****Published September 2015*** MarketVIEW: Biodefense vaccines (CAT: VAMV063)

Product Name	:	MarketVIEW: biodefense vaccines
Description	:	Global vaccine overview
Contents		Executive presentation (.pdf)
Therapeutic Area	:	Existing vaccines
Publication date	:	September 2015
Catalogue No	:	VAMV063

Background

Since the 2001 terrorist attacks and continued threats at a global level against many Western governments, the concept of **biodefense** has become an important component of many national countermeasure strategies. To this end, a number of chemical, biologica1¹, radiological, and nuclear (CBRN) terrorism agents were identified as part of a new US law passed in 2004 known as the Project Bioshield Act. This act allowed the US government to guarantee a market for CBRN countermeasures, which up until June 2014 obligated approximately \$3.309 bn in funding.

Despite Project Bioshield and The Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (PAHPRA), which has effectively extended the Project BioShield procurement program to FY2018, the US HHS has obligated 90% to just three threats: anthrax, smallpox, and botulinum toxin. Project BioShield did not acquire any countermeasures against the other eight material CBRN threats, meaning that a significant amount of research and development is still required.

The **MarketVIEW** report covers in depth the background, legislation and current US capabilities with regard to biodefense vaccines with a focus on anthrax, smallpox and other biodefense vaccines. For anthrax and smallpox, detailed coverage is provided on disease epidemiology, past and current vaccines/associated recommendations/policy and corporate development of new generation vaccines for inclusion to the future US Strategic National Stockpile. The objective of this report is to give the reader a full background into the biodefense industry so that future dynamics/trends can be visualized for potential strategy development or market entry.

Bringing life to vaccine strategy...

www.vacZine-analytics.com

¹ Bacillus anthracis and multi-drug resistant Bacillus anthracis, Burkholderia mallei, Burkholderia pseudomallei, Botulinum toxins, Ebola virus, Francisella tularensis, Junin virus, Marburg virus, Rickettsia prowazekii, Variola virus, Yersinia pestis

Methodology

VacZine Analytics has closely monitored all significant source material pertaining biodefence vaccines and related pathogens e.g. smallpox, anthrax. Source materials used are literature articles, government websites, medical bodies and associations, conference proceedings etc. Previously published research by VacZine Analytics in the field of novel vaccines has also been utilised.

PRODUCT CONTENTS:

Published September 2015 (CAT No: VAMV063)

****This product is composed of a summary presentation (.pdf) only

Author's note Contents **Executive summary** Summary table of biodefence vaccines Authors note What is biodefense? Key events in US biodefense policy The US Project Bioshield Act CBRN Agents Determined to Pose a Material Threat Use of FY2004-FY2013 advance appropriations (\$m) Project BioShield Acquisition Activity Project BioShield Countermeasure Acquisition by Threat FY2004-FY2014 (\$m) The Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (PAHPRA) Other important US Biodefense legislation Biomedical Advanced Research and Development Authority (BARDA) BARDA - progress since 2004 Attributes of biodefense vaccines Technology support to biodefense vaccines (US BARDA) Next generation concepts (US BARDA) **Biodefense vaccines: US Capabilities** US HHS Centers for Innovation in Advanced Development and Manufacturing (CIADMs) CIADM: Texas A&M University System (TAMUS) CIADM: ex-Novartis Vaccines and Diagnostics, Cambridge MA CIADM: Emergent Biosolutions, Gathersburg, MD CIADMs - summary map US Department of Defense (DoD) - CBD program Biodefense vaccines: anthrax Anthrax: disease background Types of anthrax Anthrax: US incidence Anthrax and bioterrorism Anthrax: management (general) History of anthrax vaccines: US History of anthrax vaccines: detailed timeline Anthrax vaccine: recommended groups (ACIP - 2009)

Bringing life to vaccine strategy...

www.vacZine-analytics.com

VacZine Analytics[®] Bringing life to vaccine strategy...

Continued.....

