Latest review of the vaccine R&D pipeline (Autumn '12)

LONDON, UK----7th October 2012----ExpertREACT. Despite no truly "new" product launches for sometime the vaccine industry R&D pipeline is still highly dynamic retaining a good level of innovation. All eyes still await news regarding Novartis' Bexero and the potential implications of the latest ChimeriVAX-dengue (CYD) clinical data. Japanese players continue a slow but certain entry to the global stage.

According to our latest analysis **(1)** of the current vaccine R&D pipeline there are around 90 vaccine projects in clinical development Phases I, II and III. This figure excludes numerous additional projects we term "global initiatives" e.g. tuberculosis and malaria and those focused on pandemic influenza and therapeutic vaccine approaches for non communicable diseases. Analysis of intellectual property(IP)/patent data and company reporting also suggests that there is still significant investment in new projects at the preclinical stages. This indicates R&D momentum in the vaccine industry is still high with companies still keen to invest in innovation.

Analysis shows that the majority of vaccine projects at the clinical stages are within the "novel adult" category. Examples here are the vaccine candidates targetting "nosocomial" of hospital acquired infections such as *Clostridium difficile* (Phase II), *P.aeruginosa* (Phase II/III) and *Staphylococcus aureus* (Phase II). Other notable novel adult programs are Montana US based LigoCyte's clinical stage norovirus VLP vaccine where a Phase II study (NCT01609257) began recruitment in 2012. LigoCyte's program has generated some interesting news recently since it became the target for a $60m milestone payment from Japanese giant Takeda's fledging global vaccine business unit **(2)**. Takeda's division already is investigating a a Haemophilus Influenza type b (Hib) vaccine and combination vaccine containing a Sabin-inactivated poliovirus (s-IPV) vaccine. Last year, another Japanese company Astellas Pharma had previously in-licensed Vical's Therapeutic CMV vaccine (Transvax). Both acquisitions signify Japanese companies willingness to expand their global footprint investing in programs most likely not meeting high thresholds imposed by EU/US industry incumbents.

Also in the **novel adult segment** Pevion Biotech (PEV7) and Novadigm Pharmaceuticals (NDV-3) are developing therapeutic Candida vaccines to reduce the incidence of vulvovaginal candidiasis (RVVC). RVVC affects millions of women each year causing significant discomfort. A safe and effective vaccine would satisfy a great unmet need but could also establish a new "over the counter" product concept unique to vaccines which are either recommended (by schedule) or related to travel.

Insect borne/endemic diseases also contribute a significant number of projects to the current vaccine R&D pipeline. Here diseases such as Dengue, Enterovirus-71, Chikungunya virus, Lyme Borreliosis and Ross River Virus are being investigated in addition to malaria which falls into our "global initiatives" category. Sanofi's ChimeriVAX™-dengue (CYD) which is currently in Phase III testing in Latin America and Asia made the news recently when results from a Phase IIb study in Thailand (Ratchaburi Province) indicated the vaccine was efficacious in children (n=4,002 4-11 yrs) but only afforded efficacy in 3 out of 4 dengue (DEN) serotypes **(3)**. For Enterovirus-71 which is a frequent cause of Hand, Foot and Mouth Disease (HFMD) in Asia; a Phase III trial conducted by Sinovac Biotech is expected to be completed in 2013.

The **infant/adolescent segment** promises to deliver the most near term commercial value to vaccine industry revenues with the filing and continued development of two meningococcal serogroup B vaccines. Novartis filed for European approval of the meningococcal B vaccine, Bexsero (4CMenB) back in December 2010 and has since submitted for approval to health authorities in Canada, Brazil and Australia **(4)**. Pfizer has posted several phase III trials for the meningococcal B vaccine PF-05212366 (MnB rLP2086) and appears now to be concentrating on an adolescent based strategy. Development of MedImmune's (AstraZeneca) respiratory syncytial virus (RSV) vaccine candidate, MEDI-534, was discontinued for safety/efficacy reasons in June 2012 **(5)**. However, development continues with MEDI-559 another live attenuated vaccine which completed a Phase I trial in August 2012. US-biotech Novavax are developing a recombinant RSV-F fusion protein vaccine. Also in the infant segment Merck & Co is developing a *Streptococcus pneumoniae* conjugate vaccine, V114, which completed a phase II trial in infants in August 2012 (NCT01215188).

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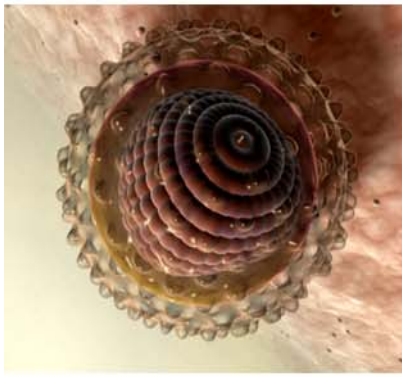

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Based on patent analysis V114 maybe a 15-valent pneumococcal conjugate vaccine hoping to supercede Pfizer's PCV-13. GSK, Sanofi Pasteur and Novartis/Intercell are developing novel *Streptococcus pneumoniae* vaccines (the development status of the latter is uncertain).

In the sexually transmitted diseases (STD) segment Merck & Co is conducting a Phase III multi-national trial with V503, a broad spectrum HPV vaccine (NCT00543543). The HPV types covered by V503 include types in Gardasil (6, 11, 16, 18) and possibly 2, 31, 45 and 58. Several therapeutic HPV vaccines are also in clinical development. As yet no *Chlamydia trachomatis* vaccines have entered clinical development although Sanofi, Novartis and GSK have Intellectual Property (IP) assets. For HSV-2 the most clinically advanced Herpes simplex 2 virus (HSV-2) TX vaccine candidate is Genocea's GEN-003, which entered Phase II development in August 2012 **(5).**

Outside of the main areas other new vaccine projects of future interest include Chandipura virus, Acne vulgaris (P.acnes), *Porphyromonas gingivalis* and Parvovirus.

***Top 5 companies:** GSK Biologicals, Sanofi Pasteur, Merck & Co, Pfizer (Wyeth) and Novartis Vaccines and Diagnostics.

References and Notes:

1) **VacZine Analytics**. Vaccine Pipeline Review (CAT No: VAVS016), published October 2012.
2) Takeda to Acquire LigoCyte Pharmaceuticals Inc. October 5th 2012. Available at: http://www.ligocyte.com/news/documents/Takeda%20Acquires%20LigoCyte%20Pharmaceuticals,%20Inc..pdf. Accessed October 2012
3) Sanofi Pasteur announces publication in the Lancet of world's first efficacy results for its dengue vaccine candidate. September 11, 2012. Available at: http://www.sanofipasteur.com/articles/1136-sanofi-pasteur-announces-publication-in-the-lancet-of-world-s-first-efficacy-results-for-its-dengue-vaccine-candidate.html. Accessed October 2012
4) Novartis Vaccines Corporate Website. Available at: http://www.novartisvacines.com. Accessed October 2012
5) Clinicaltrials.gov. A service of the US National Institutes of Health

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