



Protein Therapeutics to Amp Up Outsourcing in Animal Health

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The rapidly evolving vet business underscores the centrality of CDMOs and CROs.

This is the final installment of a nine-part series of articles addressing pharmaceutical outsourcing industry trends.

Humankind is growing increasingly fond of pet animals. According to the American Pet Products Association, pet ownership rose to almost 70% of U.S. households in 2020. Another report appeared in 2021 by the Pet Food Manufacturers' Association and showed a total of 3.2 million households in the UK acquired a pet since the start of the Covid-19 pandemic.

Having pets in the home not only does nurture cognitive, emotional, social, and physical development, but studies indicate that human-animal interactions are also proven to reduce anxiety, depression, and loneliness. As pets increasingly become part and parcel of families, people are ready to sacrifice anything for their beloved four-legged companions that help

them live longer and healthier lives.

The boom in pet ownership has resulted in an unprecedented interest in animal health.

Companion animal health, which comprises dogs, cats, horses, etc., is currently the fastest growing segment in the rapidly evolving global animal health market which was valued at a little over \$40 billion in 2022 by PS Market Research. Large animals represent approximately 60% of total animal health sales propelled by increased protein consumption and a growing global population.

BIOLOGICS — THE BIG BET

Among the product categories, veterinary drug makers are now betting big on biologics as adoption rates rise and awareness level of pet health grows.

The interest in biologics kick-started with the introduction of lokivetmab (Cytoint) in 2017 by Zoetis. The monoclonal antibody drug has been approved to treat atopic and allergic dermatitis in dogs. Today, lokivetmab, a blockbuster, delivers over \$100 million in annual revenue. Again in 2022, Zoetis launched frunvetmab (Solensia) for treating osteoarthritis in cats. Companion animal health products accounted for nearly 65% of the total revenues for Zoetis, the world's largest veterinary drug maker, for the year ended 31 December 2022.

"Protein therapies are now a very major part of the human pharmaceutical landscape, but they are just now being introduced to animal health. We see great opportunity in being a leader in this revolution for disease treatment," says Todd Zion, president and CEO of Akston Bioscience Corporation, a Beverly, MA-based company that invents, develops, and manufactures breakthrough protein therapeutics for companion animal health.

Antibody treatments could offer a range of benefits to several chronic disorders dogs and cats suffer from including diabetes, cancer, lymphoma, arthritis, allergic disorders, and chronic pain.

Akston's most advanced candidates are AKS-321d and AKS-425c, once-a-week insulins to treat canine and feline diabetes. Both are licensed to and are being developed in partnership with Dechra Pharmaceuticals, Plc, a global veterinary pharmaceuticals company.

The dog and cat once-weekly insulins will have a dramatic effect on treating diabetes in companion animals, avers Zion. "Imagine having to inject your cat with insulin twice a day and then think about being able to do that only once a week. We have seen this benefit in our early testing at academic veterinary clinics. The owners and veterinarians are extremely excited about the change," he says.

So many dogs and cats are euthanized when they are diagnosed with diabetes, adds Zion emphasizing that Akston believes its insulins can reduce these numbers significantly.

Other candidates in the company's development pipeline

include AKS-544d, which targets chronic pain in canines, and AKS-197d, an insulin receptor down-regulator for treating canine cancers.

While there is a lot of interest in long-term non-infectious debilitating diseases such as arthritis, there is also interest in next-gen vaccines spurred by new-wave technologies like mRNA and novel peptide-based antimicrobials.

COVID-19, with its high rate of transmission, has turned the spotlight on zoonotic diseases more glaringly than ever highlighting the need for animal health surveillance.

According to the World Organization for Animal Health, 75% of emerging infectious diseases have an animal origin.

Diseases that can be shared between animals and people are not new, however, infectious, zoonotic diseases are being identified with increasing frequency.

Many companies are looking for alternatives or substitutes for antimicrobials as the use of antibiotics in livestock finds their way to the food chain contributing to the emergence of "super bugs."

Unsurprisingly, the health of animals has become more or less synonymous with that of humans.

In view of this, contract research organizations (CROs) need to upskill and expand their offerings to clients to cover new or re-emerging diseases, opine experts.

DEMAND FUELS PARTNERING

Growing demand for advanced protein therapeutics and other animal health products expands the opportunities for outsourcing.

Industry surveys show that almost all animal health organizations are outsourcing services and operations underscoring the critical importance of contract development and manufacturing organizations (CDMOs) in animal health drug development and manufacturing.