Focus on AVA vaccine: Biothrax pre-exposure schedule Anthrax: Post-exposure prophylaxis (PEP) Anthrax vaccines: current and future research HHS PHEMCE anthrax programmatic priorities Next generation Anthrax vaccines: NuThrax[™] Next generation Anthrax vaccines: PreviThrax[™] Next generation Anthrax vaccines: Soligenix Ad5 Vectored Anthrax vaccine - NasoShield (VAXIN) Pfenex Inc (Px563L) PharmAthene: SparVax rPA Anthrax Vaccine Market for Anthrax vaccines Anthrax supply contracts: Emergent Biosolutions Emergent Biosolutions: product sales 2012 - 2014, Biothrax **Emergent Biosolutions – spinout** Biodefense vaccines: smallpox Smallpox: disease background Types of smallpox Smallpox disease symptoms Vaccination and smallpox Conventional smallpox vaccines WHO smallpox eradication campaign Smallpox: six preconditions for eradication met Smallpox vaccines and biodefense Smallpox as a weapon: former USSR Global smallpox vaccine stockpiles (2005) Second generation smallpox vaccines Third generation smallpox vaccines Bavarian Nordic: MVA-BN MVA-BN and US Project Bioshield Bavarian Nordic: US contracts awarded to date MVA-BN and Canada/EU/ROW IMVANEX: revenue potential at high threat level IMVAMUNE: life cycle management Other key vaccines: Kaketsuken Japan: LC16m81 History of Smallpox Vaccine Preparedness in Japan Kaketsuken Japan: LC16m8 - US BARDA program Other biodefense vaccines Botulinum toxin vaccine **Tularemia vaccines Ricin vaccines** Burkholderia vaccines Alphaviruses and biodefense vaccines Bibliography About VacZine Analytics Disclaimer

PAGES: ~90 slides, fully referenced/sourced. Available in .pdf form

Bringing life to vaccine strategy...

www.vacZine-analytics.com



PRODUCT COST:

VacZine Analytics will grant a [enter region] license to [enter client name], for the price of:

FULL PRODUCT - USD \$5995.00/ GBP £3865.00[#] (Region license)*

[#] Indicative rate only. Prevailing rate applied to date of transaction.
 *A region is North America, Europe or ROW
 For orders in the UK, VAT at 20.0% will be added to final invoice total

HOW TO ORDER:

To order please contact your region account manager or order direct at <u>orders@vaczine-analytics.com</u> This report can also be purchased on-line. Please review the **TERMS and CONDITIONS** of purchase.



VacZine Analytics (R) is a trading division of Assay Advantage Ltd, UK Company Number: 5807728 VacZine Analytics (R) and the "spiral logo" are UK Registered Trademarks, 2009

Bringing life to vaccine strategy...

www.vacZine-analytics.com

BIBLIOGRAPHY

- 1. The Project Bioshield Act: Issues for the 113th Congress. By Frank Gotton (June 2014). Congressional Research Service
- US Department of Health and Human Services. BARDA unveils path forward in the BARDA Strategic Plan 2011-2016. Available at: <u>http://www.phe.gov/about/barda/Pages/2011barda-stratplan.aspx</u>. Accessed June 2015
- Renewing the Project Bioshield Act. What has it Brought and Wrought? Policy Brief. Center for a New American Security. January 2013
- 4. US Department of Human and Health Services. Fact sheet. Centers for Innovation in Advanced Development and Manufacturing (CIADM). Available at:

https://www.medicalcountermeasures.gov/media/8862/aspa_0420_20120615_aspr_pr_countermeasures_fact_sheet_combi ned508.pdf. Accessed August 2015

