapy based on their previous experience of it [2].

Beyond cancer, there are many possible applications of antibody therapeutics to animal health. In fact, the only currently available antibody therapeutic in the veterinary space is one against IL-31 that is used in the treatment of atopic dermatitis. This drug, called Cytopoint™, has been incredibly successful, reaching blockbuster status (which is >$100M annual sales in the animal

health world) in its second year of sales. This therapy has also helped demonstrate willingness from veterinarians and owners to use antibody therapies with pets, as well as the fact that it can be done cost effectively. Cytopoint treatment costs on the order of $100 per month, far less than tens of thousands that many human antibody treatments can amount to over a year. This has helped change perceptions within the industry, as it was incorrectly assumed that it would be impossible to develop antibody treatments that pet owners could afford.

Whilst Cytopoint is a very successful drug, it was made by an older antibody technology than the one being used by PetMedix. The process, called CDR-grafting, involves labour- and cost-intensive antibody engineering to take a mouse antibody and make it more (but never fully) dog-like. Whilst building the PetMedix platform is a huge scientific challenge that requires a great deal of technical skill and know-how, the platform once complete can rapidly and readily yield drug-quality antibodies that need no further manipulation. This will bring the overall times and costs of drug discovery down, as well as improving the chance of success of each project. Kymab is a close partner of PetMedix and we are able to leverage their expertise and experience in order to help bring the very best of human antibody medicine to animal health.

4. The journey so far

Having initially budded off from Allan's academic laboratory in the spring of 2019, the team took up residence in labs at Granta Park. There, work continued to build out and improve on the platform that had started as Jolyon's PhD project. Since then this work has advanced sufficiently that the mouse platform is being used for drug discovery, and at the start of 2021 PetMedix has a number of internal discovery programmes underway targeting a range of different indications in canine health.

Figure 2. PetMedix Scientific Team Leaders Dr Daniel Alanine (left) and Dr Andy Thompson (right) working at our Babraham campus facility.

Over the last 18 months, the team has grown considerably and PetMedix now has nearly 40 staff, the majority of which are PhD scientists. Not only has the murine platform advanced, but so has the entire workflow of antibody discovery. PetMedix has honed and refined the entire process, building in part from the know-how and understanding of Kymab, to ensure that every step from antigen preparation to in vitro screening of lead candidates is optimised. This work has taken a great deal of ingenuity and skill from our team, in part because significantly less basic research has been carried out in canine or feline systems. What this means in practice is that a human antibody scientist can generally order a kit or reagent to assist them in their experimental goals, whereas our team have had to develop that approach de novo.

Alongside all the technical development, PetMedix moved to brand new facilities on the Babraham campus in the middle of lockdown. That this could happen safely and efficiently, science was only paused for one week and the move itself took less than one day, was a testament to everyone within the company pitching in and working together to help achieve our common goal. It is somewhat cliché to extoll the virtues of a team within a start-up company, but we are certainly very proud of the people that make up PetMedix, both for their technical skill, but also for their approach to everything we do.

Alongside this move we brought in additional venture investment from Cambridge Innovation Capital in May 2020, and are excited to have them on our board. Our progress has also been recognised by a number of awards, the most significant were being named ‘Best Start-up 2019’ by Animal Pharm (the principle news outlet for the animal health industry) and then to be longlisted by Nature Research as ‘Best Spin-out 2020’.

5. Who is involved?

Professor Allan Bradley, CSO. Allan is a world-renowned researcher and entrepreneur. He is Emeritus Director of the Wellcome Trust Sanger Institute, and was responsible for transitioning its high-throughput genome-sequencing infrastructure into an academic genome centre with a focus on primary research. Central to this transition was the creation of a mouse genome-engineering research program leading to discoveries and techniques for humanizing mouse immune systems. These proprietary technologies formed the foundation in 2010 of Kymab Ltd. Kymab was conceived as a platform-to-product company, where the first few years were focused on building the platform. Kymab have used this platform to discover novel human antibody therapeutics that it has validated pre-clinically and is now testing the first of these in human clinical trials. In his academic role, Allan has published widely in high impact journals and is a respected expert in the monoclonal antibody and mouse engineering fields. Previously he was a Howard Hughes Medical Institute Investigator at Baylor College of Medicine (Houston, USA) where he built up one of the biggest transgenic mouse facilities in the USA and also spun out Lexicon Genetics, another successful pharmaceutical company based on mouse genetic technology. Allan is a Fellow of the Royal Society.

Dr Thomas Weaver, CEO. Tom has a proven track record of creating value in genetic based start-up companies, including Hexagen Genetics (acquired by Incyte Plc), Geneservice (acquired by Source Bioscience Plc), and Congenica (still private). He has experience in technology development, business and operational planning, building multi-disciplinary teams, including operational, IT, BD, sales, finance, and quality, and management at both operational and C-levels. Tom also has academic and government science experience, having been a Medical Research Council (MRC) Director in Oxford overseeing a team of 130 mammalian geneticists and animal technicians undertaking one of the world's largest mouse mutagenesis and clinical phenotyping infrastructures. He trained in experimental oncology (Madison, USA) and did post-doctoral research at the MRC Lab for Molecular Biology (Cambridge, UK) and University of Cambridge (UK).

Dr Jolyon Martin, Head of Business Development. Jolyon carried out his PhD (Cambridge, UK) in Professor Bradley's laboratory under his mentorship. He led the research and operational teams that made an in vivo model for caninizing the mouse immune system. This research includes the first complete annotation of all relevant canine genes that are the essential components necessary to generate fully functional antibodies. This mouse platform and the know how associated with the research program untaken at the Sanger Institute as part of Jolyon's PhD forms the basis of the PetMedix technology. Previously Jolyon ran business development for Simprints, a social enterprise start-up, and worked in operations at Horizon Discovery. He was named Cambridge University Entrepreneurs Young Entrepreneur of the Year Award in 2017 and '30 under 30' in Europe for Science and Healthcare by Forbes in 2021

6. Look into the future

To date, PetMedix has built an industry leading canine mAb discovery platform, with a stellar team working to apply it to drug discovery. Over the next few years, PetMedix's assets will be advanced through clinical development and on to regulatory approval. Work is also underway on the feline platform and over the next few years that will also be applied to drug discovery for novel cat medicines. The USA is the likely first market that the therapies will be registered in, and so the team is likely to develop a small commercial and regulatory presence there. However, the heart of the Cambridge biotech cluster is where PetMedix began and where its core research and development shall remain.

References

[1] Schiffman, Joshua and Matthew Breen, Comparative oncology: what dogs and other species can teach us about humans with cancer, Philosophical transactions of the Royal Society of London. Series B, Biological sciences, Vol. 370, No. 1673, Jul. 2015.

[2] Williams, Jane et al., Factors Which Influence Owners When Deciding to Use Chemotherapy in Terminally Ill Pets, Animals : an open access journal from MDPI, Vol. 7, No. 3, Mar. 2017.

The company

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