

NUVELO INC  
Form 424B3  
December 08, 2005  
PROSPECTUS SUPPLEMENT NO. TWO

(TO PROSPECTUS DATED October 13, 2005)

This filing is made pursuant to Rule 424(b)(3)  
under the Securities Act of 1933 in connection with  
Registration No. 333-128316

## NUVELO, INC.

### Common Stock

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This Prospectus Supplement No. Two supplements and amends the prospectus dated October 13, 2005 relating to the resale by certain stockholders of up to 8,425,000 shares of our common stock.

This prospectus supplement should be read in conjunction with the prospectus dated October 13, 2005, as supplemented by Prospectus Supplement No. One dated November 18, 2005, both of which are to be delivered with this prospectus supplement. This prospectus supplement is not complete without, and may not be delivered or utilized except in connection with, the prospectus, including any amendments or supplements to it.

We are filing this prospectus to reflect a draw down by us pursuant to the common stock purchase agreement by and between us and Kingsbridge Capital Limited, dated August 4, 2005.

The table appearing under the caption **Selling Stockholder** on pages 24-25 of the prospectus is hereby supplemented by adding the following to the end of that table, immediately after the paragraph and bullet point added by Prospectus Supplement No. One:

On November 23, 2005 we delivered notice to Kingsbridge to effect a draw down of up to \$9,400,000. The first trading day of the eight day pricing period for this draw down was November 25, 2005 and, in connection with this draw down, on December 7, 2005 we issued an aggregate of 1,186,297 shares of our common stock to Kingsbridge at an aggregate purchase price of \$9,400,000.

**Investing in our common stock involves a high degree of risk. Please carefully consider the Risk Factors beginning on page 4 of the prospectus, as well as the section entitled Risk Factors included in our recent quarterly and annual reports filed with the Securities and Exchange Commission.**

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.

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The date of this Prospectus Supplement is December 8, 2005.