Application No.	Drug	Applicant
NDA 18–154	LONITEN (minoxidil) Tablets, 2.5 mg and 10 mg	Pharmacia & Upjohn Co., c/o Pfizer, Inc.
NDA 18–285	VISKEN (pindolol) Tablets, 5 mg and 10 mg	Novartis Pharmaceuticals Corp.
NDA 18–445	DOLOBID (diflunisal) Tablets, 250 mg and 500 mg	Merck & Co., Inc., Sunneytown Pike, P.O. Box 4, BLA–20, West Point, PA 19486
NDA 19–661	CYTOVENE IV (ganciclovir sodium) Injection, EQ 500 mg base/vial	Roche Laboratories, Inc., 340 Kingsland St., Nutley, NJ 07110–1199
NDA 20–027	CARDIZEM (diltiazem HCl) Injection, 5 mg/mL and 25 mg/vial	Biovail Pharmaecuticals, Inc.
NDA 20–137	DEMADEX (torsemide) Injection, 20 mg/2 mL (10 mg/mL) and 50 mg/5 mL (10 mg/mL)	Roche Laboratories, Inc.
NDA 20–154	VIDEX (didanosine) Chewable Tablets, 25 mg, 50 mg, 100 mg, 150 mg, and 200 mg	Bristol-Myers Squibb Co., P.O. Box 5100, Wallingford, CT 06492–7660
NDA 20–225	IMDUR (isosorbide mononitrate) Extended-Release Tablets, 30 mg, 60 mg, and 120 mg	Schering Corp., 2000 Galloping Hill Rd., Kenilworth, NJ 07033
NDA 21–238	KYTRIL (granisetron HCl) Oral Solution, EQ 2 mg base/10 mL	Roche Laboratories, Inc.
NDA 21–301	LEVOXYL (levothyroxine sodium) Tablet, 0.3 mg	King Pharmaceuticals, Inc., 501 Fifth St., Bristol, TN 37620

FDA has reviewed its records and, under § 314.161, has determined that the drug products listed in this document were not withdrawn from sale for reasons of safety or effectiveness. Accordingly, the agency will continue to list the drug products listed in this document in the ''Discontinued Drug Product List'' section of the Orange Book. The ''Discontinued Drug Product List'' identifies, among other items, drug products that have been discontinued from marketing for reasons other than safety or effectiveness.

Approved ANDAs that refer to the NDAs listed in this document are unaffected by the discontinued marketing of the products subject to those NDAs. Additional ANDAs that refer to these products may also be approved by the agency if they comply with relevant legal and regulatory requirements. If FDA determines that labeling for these drug products should be revised to meet current standards, the agency will advise ANDA applicants to submit such labeling.

Dated: June 5, 2009.

Jeffrey Shuren,

Associate Commissioner for Policy and Planning.

[FR Doc. E9–14000 Filed 6–12–09; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, Public Health Service, HHS.

ACTION: Notice.

SUMMARY: The inventions listed below are owned by an agency of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of Federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

ADDRESSES: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804; telephone: 301/496–7057; fax: 301/402–0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Improved Antibodies Against ErbB4/Her4

Description of Technology: ErbB4/Her4 is a receptor tyrosine kinase that regulates cell proliferation, cell differentiation and cell survival. ErbB4 has been implicated in the pathology of numerous cancers (*e.g.,* breast cancer, non-small cell lung carcinoma, adenocarcinoma), as well as psychiatric disorders (*e.g.,* schizophrenia). As a result, ErbB4 is an excellent target for developing therapies against these diseases. Unfortunately, the study of ErbB4 has been slowed by the lack of highly specific and functional antibodies against the receptor.

In order to overcome the deficiencies with current ErbB4 antibodies, NIH inventors have generated three rabbit monoclonal antibodies with improved properties and versatility. Specifically, the mAb-6, mAb-7 and mAb-10 hybridomas produce antibodies with a high degree of specificity and affinity for ErbB4. These antibodies recognize specific epitopes on the intracellular domains of ErbB4 without cross-reaction against other proteins, and can be used successfully in the immunostaining of fixed tissue. Each antibody recognizes both human and mouse ErbB4, whereas only mAb-7 and mAb-10 recognize rat ErbB4.

