

HYBRIDON, INC.

**Prospectus Supplement No. 1 dated January 26, 2005
to the Prospectus Dated December 9, 2003**

The information in this prospectus supplement concerning the selling stockholders supplements the statements set forth under the caption "Selling Stockholders" in the prospectus. This prospectus supplement should be read in conjunction with the prospectus, which is required to be delivered with this prospectus supplement.

Investing in our common stock involves a high degree of risk. See "Risk Factors" beginning on page 3 of the prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement is truthful or complete. Any representation to the contrary is a criminal offense.

Selling Stockholders

The table below sets forth, to our knowledge, information about the selling stockholders listed in the table as of December 31, 2004 and supersedes the information regarding Bruce Alexander, Optima Life Sciences Limited, Spencer Trask & Co. and Sam V. Vail in the table appearing under the heading "Selling Stockholders" in the prospectus. In addition, the table below reflects the transfer by Don & Sheri Yohe JTWR0S, who are listed in the table appearing under the heading "Selling Stockholders" in the prospectus, to the Donald E. & Sheri J. Yohe Revocable Trust, U/A dtd. 11/16/2000 of beneficial ownership of the shares of common stock set forth in the table below.

We do not know when or in what amounts a selling stockholder may offer shares for sale. The selling stockholders may not sell any or all of the shares offered by the prospectus, as supplemented by this prospectus supplement. Because the selling stockholders may offer all or some of the shares pursuant to this offering, and because there are currently no agreements, arrangements or understandings with respect to the sale of any of the shares, we cannot estimate the number of shares that will be held by the selling stockholders after completion of this offering. For purposes of this table, however, we have assumed that, after completion of the

offering, none of the shares covered by the prospectus, as supplemented by this prospectus supplement, will be held by the selling stockholders.

Beneficial ownership is determined in accordance with the rules of the SEC, and includes voting or investment power with respect to shares. Shares of common stock issuable upon exercise of warrants that are exercisable within 60 days after December 31, 2004 are deemed outstanding for computing the percentage ownership of the person holding the warrants but are not deemed outstanding for computing the percentage ownership of any other person. Unless otherwise indicated below, to our knowledge, all persons named in the table have sole voting and investment power with respect to the shares of common stock beneficially owned by them, except to the extent authority is shared by spouses under applicable law. The inclusion of any shares in this table does not constitute an admission of beneficial ownership for the person named below.

Name of Selling Stockholder (1)	Shares of Common Stock Beneficially Owned Prior to Offering		Number of Shares of Common Stock Being Offered	Shares of Common Stock to be Beneficially Owned After Offering	
	Number	Percentage		Number	Percentage
Bruce Alexander	28,764(2)	*	28,764(2)	—	—
Amor Ltd.	1,030,050	*	745,891	284,159	*
Banque Saudi Fransi	7,798,602(3)	6.98%	1,322,260	6,476,342	5.79%
Optima Life Sciences Limited	7,725,982(4)	6.83%	4,404,262(5)	3,321,720	2.94%
Mohammad Salaheddine Seifeddine Salhab & Shafya Al-Dughithar Salhab	1,468,767	1.32%	678,082	790,685	*
Spencer Trask & Co.	1,135,259(6)	1.01%	1,135,259(6)	—	—
Sam V. Vail	35,671(7)	*	35,671(7)	—	—
Donald E. & Sheri J. Yohe Revocable Trust, U/A dtd. 11/16/2000	89,041(8)	*	89,041(8)	—	—

* Less than one percent.

(1) The term “selling stockholders” includes donees, pledgees, transferees or other successors-in-interest selling shares received after the date of this prospectus supplement from a selling stockholder as a gift, pledge, partnership distribution or other non-sale related transfer.

(2) Consists of shares of common stock issuable upon the exercise of warrants held by Bruce Alexander.

(3) Includes 865,040 shares of common stock issuable upon the exercise of warrants held by Banque Saudi Fransi.

(4) Includes 2,203,734 shares of common stock issuable upon the exercise of warrants held by Optima Life Sciences Limited.

(5) Includes 1,650,114 shares of common stock issuable upon the exercise of warrants held by Optima Life Sciences Limited.

(6) Consists of shares of common stock issuable upon the exercise of warrants held by Spencer Trask & Co.

(7) Consists of shares of common stock issuable upon the exercise of warrants held by Sam V. Vail.

(8) Includes 20,548 shares of common stock issuable upon the exercise of warrants held by the Donald E. & Sheri J. Yohe Revocable Trust, U/A dtd. 11/16/2000.