- US Department of Human and Health Services. TAMUS Fact sheet. Centers for Innovation in Advanced Development and Manufacturing (CIADM). Available at: <u>https://www.medicalcountermeasures.gov/media/8871/aspa_0420_20120615_aspr_pr_countermeasures_fact_sheet_tamus_508.pdf</u>. Accessed August 2015
- US Department of Human and Health Services. Novartis Fact sheet. Centers for Innovation in Advanced Development and Manufacturing (CIADM). Available at: <u>https://www.medicalcountermeasures.gov/media/36752/aspa_0420_20120615_aspr_pr_countermeasures_fact_sheet_nova</u> rtis_v02 - 508.pdf. Accessed August 2015
- US Department of Human and Health Services. Novartis Fact sheet. Centers for Innovation in Advanced Development and Manufacturing (CIADM). Available at: <u>https://www.medicalcountermeasures.gov/media/8865/aspa_0420_20120615_aspr_pr_countermeasures_fact_sheet_emerg</u> ent508.pdf. Accessed August 2015
- US Department of Human and Health Services. Map. Fact sheet. Centers for Innovation in Advanced Development and Manufacturing (CIADM). Available at:
- <u>https://www.medicalcountermeasures.gov/media/34653/ciadm_map_1aug2013_508.pdf</u>. Accessed August 2015
 2014 Department of Defense Chemical and Biological Defense Annual Report to Congress. Department of Defense Chemical and Biological Defense Program. March 2014
- 10. Nanotherapeutics to create 150 jobs at new Alachua manufacturing facility. April 2013. Available at: http://www.gainesvillechamber.com/2013/04/nanotherapeutics-to-create-150-jobs-at-new-alachua-manufacturing-facility/. Accessed August 2015
- 11. PharmAthene and Nanotherapeutics Form Strategic Alliance to Advance Biodefense Programs. Sept 2014. Available at: http://ir.pharmathene.com/phoenix.zhtml?c=191999&p=irol-newsArticle&ID=1964759. Accessed August 2015
- US Centers For Disease Control and Prevention. CDC. Basics what is anthrax? Available at: <u>http://www.cdc.gov/anthrax/basics/index.html</u>.Accessed June 2015
 Diseases and conditions. Anthray. Definition. Available at: http://www.doc.gov/anthray/basics/index.html. Accessed June 2015
- 13. Diseases and conditions. Anthrax. Definition. Available at: <u>http://www.mayoclinic.org/diseases-</u> conditions/anthrax/basics/definition/con-20022705. Accessed June 2015
- 14. US Centers For Disease Control and Prevention. CDC. Basics what is anthrax? Available at: http://www.cdc.gov/anthrax/basics/index.html. Accessed June 2015
- 15. US Centers For Disease Control and Prevention. CDC. Basics what is anthrax? Available at: http://www.cdc.gov/anthrax/basics/index.html. Accessed June 2015
- 16. Use of Anthrax Vaccine in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2009
- 17. Rotz LD, Khan AS, Lillibridge SR, Ostroff SM, Hughes JM. Public health assessment of potential biological terrorism agents. Emerg Infect Dis 2002;8:225–30
- 18. Meselson M, Guillemin J, Hugh-Jones M, et al. The Sverdlovsk anthrax outbreak of 1979. Science 1994;266:1202--8.
- 19. World Health Organization. Health aspects of chemical and biological weapons: a report of a WHO group of consultants. Geneva, Switzerland: World Health Organization; 1970.
- 20. Office of Technology Assessment; US Congress. Proliferation of weapons of mass destruction. Publication OTA-ISC-559, no. 53-55.Washington, DC: Government Printing Office; 1993:53--5.
- Tigertt WD. Anthrax. William Smith Greenfield, M.D., F.R.C.P, Professor Superintendent, the Brown Animal Sanatory Institution (1878--81). Concerning the priority due to him for the production of the first vaccine against anthrax. J Hyg (Lond) 1980;85:415--20.
- 22. Brachman PS, Gold H, Plotkin SA, Fekety FR, Werrin M, Ingraham NR. Field evaluation of a human anthrax vaccine. Am J Public Health Nations Health 1962;52:632--45.
- 23. Anthrax vaccine adsorbed. United States patent US 3208909. September 28, 1965.

Bringing life to vaccine strategy...

