

Prospectus Supplement No. 1
(To Prospectus dated May 31, 2006)



ZIOPHARM Oncology

ZIOPHARM Oncology, Inc.

11,187,774 Shares

Common Stock

This prospectus supplement (this “Supplement”) supplements and amends the prospectus dated May 31, 2006 and included in our registration statement on Form S-3 (File No. 333-134279) filed on May 19, 2006 and declared effective by the U.S. Securities and Exchange Commission on May 30, 2006 (the “Prospectus”). The Prospectus initially related to the sale of up to 11,187,774 shares of our common stock by the selling shareholders named in the Prospectus or their donees, pledgees, transferees or other successors in interest, including 7,991,256 shares issued in a private placement transaction that we completed on May 3, 2006 (the “May 2006 Private Placement”) and 3,196,518 additional shares issuable upon the exercise of warrants that were issued in the May 2006 Private Placement. This Supplement does not relate to our issuance of additional shares of common stock beyond the 11,187,774 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.

Our common stock trades on the NASDAQ Capital Market under the symbol “ZIOP.”

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

The date of this prospectus supplement is March 4, 2011.

SELLING STOCKHOLDERS

The information in the table appearing under the caption “Selling Shareholders” commencing on page 15 of the Prospectus is hereby superseded in its entirety by the information set forth in the table below. **The information has been updated only to reflect assignments and other transfers of warrants to purchase our common stock that were initially acquired in the May 2006 Private Placement by the holders thereof.**

The information set forth in the table below is current as of March 4, 2011. Since the date on which we were provided with the information regarding their security ownership in ZIOPHARM Oncology, Inc., selling stockholders may have acquired, sold, transferred or otherwise disposed of all or a portion of their securities. Accordingly, the information provided herein for any particular selling stockholder may understate or overstate, as the case may be, such stockholder’s current ownership.

Selling Stockholder	Shares Beneficially Owned Before Offering ⁽¹⁾	Number of Outstanding Shares Offered by Selling Stockholder	Number of Shares Offering by Selling Stockholder Upon Exercise of Certain Warrants	Percentage Beneficial Ownership After Offering ⁽²⁾
ACM SPV LLC’s	2,119	0	2,119	—
Alastair Muir-Taylor	7,019	5,399	1,620	—
Albert M. Leftkovits, M.D.	7,019	5,399	1,620	—
Albert Sebag	291	0	291	—
Alfred J. Smith	7,019	5,399	1,620	—
Amgis Capital International I LP	2,200	0	2,200	—
Amgis Capital International I Ltd.	1,100	0	1,100	—
Amita Rodman Mehta F/B/O ARM-TDA	467	0	467	—
Amita Rodman Mehta IRA and IRA R/O	99	0	99	—
AMP CAPITAL INVESTORS LIMITED AS RESPONSIBLE ENTITY FOR ENHANCED INDEX INTERNATIONAL SHARE FUND	37,516	0	37,516	—
Andrew W. Alstein	14,039	10,799	3,240	—
Andrew W. Schonzeit	8,423	6,479	1,944	—
Andy Miles	74	0	74	—
Anjali Doshi, minor, c/o Navin Doshi	69	0	69	—
Anthony J. Ottavio	8,423	6,479	1,944	—
Anthony Vitale	39,832	0	39,832	—
Arthur Greco	7,019	5,399	1,620	—
ARTUS GMBH & CO. KGaA ^(a)	70,194	53,995	16,199	—
Barclays Bank (Suisse) S.A.	3,300	0	3,300	—
Barry M. Pearl	7,615	4,319	1,296	*
Basil Christakos	8,678	0	2,606	*
BCMF Trustees, LLC	10,551	0	10,551	—
Ben and Sophie Reuben	16,845	12,958	3,887	—
Ben Heller	100,116	32,397	9,719	*
Bernard S. Carrey	4,211	3,239	972	—
Brenda M. Hackney	7,019	5,399	1,620	—
Broadlawn Master Fund, Ltd. ^(b)	28,077	21,598	6,479	—
Bruce W. Jaeger	45,401	34,924	10,477	—
Bushido Capital Master Fund, LP ^(c)	71,284	64,794	6,490	—
Carl Belczynski	54	0	54	—
Carucci Family Partners ^(d)	81,155	32,397	9,719	*
CFRR Holdings, LLC	161	0	161	—