The global veterinary CRO and CDMO market size was valued at \$5.80 billion in 2022 and is expected to grow at a CAGR of 8.94% from 2023 to 2030, according to a report by Grand View Research.

cGMP manufacturing of protein therapeutics is currently the fastest-growing segment. The key trend, according to Zion, is that the larger companies in the field can develop and manufacture them, but the others do not. So, they are looking to outsourced service providers for this capability.

Akston Bio, which also provides CDMO services, uses the company's proprietary Ambifect Fc-fusion platform to design species-specific therapeutics. "It allows us to 'swap' components of therapeutic proteins that we have used for other candidates," comments Zion. This reduces risk, development time, and cost as it can allow the same facility to produce different products.

Meanwhile, CROs operating in veterinary research find that their roles as service providers are getting broader and broader as a lot of companies are looking for support in regulatory and other related aspects besides animal studies.

"Clients are seeking 'value added' services from CROs. In addition to actual animal studies clients are also looking for advice and guidance on regulatory aspects of the studies plus future application submissions to regulators," says Dr. Peter Holdsworth, consultant to Veterinary Research Management Limited (VRM), a specialist firm providing project management expertise to animal health companies, headquartered in Worcestershire, UK.

The UK is being accepted as a location for European-focused studies, he adds.

VRM supplies a personalized service with flexibility in study offerings plus assistance in developing study designs and models that may not already exist in practice.

Obviously, animal health companies are increasingly exploring opportunities to work with CDMOs having relevant therapeutic experience and technical know-how as equal partners and not mere fee-for-service providers.

The partnership is very valuable if both parties are open to it, say CDMO experts. Instead of doing bits and pieces for a company, partnerships work well when the clients have a clinical candidate identified and they want to develop it moving through regulatory approval to commercialization. It is a big win for both parties.

SPECIES-SPECIFIC MODEL

Despite outsourced manufacturing having a clear edge in the animal health market, the penetration of outsourcing activities in animal health is much less compared to the human health sector.

Experts cite various reasons for this gap explaining some of the factors that determine outsourcing opportunities in animal health.

Dr. Holdsworth holds that the traditional animal health industry is still, in part, working through the phase of separating its business models totally from human health parent companies. With this transition occurring, there are still no strong market signals for third parties to stand up in animal health to accommodate outsourcing, as there is in the mature human health sector.

Meanwhile, Zion of Akston Bio explains how the drug development patterns of both industries are not the same—developing and testing human and animal health therapies are very different. Clinical testing of human candidates is a very long and expensive process while testing candidates for animal health is faster and much less expensive. However, the regulatory requirements for manufacturing development and commercial production are basically the same.

Unlike human health where there is a well-defined model, the biggest challenge in animal drug research, is developing an efficacious model, points out a drug development services expert associated with an Indian CDMO. Things are far too different with animal health, where each animal is a unique model in itself. The physiology of a dog is not exactly

the same as that of a cat. The receptors or drug target of a cat is different from what a horse has and so on. So, a medicine meant for a dog may not work for a cat. This complexity makes outsourcing in the early part of drug discovery biology often cumbersome.

From the development perspective, because all are innovative drugs, there is always the concern that proprietary information is being lost. When it comes to manufacturing, the question of volumes comes foremost. The necessity to outsource in human health is the volumes, he maintains. There, the requirement is large, especially for the cardiovascular or diabetes categories. That is not the case with animal health. Here the therapeutic volumes are small and that can be taken care of in-house.

The complexity of veterinary formulations is yet another factor. Many small molecule veterinary medicines contain multiple components and the CROs must struggle with these complex formulations as regulatory scrutiny is very hard when a product has five or six components, notes Zion.

VET GENERICS ON THE WAY?

The scenario, however, is rapidly changing. Outsourcing in drug development and manufacturing processes has already started to happen.

Leading players are currently outsourcing many of their processes, though extremely cautious, with the processes crucial to innovative products.

Zoetis' global manufacturing and supply chain was supported by 132 CMOs, as of 31 December 2022, shows the company's 2022 annual report.

In the same year, around 75 CMOs/CDMOs manufactured medicines for Boehringer Ingelheim Animal Health, in addition to the German major's own network of 15 production facilities in nine countries.

Not only the big players, but the experts also see many smaller companies entering the animal health space in the coming days just like the biotech companies emerged in human health.

They also envision the generics as well as biosimilars coming up in animal health soon. **CP**

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