Future game-changers in drug discovery for companion animals

By **Dr. Linda Rhodes / Published:** 21 February 2013

There is a dearth of new animal health drugs coming to market. But why is this the case? And how is the industry tackling this issue? Dr. Linda Rhodes of Aratana Therapeutics addresses these questions with an overview of innovation in the new small molecule chemical entities field.

The animal health industry is part of the bigger pharmaceutical industry, and yet our path to the discovery of new drugs is different.

The human pharmaceutical and biotechnology sector sources new small molecule chemical entities from primary screening, based on basic biology and the discovery of new drug targets. Robotic screening, large chemical libraries and talented medicinal chemists have uncovered new chemical entities (NCEs) that have changed the face of human health.

Animal health is different. With the exception of some clever flea, tick and parasitic worm screens, there has been very little effort to screen human drug libraries against veterinary targets. In addition, there is no biotechnology industry feeding NCEs into the pipelines of the major animal health companies and the result is few truly new drugs coming to market.

New products recently approved in the US have been novel re-formulations of 'old molecules', such as: the recent approval of the gonadotrophin-releasing hormone agonist triptorelin in a gel formulation for intra-vaginal use to stimulate ovulation in swine (OvuGel); meloxicam in an oral transmucosal spray formulation (OroCAM); and eprinomectin in a slow-releasing, long-acting formulation for several months of parasite control (Longrange).

In fiscal 2012, 11 original New Animal Drug Applications (NADAs) were approved by the US Food and Drug Administration's Center for Veterinary Medicine. Of the 11, six were for companion animals, five for dogs and one for both dogs and cats. All the molecules for companion animals are either reformulations of old animal health drugs (meloxicam, two formulations of milbemycin) or generic human drugs (fentanyl, cephalexin). Most importantly, there was not one new chemical entity (defined as a molecule new to both human and animal health, reflecting innovation technology) approved.

In 2013, we now have one new chemical entity approved – pradofloxacin (Veraflox) is an antibiotic recently launched by Bayer Animal Health for the treatment of skin and wound infections in cats.

What's getting in the way of increased innovation in pet therapies?

The major US sources of funding for basic research in biomedical sciences are the National Institutes of Health, and the National Science Foundation, both of which focus on human health. The biotechnology industry gets funding from private capital and, for the most part, these companies also focus on human health research.

Just browse the programs of human health conferences or the Biotechnology Industry Organization meetings – there are many companies focusing on disease targets that are human exclusive: Alzheimer's; cholesterol lowering; Parkinson's; and Hepatitis C. Furthermore, there are types of human drugs, such as humanized monoclonal antibodies, siRNA, antibody-toxin conjugates and other human specific proteins, such as erythropoietin, that cannot be used cross-species.

So the focus for finding compounds for veterinary use is on small molecule NCEs for drug targets shared by both animals and humans, and there certainly are compounds that could work in multiple species – pain medications, antibiotics, obesity drugs, small molecule anemia drugs and many others.

In the past, there has been reluctance by human pharmaceutical companies to allow their lead compounds to be used for veterinary medicine. Even back-up compounds were usually off limits, in case they might be needed if the lead compound failed. Biotechnology and small pharmaceutical companies showed a lack of interest and understanding of animal health.

Years ago, there was a perception that if you had to take your molecule to veterinary medicine, it was a mark of weakness and failure – it meant that you thought you couldn't move forward in human health. Add to this the risk aversion to anything new and particularly the fear of regulatory risk, and the likelihood of an NCE being available for veterinary use was about nil.

The large animal health companies, similar to their human health 'parents' have rarely managed to innovate. Much of their R&D budgets are spent on life cycle management.

For example, the Zoetis public offering filing document that preceded Pfizer's successful spin-off, said: "The majority of our R&D investment is focused on brand lifecycle development." Zoetis will expand its product line by "adding new species or claims, achieving approvals in new countries and creating new combinations and reformulations". It is likely the rest of the larger animal health companies are taking a similar approach.

What's changing?

We've all heard the phrase 'One Health' over the last few years. This represents a profound shift in the understanding of the relationship of biology and medicine among the species. Now that not only the human genome has been sequenced but genomes of most of the important domestic animals, it is easier to demonstrate inter-relationships with our mammalian 'cousins', particularly for drug targets.