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Charles D. Kleinow	28,600	22,000	6,600	—
Citigroup Global MKT Inc. as IRA Rollover Cust FBO Mai N. Pogue	14,300	11,000	3,300	—
Clarion Capital Corporation ^(e)	98,271	75,593	22,678	—
Common Fund Hedged Equity Company ^(f)	24,100	24,100	0	—
Cooper A. McIntosh MD	11,231	8,639	2,592	—
Cordillera Fund L.P. ^(g)	42,116	32,397	9,719	—
Cranshire Capital, LP ^(h)	42,116	32,397	9,719	—
Cycad Group, LLC ⁽ⁱ⁾	140,390	107,992	32,398	—
Daniel A. Bachtle	11,231	8,639	2,592	—
David A. Dent	22,557	16,198	4,859	*
David Jaroslawicz	69,616	32,397	9,719	*
David S. Hannes	7,019	5,399	1,620	—
DIVALVEST INC	3,502	0	3,502	—
DKG Leasing-2000, LLC.	398	0	398	—
Dr. G. Bruce Miles IRA R/O	2,807	2,159	648	—
Drs. Maya and Mehul Shah	125	0	125	—
Edmund Debler	3,012	0	3,012	—
Edward and Sandra Meyer Foundation, Inc.	4,050	0	4,050	—
Erich W. Wouters, M.D.	7,019	5,399	1,620	—
Esther Stahler	28,077	21,598	6,479	—
ETP/FBR Venture Capital II, LLC ⁽ⁱ⁾	213,109	163,930	49,179	—
Fernando Ahumada	11,231	8,639	2,592	—
Finderne, LLC ^(k)	8,100	8,100	0	—
FIRS Management, LLC ^(l)	11,231	8,639	2,592	—
Fred Vitale	5,824	4,319	1,505	—
Globe Capital Investors Biotech LLC ^(m)	143,477	110,367	33,110	—
Good Steward Trading Company SPC	7,500	7,500	0	—
Griffin Securities, Inc.	138,977	0	138,977	—
Hackney One Investments, LLC ⁽ⁿ⁾	7,019	5,399	1,620	—
Harewood Nominees Ltd. A/C 4689000 ^(o)	125,053	125,053	0	—
Harewood Nominees Ltd. A/C 4721300 ^(p)	42,116	32,397	9,719	—
Harris Lydon	58,931	0	36,582	*
Harry and Susan Newton JTWROS	38,591	16,198	4,859	*
Hartwell Davis, Jr.	14,039	10,799	3,240	—
Hauck & Aufhauser Banquiers Luxembourg S.A. ^(q)	22,461	17,278	5,183	—
Henderson North American Multi-Strategy Equity Fund ^(r)	132,245	101,727	30,518	—
Hollis Capital Partners, LP ^(s)	21,057	16,198	4,859	—
Hollis N. Geiger, Jr.	7,019	5,399	1,620	—
Investment Strategies Fund LP ^(t)	42,116	32,397	9,719	—
Iroquois Master Fund Ltd. ^(u)	11,231	8,639	2,592	—
J. Jay Lobell	94,252	26,997	8,099	*

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J. Rainer Twiford	14,039	10,799	3,240	—
Jacqueline P. Tanner	20,800	16,000	4,800	—
James A. and Rosemarie Ingrassia JTWROS	19,655	15,119	4,536	—
James B. Metzger	2,069	0	2,069	—
James E. Cantrell, Jr.	14,039	10,799	3,240	—
Jane R. Shoup IRA	7,019	5,399	1,620	—
Jay Lobell	630	0	630	—
Jeanne Marie Kiss IRA	467	0	467	—
Jeff Eisenberg	7,019	5,399	1,620	—
Jeffrey R. Johnson	5,615	4,319	1,296	—
Jeffrey R. Marshall	18,323	0	18,323	—
Jennifer & John McNealey	63	0	63	—
Jimmie H. Harvey SEP IRA	5,399	5,399	0	—
John Knox	19,470	0	10,362	*
Jorge Ahumada	14,039	10,799	3,240	—
Jorge Altschuler	11,231	8,639	2,592	—
Joshua Moskowitz	42	0	42	—
Julia R. Lucian	15,000	0	15,000	—
Karl Ruggenberg	9,924	0	2,074	*
Kazuaki Yonemoto	14,039	10,799	3,240	—
Kenneth E. Bush, Jr.	7,019	5,399	1,620	—
Kieran MacCarthy, minor, c/o Navin Doshi	69	0	69	*
Klaus Kretschmer	28,077	21,598	6,479	—
Knott Partners, L.P. ^(v)	200,900	200,900	0	—
Lab Partners ^(w)	5,615	4,319	1,296	—
Lakeside Partners LLC ^(x)	28,077	21,598	6,479	—
Larry Gellman	70,194	53,995	16,199	—
Laurie Widder Revocable Trust 2004	261	0	261	—
LBI Group, Inc. ^(y)	1,123,109	863,930	259,179	*
Les Fils Dreyfus & Cie S.A.	1,455	0	1,455	—
Lewis Opportunity Fund, LP ^(z)	53,347	41,036	12,311	—
Lindsay A. Rosenwald, M.D. ^(aa)	1,573,794	0	250,449	2.01%
Louis Smookler	17,326	0	5,181	*
Mai N. and Gerald A. Pogue JTWROS	42,900	33,000	19,906	*
Man Mash Limited	100	0	100	—
Manali MacCarthy, minor, c/o Navin Doshi	69	0	69	—
Mario Pasquel and Begona Miranda	23,254	5,399	1,620	*
Mark Ahn	209	0	209	—
Mark Zizzamia	44,956	0	44,956	—
Mattherhorn Offshore Fund Limited	283,348	283,348	0	—
Matthew A. King	7,019	5,399	1,620	—
Michael A. Lindley	10,799	10,799	0	—