Applications:

• Basic research tool for the study of ErbB4;

• Reagent for diagnostic applications such as Western Blotting, ELISA, immunofluorescence and immunohistochemistry in fixed tissue samples;
• Reagent for biochemical techniques such as immunoprecipitation.

Advantages:

• Potential to be the gold standard for ErbB4 antibodies due to its specificity and affinity;
• Greater affinity for ErbB4 than currently available antibodies, giving them superior properties in diagnostic and biochemical applications;
• Unlike currently available polyclonal antibodies to ErbB4, the monoclonal antibodies do not cross-react with other proteins;
• Unlike currently available antibodies, these antibodies are capable of immunostaining fixed tissue samples;
• The epitopes on ErbB4 that are recognized by each monoclonal antibody have been mapped.

Relevant Publications:

1. G Carpenter. ErbB-4: mechanism of action and biology. Exp Cell Res. 2003 Mar 10;284(1):66–77.
2. S Britsch. The neruregulin-1/ErbB signaling system in development and disease. Adv Anat Embryol Cell Biol. 2007;190:1–65.

Inventors: Andres Buonanno and Detlef Vullhorst (*NICHD*)

Patent Status: HHS Reference No. E–171–2009/0—Research Material. Patent protection is not being pursued for this technology.

Licensing Status: The technology is available under a biological materials license.

Licensing Contact: David A. Lambertson, PhD; 301–435–4632; *lambertsond@mail.nih.gov.*

Collaborative Research Opportunity: The Eunice Kennedy Shriever National Institute of Child Health and Human Development, Section on Molecular Neurobiology, is seeking statements of capability or interest from parties interested in collaborative research to further evaluate or commercialize specific rabbit monoclonal antibodies generated against the ErbB4 receptor (also known as HER4). Please contact Joseph Conrad III, PhD at 301–435–3107 or *jmconrad@mail.nih.gov* for more information.

Mouse Model of Individual Unresponsive to Interferon

Description of Technology: NIAID has developed a mouse model that produces very high levels of Interferon-alpha-receptor 2 (IFNAR2), both in liver cells and free-floating in serum.

Chronic co-infection of HIV and hepatitis C virus (HCV) is associated with increased overall morbidity and mortality compared to those infected with just one virus. Recent data further suggests that co-infection is also associated with a more rapid progression of liver disease, higher HCV RNA viral levels, decreased cure rate of HCV, and increased toxicities of anti-HCV therapy. Finally, clinical trials have shown that many patients infected with both viruses do not respond to Interferon-based therapy. Research strongly suggests that non-responding patients have an increased level of a free-floating form of IFNAR2, which could block Interferon activity.

Resistance to Interferon therapy also occurs in other diseases, such as autoimmune diseases (*e.g.,* lupus, scleroderma, psoriasis, vasculitis) and certain forms of cancer (*e.g.,* Kaposi's sarcoma, follicular lymphoma). The various means by which resistance arises is currently being researched.

Applications: Study of mechanisms of resistance to Interferon therapy in selected diseases, such as HCV/HIV co-infection and certain cancers; study of Interferon-alpha in auto-immune diseases such as lupus, scleroderma, psoriasis, and vasculitis; drug design and screening.

Advantages:

• A model to screen, develop, and test drugs for HCV among HCV/HIV co-infected patients not responding to Interferon;
• A model for basic research, to study the biology and role of IFNAR2 and its function, along with the role of the Interferon receptor in the development of disease resulting from activation of the immune system.

Development Status: Proof-of-principle studies showing that the mice represent HCV/HIV co-infected individuals not responding to Interferon treatment.

Market: HIV/HCV co-infection is documented in one-third of all HIV-infected persons in the United States, an estimated 250,000 people. Moreover, certain cancers (*e.g.,* Kaposi's sarcoma, follicular lymphoma) normally treated with Interferon-alpha either show initial resistance or develop resistance during therapy, but the mechanism of resistance is highly complex; this mouse model will be useful in learning the paths through which resistance develops, and perhaps in designing strategies to overcome resistance. Finally, autoimmune diseases known to be caused (in whole or in part) by Interferon-alpha include lupus, scleroderma, psoriasis, and vasculitis.

