The current industry landscape for therapeutic vaccines

LONDON, UK----25th January 2011----ExpertREACT. Examination of the therapeutic vaccine space reveals most activity is academic, diverse and explorative. Of the major vaccine players, GSK Biologicals are giving the sector most attention with candidates in advanced clinical development. High unmet in many chronic indications such as cancer and the recent FDA approval of Provenge (sipuleucel-T) continues to provide momentum.

At the beginning of 2011 it is usual to consider new developments and directions for the vaccine industry as the year unfolds. In previous articles we have discussed the major predicted events in the prophylatic space for this coming year but have paid less attention to field of therapeutic (TX) vaccination. Here, conceptually the immune system might be harnessed to combat non-communicable chronic diseases such as cancer, cardiovascular, neurological and autoimmune pathologies. As little as 2-3 years ago, in the minds of both vaccine R&D scientists and indeed company marketing personnel, therapeutic vaccines were viewed upon with some skepticism; mainly due to their low likelihood of success. However, the promise of enormous potential commercial rewards and the recent FDA approval (April 2010) of the first therapeutic cancer vaccine, Dendreon's Provenge (sipuleucel-T) continues to give the field renewed momentum. Dendreon is now approved for the treatment of asymptomatic or minimally symptomatic metastatic castrate resistant prostrate cancer **(1)** and expected to be commercially viable.

To gauge the current level of commercial interest in therapeutic vaccination, **VacZine Analytics** has conducted a new analysis and also updated its vaccine R&D database (VaccineSTATS) previously limited only to commercial prophylatic vaccines **(2)**. Prior to commencing the analysis it did become evident that the definition of a "therapeutic vaccine" greatly influenced the quantity and scope of programs to consider for inclusion. Example points of discussion were whether the term therapeutic vaccine could be used interchangeably with immunotherapy? Where active immunotherapies induce an antigen specific response e.g. against tumor antigens, passive immunotherapy approaches such as monoclonal antibodies, antibody fragments and antibody-drug conjugates are distinctly engineered ex-vivo and were therefore not considered as vaccines in this analysis. Similarly immunotherapies can be non specific where a general systemic immune system response is evoked possibly by use of antisense drugs, oligonucleotides and other immunomodulators. Although integral to some antigen-specific based approach these programs were also excluded from our analysis.

As part of our consideration of therapeutic vaccines for oncology based indications, one could also question whether autologous based approaches are (strictly speaking) vaccines or a sophisticated immunotherapy procedure. With these approaches a cellular sample is removed from a patient, manipulated ex-vivo and reinjected. With the FDA approved Provenge (sipuleucel-T) is a mixture of autologous cells and PAP-GM-CSF fusion protein designed to boost the body's immune system to attack cancerous cells. Given, these types of approaches have been validated by licensure, and are quite common; they were included in the analysis.

Using the above described guidelines and other filtering criteria, we estimate that there are around 350 ongoing Western programs focused on therapeutic vaccination. Due to the large diversity of approaches our analysis also reveals that the majority of investigation is still within the academic sector. This is unsurprisingly given the overall immaturity of the field in terms of commercialization and the need for "unbridled" experimentation common in universities/institutions but often difficult to pursue in the commercial sector. Of the programs that were identified within the commercial (industry) sector, around ~80% of activity was found to be targeting various cancers with the main indications being melanoma, non-small cell lung cancer and prostate cancer. Example programs are GSK Biologicals interventions for melanoma (GSK2132231A and GSK 2302025A) both advanced to Phase III and Phase I respectively. These programs compliment the company's two pronged approached to melanoma alongside other small molecule investigational agents GSK2118436 (BRAF inhibitor) and GSK1120212 (MEK inhibitor) which have recently progressed to Phase III studies **(3).**

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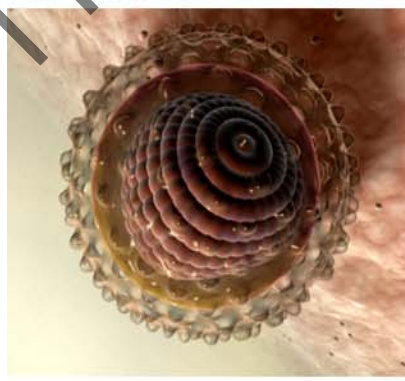

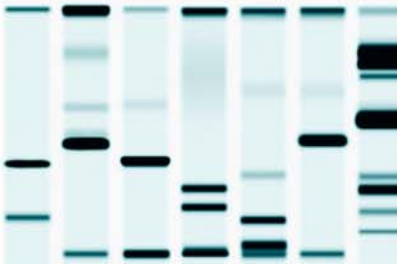

Other several candidate therapeutic vaccines were found to be in development mainly for Alzheimer's disease, smoking cessation, diabetes, hypertension and cocaine dependence. A significant number of commercial programs had also progressed beyond initial Phase I trial with 7 trials reaching advanced Phase III clinical development.

Around 45 commercial companies are investigating therapeutic vaccination indicating a reasonable level of industrial interest. However, the fact that the majority of programs are operated by smaller companies merely with a single program again suggests the sector remains immature. Of the major players GSK is undoubtedly the most active and in the past has formed alliances focused on the sector, notably with Austria-based AFFiRis (October 2008) for an exclusive license and option agreement for Alzheimers candidates **(4).** Other major players such as Merck & Co and Novartis have an interest, although for the latter it is the NVS pharmaceutical division that perpetuated arrangements with Cytos re: Smoking cessation and Alzheimer's disease rather than Vaccines and Diagnostics (V&D). Pfizer, prior to acquistion of Wyeth, also became involved with a therapeutic vaccine for Alzheimer's (ACC-001, PF-05236806) which is in Phase II clinical testing.

Overall, since our discussion of the sector back in 2008, it does appear that the sector has progressed especially with the first FDA approval of Provenge. However, after reexamination of status in 2011, **VacZine Analytics** believes therapeutic vaccination may only receive "prime time" attention within vaccine major players when (and if) GSK licenses its first candidate. This may not be far off.

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

References and Notes:

1) Dendreon Corporate Website. Available at: http://www.dendreon.com/products/. Accessed January 2011
2) VacZine Analytics. VaccineSTATS R&D database (CAT No: VAVS016), Available at: http://www.vaccinestats.com. Accessed January 2011
3) GSK Corporate Press Release. 24th January 2011. GSK announces start of two phase III studies in advanced metastatic melanoma. Available at: http://www.gsk.com/media/pressreleases/2011/2011_pressrelease_10018.htm. Accessed January 2011.
4) GSK Corporate Press Release. 23rd October 2008. Available at: http://www.gsk.com/media/pressreleases/2008/2008_pressrelease_10117.htm. Accessed January 2011

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