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Michael G. Lindley and Nina Lindley Joint Tenants by the Entireties	3,240	0	3,240	—
Michael Geschwer	104	0	104	—
Michael Hoffman	1,283	0	1,283	—
Michael Rosenman	64,797	0	32,943	*
Michael Weiser ^(bb)	318,609	0	18,319	*
Millennium Partners, L.P. ^(cc)	793,486	431,965	129,590	*
Modern Capital Fund LLC ^(dd)	36,500	28,077	8,423	—
Mosaix Ventures LP ^(ee)	210,583	161,987	48,596	—
MP Asset Management LLC	19	0	19	—
MP Asset Managers, L.P.	1,272	0	1,272	—
MP BioPharmaceutical Partners, LP	17,710	17,710	0	—
MP BioPharmaceutical Fund Ltd.	25,485	25,485	0	—
Mr. Guy Pommares	36	0	36	—
Murray J. McCabe	104,541	26,997	8,099	*
N. Dean Meyer	28,600	22,000	6,600	—
Natasha Doshi, minor, c/o Navin Doshi	69	0	69	—
NBC Securities, Inc.	2,304	0	2,304	—
Neal Polan	7,019	5,399	1,620	—
Neil Herskowitz	25,805	5,399	1,620	*
Neurosurgical Associates PC 401(k) Profit Sharing Trust FBO J. Finley McRae	5,399	5,399	0	—
Nicholas B. Kronwall Trust Dated 11/12/69 ^(ff)	11,231	8,639	2,592	—
Nicole Berg	169,923	86,393	25,918	*
Ocelot BioEquities Inc.	3,240	0	3,240	—
Oppenheim Pramerica Asset Management S.a.r.l. on behalf of FCPOP Medical BioHealth-Trends ^(gg)	224,622	172,786	51,836	—
Orest Bedrij	19,653	15,118	4,535	—
OTA LLC ^(hh)	194,384	0	194,384	—
Pam Investments LTD – I ⁽ⁱⁱ⁾	28,600	22,000	6,600	—
Pam Investments LTD – II ⁽ⁱⁱ⁾	14,300	11,000	3,300	—
Pamatlan, SA	821	0	821	—
Panacea Capital L.P. ^(jj)	7,937	7,937	0	—
Panacea Capital Offshore LTD ^(jj)	211,715	211,715	0	—
Panacea Capital QP, LP ^(jj)	44,925	44,925	0	—
Paul Boni	209	0	209	—
Paul J. Solit	14,221	6,479	1,944	*
Peter Barber	3,288	0	252	*
Philip Isaacson	9,546	7,343	2,203	—
Procific ^(kk)	1,320,004	1,079,914	323,974	*
Procific ^(kk)	55,000	55,000	0	—
ProQuest Investments III, L.P. ^(ll)	1,737,404	1,079,914	323,974	*
Quantitative BioEquities (BVI) Fund, LTD ^(mm)	10,800	10,800	0	—