Inventors: Shyamasundaran Kottilil (NIAID), Howard Young (NCI), Michael Polis (NIAID), Anthony Suffredini (NIHCC).

Patent Status: HHS Reference No. E–106–2009/0—Research Tool. Patent protection is not being pursued for this technology.

Licensing Status: Available for non-exclusive Biological Materials Licensing.

Licensing Contact: Bruce Goldstein, J.D., M.S.; 301–435–5470; *goldsteb@mail.nih.gov.*

Collaborative Research Opportunity: The National Institute of Allergy and Infectious Diseases, Laboratory of Immunoregulation, is interested in collaborative research directed toward molecular strategies for vaccine and antiviral development, and animal models of viral hepatitis C. For more information, please contact Rick Williams at 301–402–0960.

Enhanced Immune Response Against Influenza Virus by Priming With a DNA-based Vaccine

Description of Technology: Available for licensing and commercial development are compositions and methods for enhancing an immune response to influenza viruses by priming with DNA-based vaccines encoding influenza proteins. The priming compositions contain DNA constructs with inserted nucleic acids encoding influenza virus hemagglutinin (HA) or an epitope-bearing domain thereof, while the boosting compositions are inactivated influenza vaccines. The DNA constructs are based on proprietary expression systems that increase protein expression relative to commonly used alternatives.

A potential influenza pandemic caused by H5N1 strains of avian influenza virus (bird flu) is a major global concern. The seasonal influenza caused by other subtypes of influenza is also a cause of concern. Vaccination is one of the most effective ways to minimize suffering and death from influenza. However, influenza vaccination does not reduce the risk of community-acquired pneumonia in elderly nor does it decrease the rate of influenza infection in children aged 6–23 months. Strategies to elicit protective immunity with greater potency and breadth therefore remain a priority. The present invention discloses the ability of gene-based priming with influenza hemagglutinin (HA) to prime for an increase in titer and cross-reactivity of the neutralizing antibody response after inactivated influenza virus vaccine boost. After priming with a DNA vaccine encoding HA from a H1N1 strain, boosting with a seasonal influenza vaccine containing this

inactivated virus stimulated a 100-fold increase in the titer of H1 neutralizing antibodies. Of note, this combination immunization, in contrast to either component alone, elicited heterotypic neutralizing antibodies against a H5N1 strain. Similar priming was also observed with a DNA vaccine encoding an HA from a H5N1 strain, with the H5N1 subvirion vaccine boost. These results show that gene-based priming prior to vaccinating with the traditional influenza vaccine boost induced humoral immunity against different subtypes of influenza viruses that increases the potency and breadth of the neutralizing antibody response.

Applications: This invention provides a vaccine strategy for potentially controlling influenza epidemics, including avian flu should it cross over to humans, and seasonal flu strains.

Development Status: Animal studies

Inventors: Gary J. Nabel and Chih-jen Wei (VRC/NIAID)

Patent Status: U.S. Provisional Application No. 61/100,621 filed 26 Aug 2008, entitled ''DNA Prime/Inactivated Vaccine Boost Immunization to Influenza Virus'' (HHS Reference No. E–341–2008/0–US–01).

Related Technology: U.S. Patent No. 7,094,598 issued 22 Aug 2006 and associated foreign rights (proprietary expression system with CMV/R promoter) (HHS Reference No. E–241–2001).

Licensing Status: Available for licensing.

Licensing Contact: Cristina Thalhammer-Reyero, PhD, MBA; 301–435–4507; *thalhamc@mail.nih.gov.*

Use of MMP–8 as a Prognostic Marker for Melanoma

Description of Technology: Cutaneous malignant melanoma is the most common fatal skin cancer, and the incidence of this disease increases each year. The average survival time for patients diagnosed with malignant melanoma is less than ten months. Consequently, it is important to identify and understand genetic alterations leading to malignant melanoma so that new treatments strategies can be developed.

