



FOR IMMEDIATE RELEASE

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**Hybridon Successfully Completes Phase 1 Healthy Volunteer
Trial of HYB2055, Its Lead 2nd-Generation Immunomodulatory
Oligonucleotide**

-- The Drug Candidate is Safe and Biologically Active --

CAMBRIDGE, MA, March 31 -- Hybridon, Inc. (AMEX: HBY) announced today it has completed a Phase 1 trial of HYB2055 in healthy volunteer subjects. In this trial, this drug candidate was safe and biologically active. HYB2055 is a 2nd-generation immunomodulatory oligonucleotide (IMO™) that combines a novel DNA structure, referred to as an Immunomer™, and a synthetic CpR™ immunomodulatory motif.

“HYB2055 has exhibited an excellent safety profile over the 32-fold range of dosages evaluated in this Phase 1 trial,” said R. Russell Martin, M.D., Senior Vice President of Drug Development at Hybridon. “Evidence of biological activity by several parameters was seen at all dose levels administered and we have already progressed to higher dosages in a separate, on-going Phase 1 trial in oncology patients.”

“Hybridon is developing HYB2055 as IMOxine™ for oncology applications and Amplivax™ as a lower dosage product for vaccine adjuvant use,” added Stephen R. Seiler, Hybridon’s Chief Executive Officer. “Initial results of our Phase 1 cancer trial of IMOxine also have been encouraging. We expect to complete that trial and initiate a Phase 2 trial in cancer patients later this year. The first Phase 1 trial of Amplivax is anticipated to begin in the second quarter of 2004.”

Hybridon presented a poster entitled “Immunological Activity of HYB2055, a TLR9 Agonist, in Healthy Volunteers” at the 95th Annual Meeting of the American Association for Cancer Research held in Orlando, FL, March 27-31, 2004. An

earlier presentation at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics in Boston, MA, (see the Hybridon press release of November 20, 2003) described the safety results of the volunteer trial.

The authors of the current poster are R. Martin, T. Sullivan, L. Bhagat, E. Kandimalla, D. Wang, Q. Zhao, and S. Agrawal from Hybridon, Inc., Cambridge MA; C. Burton, P. Bryson, and T. Ng from Phase 1 Clinical Trials Unit, Plymouth, UK; and S. Binney and L. Handy from Triphasics Clinical Trials Laboratories, Plymouth, UK.

About the Trial

Twenty-eight males aged 18 to 45 years were enrolled in groups of 4 individuals. One subject per group was randomized to receive placebo (saline) and three per group received HYB2055. Each subject was to receive three weekly doses. Subjects resided within a phase 1 unit from the night prior to each dose through 72 hours post-dose for thorough safety assessment, laboratory safety evaluations (including complete differential blood count, platelet count, serum transaminases, serum proteins, triglycerides, creatinine, urea, prothrombin and activated partial thromboplastin times, complement Bb fragment, fibrinogen, C-reactive protein, erythrocyte sedimentation rate, and plasma cortisol) and frequent physical examinations. Subjects were followed for a period of 42 days from the first dose. Immunopharmacological assessments included ELISA measurement of plasma cytokines (IL-6, IL-10, IL-12, tissue necrosis factor-alpha, interferon-alpha, and interferon-gamma) and detailed flow cytometry analysis of circulating leukocyte populations (total T cells, T-helper cells, cytotoxic T lymphocytes, B cells, monocytes, activation markers [CD40, CD69, CD86, HLA-DR], and natural killer cells). Subcutaneous dosages ranged from 0.005 mg/kg/week to 0.16 mg/kg/week. One group received intravenous dosages of 0.04 mg/kg for week 1 and 0.08 mg/kg/week for weeks 2 and 3.

About Hybridon

Hybridon, Inc. is a leader in the discovery and development of novel therapeutics based on synthetic DNA. The Company is developing therapeutics independently and with partners based on two proprietary technology platforms: i) synthetic immunomodulatory oligonucleotide (IMO™) compounds that act to modulate responses of the immune system; and ii) antisense technology that uses synthetic DNA to block the production of disease-causing proteins at the cellular level.

The Company is conducting clinical trials of HYB2055, Hybridon's 2nd generation immunomodulatory oligonucleotide, in oncology patients (this application being known as IMOxine™) and in healthy volunteers. Amplivax™ (the adjuvant application of HYB2055) has been out-licensed by Hybridon for use in a potential therapeutic and prophylactic vaccine for HIV infection. The Company has an ongoing phase 1/2 clinical oncology program of GEM®231, a 2nd generation antisense oligonucleotide targeted to protein kinase A, in combination with irinotecan. Hybridon also is collaborating on the development of additional 2nd generation antisense oligonucleotides for the treatment of cancer and viral infections.

This press release contains forward-looking statements concerning Hybridon that involve a number of risks and uncertainties. For this purpose, any statements contained herein that are not statements of historical fact may be deemed to be forward-looking statements. Without limiting the foregoing, the words "believes," "anticipates," "plans," "expects," "estimates," "intends," "should," "could," "will," "may," and similar expressions are intended to identify forward-looking statements. There are a number of important factors that could cause Hybridon's actual results to differ materially from those indicated by such forward-looking statements, including risks as to whether results obtained in preclinical or early clinical studies, such as the results referred to in this press release, will be indicative of results obtained in future preclinical studies or clinical trials, or warrant further clinical trials and product development; whether products based on Hybridon's technology will advance through the clinical trial process and receive approval from the United States Food and Drug Administration or equivalent foreign regulatory agencies; whether, if such products receive approval, they will be successfully distributed and marketed; whether the patent and patent applications owned or licensed by Hybridon will protect the Company's technology and prevent others from infringing it; whether Hybridon's cash resources will be sufficient to fund product development; and such other important factors as are set forth under the caption "Risk Factors" in Hybridon's Annual Report on Form 10-K for the year ended December 31, 2003, which important factors are incorporated herein by reference. Hybridon disclaims any intention or obligation to update any forward-looking statements.

This and other Hybridon press releases can be found at <http://www.hybridon.com>.