

IsoRay, Inc.  
Form 424B5  
December 28, 2010

Filed pursuant to  
Rule 424(b)(5)  
File No. 333-162694

**PROSPECTUS SUPPLEMENT**

(To Prospectus dated November 13, 2009  
and Prospectus Supplement dated November 24, 2010)

This prospectus supplement (this "Supplement") supplements and amends the prospectus, dated November 13, 2009, included in the IsoRay, Inc. registration statement on Form S-3 (File No. 333-162694) filed on October 27, 2009 and declared effective by the U.S. Securities and Exchange Commission on November 13, 2009, as supplemented by the prospectus supplement filed on November 24, 2010 (as so supplemented, the "Prospectus"), which relates to the sale of 2,250,000 shares of our common stock and warrants to purchase up to 4,041,667 shares of our common stock (the "Securities"). This Supplement does not relate to our issuance of additional Securities beyond the 2,250,000 shares of our common stock and warrants to purchase up to 4,041,667 shares of our common stock originally covered by the Prospectus.

This Supplement should be read in conjunction with, and may not be delivered or utilized without, the Prospectus, which is to be delivered with this Supplement. This Supplement is qualified by reference to the Prospectus, except to the extent that the information in this Supplement updates and supersedes the information contained in the Prospectus. If there is any inconsistency between the information in the Prospectus and this Supplement, you should rely on the information in this Supplement.

Our common stock is traded on the NYSE Amex under the symbol "ISR." On December 27, 2010, the last reported sale price of our common stock on the NYSE Amex was \$1.11.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus supplement is December 28, 2010.

The information appearing under the caption "Description of the Securities We Are Offering – Description of the Warrants" commencing on page S-18 of the Prospectus is hereby supplemented and amended by adding the information below. All references contained in the Prospectus relating to the Series A Warrants and the Series C Warrants shall be deemed by virtue of the filing of this Supplement to refer to the Amended and Restated Series A Warrants and the Amended and Restated Series C Warrants, respectively.

#### Amendment to Series A and Series C Warrants

On November 22, 2010, IsoRay, Inc., a Minnesota corporation (the "Company"), entered into a Securities Purchase Agreement (the "Agreement") with a certain purchaser identified on the signature pages thereto (the "Buyer"). Pursuant to the terms of the Agreement, the Company sold (the "Offering") to the Buyer, in a registered offering, an aggregate of 2,250,000 shares of the Company's common stock, par value \$0.001 per share (the "Shares"). As part of the transaction, the Buyer also received four series of warrants (collectively, the "Warrants") - (i) Series A Warrants in an amount equal to \$500,000 divided by the lower of \$1.50 and 90% of the average of the 3 lowest volume weighted average prices out of the 15 trading days preceding the exercise date (with a floor of \$0.75 for a maximum of 666,667 shares of common stock issuable upon exercise of the Series A Warrants); (ii) Series B Warrants in an amount equal to 25% of the number of shares of common stock issued at the Closing, or Series B Warrants exercisable for 562,500 shares of common stock; (iii) Series C Warrants in an amount equal to 125% of the number of shares of common stock issued at the Closing, or Series C Warrants exercisable for 2,812,500 shares of common stock; and (iv) Series D Warrants in an amount equal to 125% of the number of shares of common stock issued at the Closing, or Series D Warrants exercisable for 2,812,500 shares of common stock but the Series D Warrants will only be exercisable to the extent that any of the Series C Warrants may not be exercised due to NYSE AMEX shareholder approval requirements limiting the number of overall below-market securities issuable to no greater than 4,418,026 shares of common stock. As a result of this limitation, the total number of Series A, B and C Warrants that may be issued will not exceed Warrants exercisable for an aggregate of 2,168,026 shares of common stock, and Series D Warrants are expected to be issued to purchase 1,873,641 shares of common stock, assuming the Series A Warrants are exercisable for the maximum number of shares of common stock.

The Company and the Buyer have elected to amend and restate the Series A and Series C Warrants pursuant to an Amendment Agreement entered into between the parties as of December 27, 2010 (the "Warrant Amendment Agreement"). The amended and restated Series A and Series C Warrants (collectively, the "Amended Warrants") to be revised pursuant to the Warrant Amendment Agreement contain the following revisions – (i) the Series A Warrant's expiration date is extended from 90 days to 120 days; (ii) the Series C Warrant's anti-dilution provisions are deleted and replaced with a prohibition on dilutive issuances without the warrant holder's consent; and (iii) the Series C Warrant's provision requiring payment of a cash fee upon failure to timely deliver the warrant shares has been deleted.

As a result of the extension of the expiration date of the Series A Warrant, the Company may now require the exercise of the amended Series A Warrant only on the 120th day after issuance subject to meeting certain equity conditions and to 90% of the average of the lowest three weighted average prices of the common stock during the 15 consecutive trading days preceding the expiration date being in excess of \$0.75.