Matrix Metalloproteinases (MMPs) have been associated with increased metastasis and several small molecule inhibitors have been developed as potential anticancer agents. Unfortunately, these inhibitors have been largely unsuccessful despite the research suggesting otherwise and it is clear that additional analyses are warranted. The NIH inventors have recently performed a mutational analysis of the MMP gene family in human cutaneous metastatic melanoma and have identified several novel somatic mutations, most notably mutations in MMP–8. This invention provides methods of identifying specific inhibitors to MMP–8 that could be used to treat patients with MMP–8 mutations. It also provides methods for predicting the prognosis of patients with MMP–8 mutations. Thus, this invention could not only help identify the roles of specific MMPs in melanoma, but also help further the development MMP inhibitors to treat melanoma patients.

Applications:

- Diagnostic array for the detection of MMP–8 mutations.
- Method of predicting the prognosis of melanoma patients.
- Method of identifying MMP–8 activators as therapeutic agents to treat malignant melanoma patients.

Development Status: The technology is currently in the pre-clinical stage of development.

Market:

- Approximately 160,000 new cases of melanoma are diagnosed worldwide each year. Malignant melanoma is increasing faster than any other cancer.
- Melanoma is the most prevalent cancer among women between the ages of 25–29 and the second most prevalent cancer among woman ages 30–34.
- Cutaneous malignant melanoma is the most serious form of skin cancer and accounts for about 75% of all skin cancer deaths.
- One person dies from melanoma every hour.

Inventors: Yardena R. Samuels (NHGRI).

Publication: LH Palavalli et al: Analysis of the matrix metalloproteinase family reveals that MMP8 is often mutated in melanoma. Nat Genet 2009 May;41(5):518–520.

Patent Status: U.S. Provisional Application No. 61/198,384 filed 03 Nov 2008 (HHS Reference No. E–273–2008/0–US–01).

Licensing Status: Available for licensing.

Licensing Contact: Whitney Hastings; 301–451–7337; *hastingw@mail.nih.gov.*

Collaborative Research Opportunity: The National Human Genome Research Institute's Cancer Genetics Branch is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, and/or commercialize this newly identified candidate melanoma diagnostic and prognostic marker as well as to identify and develop possible MMP–8 activators for testing as possible anti-melanoma agents. Please contact NHGRI's Technology Development Coordinator (TDC) Claire T. Driscoll at *cdriscol@mail.nih.gov* for more information.

Methods for Preparing Immunogenic Conjugates

Description of Technology: This technology describes improved methods of synthesis for conjugate vaccines, specifically those against anthrax. The inventors' method is designed to synthesize immunogenic conjugates (*i.e.,* a protein carrier conjugated to a bacterially derived synthetic peptide) that are prepared at a physiological pH, not reversible and do not require reduction with borohydride. The inventors' method comprises reacting the protein carrier with a dihydrazide, and the peptide with a benzaldehyde, or the reverse, then reacting the derivatized peptide and the derivatized protein with each other to form an immunogenic conjugate.

Application: Methods for making conjugate vaccines and reagents.

Advantages: More efficient conjugation methods, higher conjugate yields.

Development Status: Vaccine candidates have been synthesized and preclinical studies have been performed.

Inventors: Rachel Schneerson (NICHD), Joanna Kubler-Kielb (NICHD), Fathy Majadly (NICHD), Stephen Leppla (NIAID), John Robbins (NICHD), Darrel Liu (NICHD), Joseph Shiloach (NIDDK).

Related Publication: J Kubler-Kielb et al. Additional conjugation methods and immunogenicity of Bacillus anthracis poly-gamma-D-glutamic acid-protein conjugates. Infect Immun. 2006 Aug;74(8):4744–4749.

Patent Status: U.S. Patent Application No. 11/005,851 filed 06 Dec 2004 (HHS Reference No. E–040–2005/0–US–01); Foreign Rights Available.

Licensing Status: Available for licensing.

Licensing Contact: Peter A. Soukas, J.D.; 301–435–4646; *soukasp@mail.nih.gov.*

Dated: June 8, 2009.

Richard U. Rodriguez,

Director, Division of Technology Development and Transfer, Office of Technology Transfer, National Institutes of Health.

[FR Doc. E9–13943 Filed 6–12–09; 8:45 am]

BILLING CODE 4140–01–P