

Therapeutic focus - Novel HIV approaches continue to suffer lack of interest



This week's International AIDS Conference in Vienna throws the annual spotlight on the pipeline of candidates that might offer a particularly novel or radical approach to treating a disease which, in the Western world at least, is becoming an increasingly chronic and manageable one.

While the overall pipeline remains dominated by small molecule-based therapies, admittedly aimed at more novel targets, what some researchers continue to strive for is a major breakthrough from other technologies which have revolutionised other therapeutic areas, such as vaccines and antibodies. While such hopes are understandably raised each year at these conferences, the tables below reveal a distinct lack of interest and investment, particularly from big pharma players, in more novel approaches to tackling the HIV virus. In some respects, for example, the prospect of developing an HIV vaccine, one of the industry's biggest targets since the virus exploded on to the scene in the early 1980s, remain as remote as ever.

In control

Symptoms of the disease were first identified in 1981, and by 1984 the HIV virus was classified as the root cause of AIDS. Astonishingly, just three years later in 1987 the first major drug was approved, azidothymidine (AZT), a so-called nucleoside analogue reverse transcriptase inhibitor (NRTI) which remains one of the main classes of agent used in HIV therapy today.

The HIV market has grown rapidly, particularly in the Western world, and last year reached \$14.3bn globally. Indeed, despite reports that market need has largely been met and saturated, sales of HIV drugs will continue to grow 5% annually to \$19.9bn by 2016, analysts believe.

Worldwide HIV Drugs Sales		WW annual sales (\$m)			Market Share	
		2009	2016	CAGR (09-16)	2009	2016
1	Gilead Sciences	5,567	9,590	8%	39%	48%
2	Johnson & Johnson	818	2,595	18%	6%	13%
3	Merck & Co	958	2,259	13%	7%	11%
4	Bristol-Myers Squibb	1,860	1,954	1%	13%	10%
5	ViiV Healthcare (GSK + Pfizer)	2,683	1,579	(8%)	19%	8%
6	Abbott Laboratories	1,719	1,444	(2%)	12%	7%
7	Boehringer Ingelheim	433	221	(9%)	3%	1%
8	Torii Pharmaceutical	58	122	11%	0%	1%
9	Shionogi	-	96	n/a	-	0%
	<i>Other</i>	<i>157</i>	<i>89</i>			
Total HIV Drug Market		14,253	19,949	5%		

The current market remains dominated by NRTIs, NNRTIs, protease inhibitors and integrase inhibitors. Likewise, the most promising pipeline candidates are also expected to be fresher graduates from the same classes of drugs.

The table below highlights the numbers of products adopting a more novel approach to tackling HIV, either as

a prophylactic or treatment. Of the 250-odd pipeline candidates overall, just 76 are from one of four newer classes: vaccines, antibodies, gene therapies and antisense therapies.

Count of novel pipeline HIV candidates					
Status	Vaccines	MAbs	Gene therapy	Antisense	Overall
Phase III	2	-	-	-	2
Phase II	10	3	2	-	15
Phase I	20	2	1	1	24
Pre-clinical	25	6	2	2	35
Report Total	57	11	5	3	76
<i>Abandoned projects</i>	<i>38</i>	<i>13</i>	<i>3</i>	<i>2</i>	

While 57 vaccine candidates may be in active development, almost 40 projects have fallen by the wayside, a failure record perhaps indicative of the current lack of interest in the area.

Understandably the novel scene is dominated by vaccine approaches and the table below highlights some of the late-stage candidates.

However, the most advanced vaccine, Sanofi-Aventis' Alvac-HIV, is a case in point in terms of the overall neglect this field has received in recent years. Despite reporting encouraging phase III results late last year in a 16,000 patient trial in Thailand, in combination with VaxGen's Aidsvax, Sanofi, one of the biggest vaccine makers worldwide, has largely washed its hands of it, inviting further investment from public-private partnerships.

Furthermore, the vaccine candidate itself has been in development for some time now, originally developed by Rhône-Poulenc, one of the historical forerunners of Aventis and now Sanofi-Aventis. More than 25 years on from identifying HIV, Sanofi claims the clinical data from Thailand to be "the first concrete evidence...that a vaccine against HIV is potentially feasible", quite an indictment on the lack of real progress with the technology; although admittedly the constantly revolving and mutating targets presented by HIV represent one of the biggest challenges in modern medicine.

Meanwhile VaxGen's candidate failed in two phase III studies in 2004 and the company has since given up all further direct involvement, licensing it on to Global Solution for Infectious Disease, a not-for-profit group.

It seems until one of these novel approaches produces the kind of clinical data that really makes big pharma pay attention, for now it will be left to the small biotechs and public-private enterprises of the world to plough a somewhat lonely furrow.

Selected late stage novel HIV pipeline candidates

Status	Product	Company(s)	Pharmacological Class
Phase III			
Vaccine	ALVAC-HIV	Sanofi-Aventis	HIV vaccine
	AIDSVAX	VaxGen/Global Solution for Infectious Disease	HIV vaccine
Phase II			
Vaccine	AGS-004	Argos Therapeutics/Kyowa Hakko Kirin	RNA-loaded dendritic cell immunotherapy
	DNA/MVA Vaccine	GeoVax Labs	HIV vaccine
	Global HIV Vaccine	GenVec	HIV vaccine
	HIV DNA Vaccine	Vical	HIV vaccine
	HIV Vaccine (MVA-BN-Multiantigen)	Bavarian Nordic	HIV vaccine
	tgAAC09	Targeted Genetics	HIV vaccine
	TUTI-16	Thymon	HIV vaccine
	V526	Sanofi-Aventis	HIV vaccine
	Vacc-4x	Nutri Pharma	HIV vaccine
	Vacc-5q	Nutri Pharma	HIV vaccine
Monoclonal antibody			
	HIV Antibodies therapy	Polymun Scientific	Anti-HIV agent
	PRO 140	Progenics Pharmaceuticals/Abbott Laboratories	Anti-CCR5 MAb
	TMB-355 (ibalizumab)	TaiMed Biologics/Roche	Anti-CD4 MAb
Gene therapy			
	VRX496 (Iexgenleucel-T)	VIRxSYS/Takara Bio/Oxford BioMedica	Anti-HIV gene therapy
	HGTV43	Enzo Biochem	Anti-HIV gene therapy

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