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## **Hybridon Announces Oral Presentation of Results for Phase I Trial of IMOXine<sup>®</sup> at ASCO 2005**

### **- Hybridon Plans New Chemotherapy Combination Study in Non-Small Cell Lung Cancer -**

CAMBRIDGE, MA, and WASHINGTON, DC - May 16, 2004 – Hybridon, Inc. (AMEX: HBY) announced that it and the Lombardi Comprehensive Cancer Center (LCCC) at Georgetown University Hospital today presented Phase I results of a study on IMOXine<sup>®</sup>, Hybridon's lead agonist of Toll-like receptor 9, at ASCO 2005. The results were given in an oral presentation titled "Phase I Trial of Escalating Doses of the TLR9 Agonist HYB2055 in Patients with Advanced Solid Tumors" (Abstract #2503). IMOXine is currently in a Phase II single-agent study in patients with renal cell carcinoma.

The presentation was made by Daniel Moore, M.D. of the Lombardi Comprehensive Cancer Center (LCCC), Georgetown University in the session of Developmental Therapeutics: Immunotherapy. Dr. Moore was honored by ASCO as a Merit Award recipient for the IMOXine presentation.

"IMOXine is a promising cancer compound that was well tolerated in patients and showed immunopharmacological activity in the phase I trial," said John L. Marshall, M.D., Director, Developmental Therapeutics and Associate Professor of Medicine at LCCC. "We are excited about Hybridon's plans to initiate a new Phase I/II study in patients with non-small cell lung cancer (NSCLC) using IMOXine in combination with an established chemotherapy regimen as front-line treatment. This NSCLC trial will be conducted here at Georgetown with Dr. Shakun Malik as Principal Investigator."

“The Phase I results are a strong start to our development strategy for IMOxine. One Phase I patient remains on IMOxine treatment showing continued immune response of white blood cells to weekly treatment through at least 48 weeks as well as long term safety,” said Tim Sullivan, Vice President of Development Programs at Hybridon. “We anticipate expansion into multiple clinical trials in the coming months, starting with the NSCLC trial with Dr. Marshall’s group. We also are seeking collaborations with companies to initiate additional combination trials.”

### **About the Phase I Oncology Trial**

The trial was designed to evaluate the safety and immunologic activity of IMOxine as a monotherapy in patients with refractory solid tumors that had been classified as progressive disease in spite of multiple courses of prior therapies. IMOxine was administered as a monotherapy once a week by subcutaneous injection at dosages of 0.04, 0.16, 0.32, 0.48, or 0.64 mg/kg/week. Treatment duration is open-ended, based on safety and radiology assessment of tumor status at 8-week intervals.

Nineteen of 23 patients completed at least four consecutive weeks of treatment to fulfill the safety evaluation requirements of the protocol. IMOxine induced immunological activity as shown by hematology and flow cytometry parameters such as lymphocyte mobilization and increases in serum cytokines including IL-12. Although data from a Phase I oncology trial are highly dependent on baseline patient status, many of the immunology results indicate the possibility of a bell-shaped dose response curve over the range of 0.04 to 0.64 mg/kg/week.

Seventeen patients were assessed for disease status by radiology and clinical evaluation after eight weeks of treatment, and nine of these patients were determined to have stable disease. One patient with metastatic renal cell carcinoma has maintained stable disease through the Week 56 evaluation and continues on treatment.

Adverse effects have been consistent with the expected immune stimulation activity of IMOxine, and primarily have been mild to moderate injection site reactions of erythema and induration, pain, and “flu-like” symptoms (rigors/chills, fever, nausea, myalgia, headache, malaise, and fatigue). Observations that were considered serious adverse events and possibly related to IMOxine treatment have been: transient hypoxia, dyspnea, and rigors/chills 1 hour post-dose (1 patient); abdominal pain with nausea/vomiting (1 patient); and anemia requiring transfusion (2 patients).

### **About IMOxine**

IMOxine is Hybridon’s a 2nd-generation immune modulatory oligonucleotide (IMO™) that functions as an agonist of Toll-like Receptor 9 (TLR9), a specific protein receptor in certain cells of the immune system. Other receptors also may play a role in the immune system response to IMOxine. TLR9 has been shown to recognize bacterial DNA and induce a defensive immune response, producing a Th1-type cytokine profile that allows modulation of host dendritic cells and B lymphocytes. IMOxine and its murine analogue have

been studied in a variety of preclinical tumor models, as monotherapy and in combinations with selected chemotherapeutic agents and monoclonal antibodies, and with radiation. IMOXine (also known as HYB2055 for Injection) is currently in a Phase II, multi-center, open label monotherapy study in patients with metastatic or recurrent clear cell renal carcinoma.

### **About Hybridon**

Hybridon, Inc. is developing novel therapeutics based on synthetic nucleic acid chemistry for the treatment of cancer, asthma/allergies, and infectious diseases. Hybridon's proprietary IMO drug candidates are designed to modulate immune responses through Toll-like receptors, the body's first line of defense against disease. The Company's nucleic acid chemistry expertise has also generated a portfolio of partnered products and intellectual property, creating the potential for long-term value for Hybridon. For more information please visit our website at [www.hybridon.com](http://www.hybridon.com).

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 studies or early clinical trials, such as the results reported here, 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 patents 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 Quarterly Report on Form 10-Q filed on May 10, 2005, which important factors are incorporated herein by reference. Hybridon disclaims any intention or obligation to update any forward-looking statements.

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