www.vacZine-analytics.com



- Food and Drug Administration. Investigational New Drug (IND) application: development and approval process. Accessed October 27, 2009. Available athttp://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/Inve stigationalNewDrugINDApplication/default.htm.
- Anthrax Vaccine: GAO's survey of Guard and Reserve Pilots and Aircrew. September 2002. United States General Accounting Office. Available at: <u>http://www.gao.gov/new.items/d02445.pdf</u>. Accessed July 2015
- Meyerhoff A, Albrecht R, Meyer JM, Dionne P, Higgins K, Murphy D. U.S. Food and Drug Administration approval of ciprofloxacin hydrochloride for management of postexposure inhalational anthrax. Clin Infect Dis 2004;39:303--8.
- 27. Food and Drug Administration. Prescription drug products: doxycycline and penicillin G procaine administration for inhalational anthrax (post-exposure). Federal Reg 2001;66:55679--82.
- 28. Shepard CW, Soriano-Gabarro M, Zell ER, et al. Antimicrobial postexposure prophylaxis for anthrax: adverse events and adherence. Emerg Infect Dis 2002;8:1124--32.
- 29. Inglesby TV et al. Working Group on Civilian Biodefense. 2002. Anthrax as a biological weapon, 2002: updated recommendations for management. JAMA 287:2236–2252
- 30. US Department of Health and Human Services. 2014 Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Strategy and Implementation Plan
- 31. Soligenix Corporate Website. July 2015. Available at: <u>http://www.soligenix.com/prod_def_sgx204.shtml</u>. Accessed July 2015
- Soligenix Announces Publication Successfully Demonstrating Enhanced Immunogenicity of its Heat-Stable Anthrax Vaccine
 Zhang J et al. An Adenovirus-Vectored Nasal Vaccine Confers Rapid and Sustained Protection against Anthrax in a Single-
- Dose Regimen Clin Vaccine Immunol. 2013 Jan; 20(1): 1–8.
 34. Krishnan et al. Efficacy and Immunogenicity of Single-Dose AdVAV Intranasal Anthrax Vaccine Compared to Anthrax Vaccine Absorbed in an Aerosolized Spore Rabbit Challenge Model. Clin Vaccine Immunol April 2015 vol. 22 no. 4 430-439
- First Responders. Understanding The Role of First Responders and How Their Partnership With the Federal Government Is Vital To Protecting Americans and Saving Lives. Presentation by Christopher Cox, Select Committee on Homeland Security
- Emergent Biosolutions. United States Secuirty and Exchange Commission. Washington, D.C. 20549. Form 10-K for the fiscal year ended 2014
- Emergent Biosolutions Corporate Press Release. August 6th 2015. Available at: <u>http://emergentbiosolutions.com/news?page=releasetxt&id=2076514&pubdate=August%2006%2C%202015</u>. Accessed August 2015
- 38. US Centres for Disease Control and Prevention. Smallpox Disease Overview. Available at: http://www.bt.cdc.gov/agent/smallpox/overview/disease-facts.asp.Accessed August 2015
- World Health Organisation: Smallpox. Available at: http://www.who.int/csr/disease/smallpox/en/. Accessed August 2015
 Emedicine Health. Smallpox causes. Available at: http://www.emedicinehealth.com/smallpox/page2_em.htm.
- Accessed August 2015
- 41. Kennedy RB et al. Smallpox vaccines for Biodefense. Vaccine 2009 Nov 5; 27S4: D73-D79
- Center for global development. Case I: eradicating small pox. Available at: <u>http://www.cgdev.org/page/case-1-eradicating-smallpox</u>. Accessed August 2015
- 43. Artenstein AW et al. Smallpox Vaccines for Biodefense: Need and Feasibility. Expert Review of Vaccines. 2008; 7(8):1225-1237
- 44. Arita I. Smallpox vaccine and its stockpile in 2005. The Lancet infectious diseases Oct;2005 5(10): 647–52
- 45. Alibek K. Biohazard. New York. NY. Random House Inc 1999
- 46. Henderson DA et al. Smallpox as a biological weapon. Medical and Public Health Management. JAMA 1999: 2127-2137
- National Smallpox vaccine stockpiles. Atlantic Storm analysis. 14th January 2005. Available at: <u>http://www.upmchealthsecurity.org/our-work/events/2005 atlantic storm/flash/pdf/update 1000.pdf</u>. Accessed August 2005
- 48. ACAM2000 Smallpox (vaccinia) vaccine, live package insert www.fda.gov/Cber/label/acam2000LB.pdf (Accessed June, 2008)
- FDA approves second-generation smallpox vaccine www.fda.gov/bbs/topics/NEWS/2007/NEW01693.html (Accessed April, 2008)
- 50. Henderson DA, Inglesby TV, Bartlett JG et al. Smallpox as a biological weapon. JAMA 281, 2127-2137 (1999)
- 51. Bavarian Nordic Corporate Website. MVA-BN. Available at: <u>http://www.bavarian-nordic.com/what-we-do/technologies/mva-bn.aspx</u>. Accessed August 2015
- 52. The Project Bioshield Act: Issues for the 113th Congress. By Frank Gotton (June 2014). Congressional Research Service
- 53. Bavarian Nordic. Interim Financial Report. Jan 1 March 31, 2015. Available at: http://www.bavariannordic.com/media/190207/2015-q1-uk.pdf. Accessed August 2015
- 54. Bavarian Nordic Corporate presentation. June 15, 2015. Available at: <u>http://www.bavarian-nordic.com/media/192047/150615-citi-en.pdf</u>. Accessed August 2015

Bringing life to vaccine strategy...

www.vacZine-analytics.com

VacZine Analytics[®] Bringing life to vaccine strategy...

