Nanotechnology: A lifeline for drying pharma pipelines?

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What has been nanotechnology's greatest contribution to the healthcare sector in the last 5 years?

Vela: Although still far from a cure, the area of healthcare is where nanotechnology has made its greatest contributions is cancer.

Nanotechnology is enabling new applications in the areas of molecular imaging and early detection, in vivo imaging, reporters of efficacy, multifunctional therapeutics and research tools. Significant advances have been made in all of these areas thanks to the funding awarded in 2004 by the US National Cancer Institute's (NCI) Alliance for Nanotechnology, which funded eight Centers of Cancer Nanotechnology Excellence and 12 Cancer Nanotechnology Platform Partnerships.

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From a research perspective, the programme has already yielded more than 1000 peer-reviewed journal publications. From a clinical translation perspective, 50 diagnostics and therapeutic companies have collaborated with this programme and 34 new companies have been formed in the last 4 years — 10 of these new companies were formed just last year. Combined, they have a strong intellectual property portfolio of more than 200 disclosures and patents filed. Additionally, 8–10 clinical trials are associated with this programme and several companies are in pre-IND discussions with the FDA.

Drug delivery is another hot area where nanotechnology has made significant contributions. Today's drugs have issues such as systemic and non-specific delivery, side effects and the need for organic solvents. With nanotechnology, however, advances have been made towards improved localised delivery of drugs to tumour sites, improved efficacy, and reduced side effects. Several nanotech-enabled drugs can now be found on the market such as Abraxane (Abraxis BioSciences), an albumin-bound paclitaxel therapeutic for metastatic breast cancer; liposomal therapies Doxil, DaunoXome and Myocetp; and polymeric therapies, which include Genexol-PM and Oncaspar.

Outside of the NCI Alliance programme, nanotechnology has played a part in addressing an estimated 40%+ of compounds that have poor solubility, which results in reduced efficacy and also makes them difficult to develop. Elan has led the way with its acquisition of NanoCrystal Technology; the key benefits of the technology include, among others, improved biocompatibility, increased absorption rate, dose reduction, faster formulation of compounds, increased performance through variable administration routes (excluding injectable and inhalant delivery methods). Elan had its fifth product approved in late 2009 and has also licensed this technology to J&J, AstraZeneca, Roche and Bristol-Myers Squibb, to name a few.

What challenges does nanotechnology pose to the pharma industry?

Vela: The notion that companies must innovate to survive has become more commonplace as competitive pressures and economic volatility define the business landscape. For challenges affecting the nanotechnology industry, three general categories come to mind; intellectual property issues, regulatory issues and pharmacovigilance. Combined, these have the potential to create a perfect storm for the industry if not properly addressed.

Intellectual property assets are the lifeblood of companies in all industries. By 2011, the pharma industry faces the potential loss of approximately $70–$80 billion of drug revenues as various blockbuster drugs go off-patent. Critics argue that Big Pharma either fell asleep at the wheel by not building nanotech capabilities early enough or that they were more focused on shareholder profits than on innovative therapies. Add the current economic turmoil to this mix and we see pharma companies reducing headcounts to the tune of 69100 job cuts in 2009, up 60% from 2008. As a result, some are even changing their business model to include outsourcing of various functions to stay competitive, but will it be too late for some?

This is where leading biopharma or specialty pharma companies may have a slight advantage. In particular, those focused on nanotech-enabled discovery, development or platform technologies that increase benefits while reducing costs are now in a position of strength for licensing, outsourcing or other collaborative opportunities with Big Pharma. The challenge for Big Pharma will be to swiftly adapt to a new business model that has the right balance of in-house and outsourced processes. They will also need to make efficient use of resources to identify and incorporate nanopharmaceuticals and processes into their pipeline. The challenge for small/medium biopharma and specialty pharma will be to figure out the best way to get on Big Pharma's radar. If they are not properly prepared with ample data, no amount of promised benefits will help and their funding will run out, as venture capitalist funding is predicted to decrease or remain flat in the near term.

With regard to regulatory issues and pharmacovigilance, safety and toxicity concerns continue to mount. An estimated $147-billion worth of nano-enabled commercial and consumer products were sold in 2007 and this amount is predicted to top $3.1 trillion by 2015, according to market analyst firm Lux Research.[1] Concerns over the potential human health and environmental effects, however, could trigger a backlash on further development and commercialisation of product if concerns are left unchecked. The challenge is further complicated by the market's perceived slow pace of regulatory agencies, such as the FDA. While various FDA approved nano drugs have proven benefits well beyond existing therapies, some groups are not convinced that enough is being done to address the potential risks inherent specifically with nanomaterials, even though many of these concerns are felt by industry to be unfounded or over-hyped. Further, the FDA has recognised knowledge gaps and the need to develop a rational regulatory system for approving nano-enabled products. Many approaches are being analysed by agencies and active collaborations are in place to address these gaps and achieve progress.

Will pharmaceutical manufacturing processes need to be adapted in any way to work with nanomaterials?

Vela: Downstream manufacturing processes focused on scale-up, packaging, marketing and such are likely to remain unchanged for companies incorporating nanomaterials into their products. Changes in upstream processes will be required to build up enough expertise to manage the tools and approaches in the discovery process, and also know-how to evaluate and handle materials from a safety and application perspective. Companies that have decided to outsource these upstream processes will still need to understand what they are dealing with and incorporate the necessary processes and collaborative efforts with regulatory agencies to move the product along the development pathway.

How do you think nanomedicines will be regulated in the future?

Vela: The likelihood that current regulatory processes will implement radical changes in the way they evaluate nano-enabled therapeutics and devices in the future is rather low. This is because of the significant parallel efforts and progress involving industry, academia and agencies being made in the area of nanomaterial characterisation. Moving forward, regulatory agencies will benefit from the growing knowledge base and, therefore, be in a better position to evaluate products for safety and identify potential risks. Philosophically speaking, many believe that regulatory agencies should regulate products, not science.

What future advances in nanotechnology do you think will have a significant impact on the pharma and biopharma industries?

Vela: It is no coincidence that more than $18 billion was invested in nanotechnology R&D in 2008 by governments and corporations worldwide, with substantial portions in the areas of health and medicine. With an aging population and rising costs of healthcare, the focus is shifting from managing health to preventative measures. As such, preventative technologies, such as better diagnostic nanodevices, will be in high demand.

Nanotechnology also has the ability to get us closer to personalised medicine. Targeted therapeutics with smart drug delivery devices and theranostics will drive this trend forward. On the surface, these two trends are not likely to have a favourable impact on pharma's current business model, but they could if pharma adapts its business model to align more closely with scientific and market trends. The market will demand these technologies based on benefits and costs as compared to today's alternatives. Areas of nanotechnology advances with a direct benefit to pharma and biopharma are those that will not only further improve efficacy and reduce side effects of existing drugs, but that will enable a faster discovery process to eliminate non-efficacious drugs much earlier and with less investment.

References

1. *Nanomaterials State of the Market Q3 2008: Stealth Success, Broad Impact*, (Lux Research, New York, USA, July 2008).