Business development experts in the biotechnology industry, when approached about veterinary applications to their oncology NCEs are no longer asking, as they did 10 years ago, "You mean dogs get cancer?" or "Why would anyone pay for cancer treatment for a cat?"

There is an increased visibility of animal health in the human biotechnology world. This shift is fueled by a more sophisticated understanding of 'one medicine' and also by commercial considerations. Growing companion animal markets demonstrate the potential value of new veterinary treatments. Aging pets developing chronic diseases and people's willingness to spend money on these diseases is clear. Large emerging markets in China and India are developing for meat, expanding the market for treatments for cattle, pig and poultry that increase productivity.

I recently gave a talk about the commercial opportunities for novel medicines for pets and in the Q&A, a biotech executive expressed skepticism about people spending thousands of dollars on their dog or cat. When I asked the audience members to raise their hands if they had spent more than $1,000 on their pet within the last year, about half the hands went up.

These facts have changed the climate for innovation, most notably in companion animal pharmaceuticals. The biotechnology industry is realizing that some of its innovations can be licensed to provide additional value to its companies as they focus on human health. Knowing which technologies and NCEs will have a veterinary use will require them to become educated on animal health and there is a new willingness to engage.

New sources of innovation

So where will the new chemical entities come from for veterinary medicine? The large animal health companies with human pharmaceutical parents will continue to ask for compounds from human R&D and this may become more of a source in the future than it has in the past.

However, there is continued reluctance that will need to be overcome. Furthermore, as the majority of R&D funding goes to life cycle management of the current product lines, there are few resources left for innovation.

The small pharmaceutical and biotechnology companies, both early- and mid-stage, are beginning to be more interested in licensing out their compounds for veterinary uses. In the past, their customers would be the large animal health companies but these external innovations were competing for limited research budgets with lots of life cycle management and internal R&D. There was little to no venture capital available for animal health to bring these early stage molecules through development and approval.

In the last few years, a few major life sciences venture capital companies have decided that the animal health market is attractive, and have stepped up to put capital towards developing new drugs for animals. Although this trend is in its infancy, there are a few companies that are raising significant funds to support the in-licensing and development of new molecules for unmet or underserved needs in cats and dogs, with the intention of gaining full regulatory approval in major markets for new therapies.

The creation and growth of these companies shows the animal health industry can now look forward to external innovation from well-capitalized, innovative and nimble companies, to complement their internal innovation, in the same way that is now standard in the human pharmaceutical industry.

A different and interesting example of a novel source of funding for directed research is a private foundation funding basic research whose goal is a very specific product – a long acting or permanent contraceptive/sterilant for dogs and cats. The Michelson Prize and Grants program is giving out a total of $50 million in grants to fund basic and applied research to develop drugs and vaccines that could potentially be used to control pet overpopulation. In addition, for any researcher who develops a sterilant that meets some strict criteria, there is a $25m prize incentive.

This program has jump-started basic research in feline and canine reproduction, novel long acting vaccine technology and cutting edge drug delivery. Since very few animal health companies have invested in research in this area, this represents a real step forward that will very likely result in some commercially-applicable new pet contraceptives for licensing by our industry.

This level of funding from a non-profit group is unprecedented in animal health, while in human health there are several examples of non-profit body involvement, some of which are partnerships with industry to address pressing needs such as developing drugs for diarrhea (One World Health partnering with Novartis) and vaccines for malaria (PATH Malaria Vaccine Initiative, funded by the Bill and Melinda Gates Foundation).

Conclusions

This is an exciting time in the animal health industry. The creation of Zoetis as the first large stand-alone animal health company is an important development – as an independent public company, it will be looking for new sources of innovation for its pipeline to meet the demand for growth.

In addition, there are significant drivers of new innovation: the new-found interest of venture capital and human biotechnology in the veterinary world; the growing realization that as animals become more central to our families we are expecting that their medical treatments will be science and evidence-based, just like our own; and the expanding need for increased productivity from farm animals world-wide. These trends will increase the pace of innovation and the availability of new therapies for our industry.

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