- 55. Bavarian Nordic Corporate Press Release. August 26th 2014. Available at: <u>http://globenewswire.com/news-release/2014/08/26/661130/0/en/Bavarian-Nordic-Receives-Order-from-the-Canadian-Government-to-Supply-IMVAMUNE-Smallpox-Vaccine.html</u>. Accessed August 2015
- 56. Bavarian Nordic. US Imvamune Contract confirmed. ADR Research H114 results
- 57. Medical countermeasures against smallpox and botulism. A presentation by Hiroyukii Yokote. Kaketsuken (Chemo-Sero-Therapeutic Research Institute)
- M. Yamaguchi, et al. Vaccination research group research report: Ministry of Health and Welfare special research: postvaccination side effects and research regarding treatment of complications. Rinsho to Uirusu 1975, 3: 269-79
- Saito, T. et al. Clinical and immunological response to attenuated tissue-cultured smallpox vaccine. LC16m8.JAMA 2009;301:1025-1033
- 60. T Saito et al. Research on Preparedness for Bioterrorism Associated Events in Japan: Smallpox Vaccine Preparedness Journal of Disaster Research, Vol.4, No.5 pp. 329-336, 2009
- 61. Kaketsuken (Chemo-Sero-Therapeutic Research Institute). KAKETSUKEN Awarded HHS Contract Valued at up to \$34 Million for the Development of a Live Attenuated Smallpox Vaccine (LC16m8). January 12, 2011. Press release.
- 62. Notice of CDC's Discontinuation of Investigational Pentavalent (ABCDE) Botulinum Toxoid Vaccine for Workers at Risk for Occupational Exposure to Botulinum Toxins. MMWR Weekly October 28, 2011. 60 (42);1454-1455
- 63. Byrne, M. P., and L. A. Smith. 2000. Development of vaccines for prevention of botulism. Biochemie 82:955-966 64. Byrne, M. P., T. J. Smith, V. A. Montgomery, and L. A. Smith. 1998. Purification, potency and efficacy of a botulinum
- neurotoxin type A binding domain from Pichia pastoris as a recombinant vaccine candidate. Infect. Immun. 66:4817-5011 65. Smith, L. A., and J. M. Rusnak. 2007. Botulinum neurotoxin vaccines: past present and future. Crit. Rev. Immunol.
- Dennis DT et al. Tularemia as a Biological Weapon. Medical and Public Health Management. JAMA June 6, 2001 Vol 285, No 21
- 67. NIH News. October 3rd 2005. Large Tularemia Vaccine Contracts Among New NIAID Biodefense Awards.
- 68. Marohn ME et al. Live attenuated tularemia vaccines: recent developments and future goals. Vaccine. 2013 Aug 2; 31 (35): 3485-91
- 69. Roy et al. Thermostable ricin vaccine protects rhesus macaques against aerosolized ricin: Epitope-specific neutralizing antibodies correlate with protection. PNAS. 3782-3787 March 24th 2015 Vol 112 No 12
- 70. Vitetta et al., 2006, PNAS, 105:2268-2273
- 71. Vitetta et al., 2012, Recombinant Ricin Vaccine Phase 1B Clinical Trial, Clin. Vaccine Immunol. 10:1697-9
- Silva EB et al. Development of Burkholderia mallei and pseudomallei vaccines. Cellular and Infection Microbiology. 11th March 2013
- Corporate News Release. Bavarian Nordic to Develop Biodefence Vaccine. February 24th 2014. Available at: <u>http://globalbiodefense.com/2014/02/24/bavarian-nordic-to-help-develop-biodefense-vaccine/</u>. Accessed August 2015
- 74. Spurgers KB et al. Vaccine development for Biothreat Alphaviruses. J Bioterr Biodef 2011, S1
- 75. Pittman PR. Long term duration of detectable neutralizing antibodies after administration of live-attenuated VEE vaccine following booster administration with inactivated VEEV vaccine. Vaccine 1996; 14:337-343

www.vacZine-analytics.com

TERMS and CONDITIONS:

VacZine Analytics – a trading division of Assay Advantage Ltd UK Company Number: 5807728 (Herein refered to as "The Company"). (Herein [enter client name] to as "The Client").

1. This finished research product is provided is provided as a Service. Any additional Service required by the client will be subject to a new proposal being prepared.

2. The Service will commence after written (e-mail) or Fax confirmation stating the Client's acceptance of the Service according the description proposed by the Company.

3. Cancellation policy. The Company's cancellation policies are in accordance with the EU Consumer Protection (Distance Selling) Regulations 2000 (DSRs). Prior to acceptance of an order the Company will make available written information regarding Clients cancellation rights. This is posted on the Company website and is available for public review.

4. Cancellation rights: For finished documents - a Clients cancellation rights will last for **seven working days** counting from the day that the order was concluded. If the Services i.e. provision of the documents has taken place with the Clients agreement before this period the Client's cancellation rights have ended.

5. Invoicing will 100% after submission of deliverables to the Client in a form reasonably acceptable to the Client.

6. If not purchased on line invoices are payable within thirty days of the invoice date.

7. All proposals are quoted in **\$USD dollars or £GBP** and invoices are to be settled in the same currency.

8. The Company agrees not to disclose to any third party confidential information acquired in the course of providing the services listed without the prior written consent of the Client. Exception occurs when the information is already in the public domain or when disclosure is necessary to help the Company's employees and agents with the performance of the Company's obligations to achieve satisfactory completion of the project and approved in writing by the Client.

9. Force Majeure: The Company will not be liable for any delay or failure to perform any obligation under this Agreement insofar as the performance of such obligation is prevented by an event beyond our reasonable control, included by not limited to, earthquake, fire, flood or any other natural disaster, labour dispute, riot, revolution, terrorism, acts of restraint of government or regulatory authorities, failure of computer equipment and failure or delay of sources from which data is obtained.

10. Please also refer to Master TERMS and CONDITIONS available upon request.

VacZine Analytics Warren House Bells Hill Bishops Stortford Herts CM23 2NN United Kingdom Tel: +44 (0) 1279 654514 / +44 (0) 7952470582 / Fax: +44 (0) 1279 655926 E-mail: info@vacZine-analytics.com

Bringing life to vaccine strategy...

www.vacZine-analytics.com

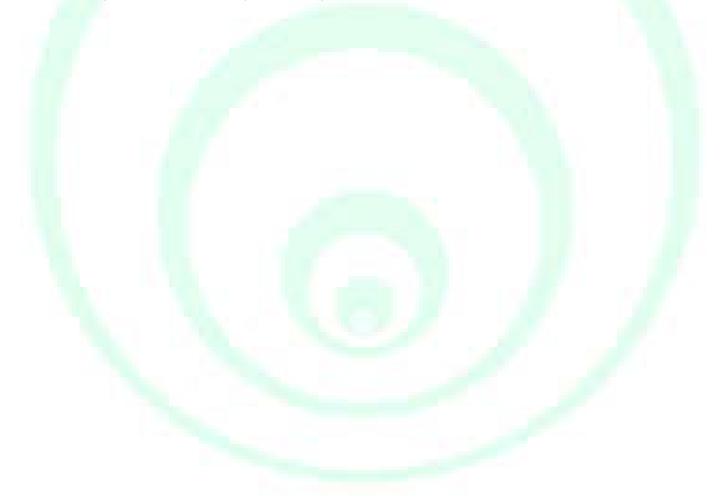


About VacZine Analytics:

VacZine Analytics is an established strategic research agency based in the United Kingdom. Its aim is to provide disease and commercial analysis for the vaccine industry and help build the case for developing new vaccines and biologics.

For more information please visit our website www.vacZine-analytics.com

VacZine Analytics (R) is a trading division of Assay Advantage Ltd, UK Company Number: 5807728 VacZine Analytics (R) and "the spiral logo" are UK Registered Trademarks, 2009



Bringing life to vaccine strategy...

www.vacZine-analytics.com