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Ralph Rabman	117	0	117	—
Reuben Taub	28,039	10,799	3,240	*
Richard J. Kasten	7,559	7,559	0	—
Richard J. Kasten 2005 Living Trust, Karen L. Kasten, Trustee	2,268	0	2,268	—
Richard Maraviglia	470	0	470	—
Riverside Contracting LLC ^(nm)	25,805	5,399	1,620	*
Robert Friedman	777	0	777	—
Rodney Cawood	7,019	5,399	1,620	—
Roger Philipp	28,600	22,000	6,600	—
Ropa Investments, Ltd	4,093	0	4,093	—
Ruth Widder	209	0	209	—
S.L. Goldblatt, Inc. Frozen Retirement Trust	615	0	615	—
Salvatore Saraceno	44,956	0	44,956	—
Sam J. Lewis	7,019	5,399	1,620	—
Sanjan Dhody	8,423	6,479	1,944	—
Scott G. Sink	7,019	5,399	1,620	—
Scott Katzmann	65,760	0	36,943	*
Sergio Masdival	7,019	5,399	1,620	—
Shoshone Partners, L.P. ^(oo)	124,000	124,000	0	—
Smithfield Fiduciary, LLC ^(pp)	512,708	215,982	64,795	*
South Ferry #2, LP ^(qq)	140,388	107,991	32,397	—
Stephen Rocamboli	51,039	0	10,362	*
Sterling Securities Int. Ltd. ^(rr)	37,623	28,941	8,682	—
Stern Agee & Leach Inc. C/F J. Finley McRae R/O IRA	1,620	0	1,620	—
Stern Agee & Leach Inc. C/F William A. Legg, Jr. IRA	14,039	0	3,240	*
Stern Agree & Leach Inc. C/F Jimmie H. Harvey Jr. SEP IRA	1,620	0	1,620	—
Steve Lisi	2,156	0	2,156	—
Steven Tish	107	0	107	—
Stuart Gollomp	5,138	3,952	1,186	—
Susan Rho	14,300	11,000	3,300	—
Sushant Kumar	68	0	68	—
Suzanne Brandt	7,019	5,399	1,620	—
Tanna Enterprises, LLC ^(ss)	7,019	5,399	1,620	—
The Weyers Group, LLC ^(tt)	14,039	10,799	3,240	—
Thomas A. Lambert, III	7,019	5,399	1,620	—
Thomas J. Curtin, Sr.	14,039	10,799	3,240	—
Timothy McInerney ^(uu)	626,923	0	80,737	*
Tokenhouse Trading Pte Ltd ^(vv)	74,463	21,598	6,479	*
Tony Nikolich	8,423	6,479	1,944	—
Vanac Industries, Inc.	89	0	89	—
Vidacos Nominees Designation Misefl	52,295	0	52,295	—

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Viram Foundation	1,271	0	1,271	—
Viram Foundation	1,069	0	1,069	—
Viren Mehta and Amita Rodman Mehta	1,582	0	1,582	—
Viren Mehta IRA and R/O IRA	770	0	770	—
Visium Balanced Fund, LP ^(ww)	241,409	185,699	55,710	—
Visium Balanced Offshore Fund, LTD ^(ww)	360,792	277,532	83,260	—
Visium Long Bias Fund, LP ^(ww)	72,593	55,841	16,752	—
Visium Long Bias Offshore Fund, LTD ^(ww)	243,348	187,191	56,157	—
W. Charles Mayer III	7,019	5,399	1,620	—
W.S. Investments, L.P.	6,027	0	6,027	—
Wiley H. Cooper IV	7,019	5,399	1,620	—
William A. Legg, Jr.	10,799	10,799	0	—
William Odenthal	7,000	0	7,000	—
Total		<u>7,991,256</u>	<u>3,196,518</u>	

(1) Beneficial ownership is determined in accordance with SEC rules, beneficial ownership includes any shares as to which the security or stockholder has sole or shared voting power or investment power, and also any shares which the security or stockholder has the right to acquire within 60 days of the date hereof, whether through the exercise or conversion of any stock option, convertible security, warrant or other right. The indication herein that shares are beneficially owned is not an admission on the part of the security or stockholder that he, she or it is a direct or indirect beneficial owner of those shares.

(2) Assumes sales of all shares by the selling stockholders.

- (a) Bernd Fortson has voting and investment control over the shares held by the selling stockholder.
- (b) Jon Bloom, Managing Partner of the selling stockholder, has voting and investment control over the shares held by the selling stockholder.
- (c) Christopher Rossman, Managing Partner of Bushido Capital Partners, Ltd., a Cayman Islands company and the General Partner of the selling stockholder, has voting and investment control over the shares held by the selling stockholder.
- (d) Walter Carucci has voting and investment control over the shares held by the selling stockholder.
- (e) Morton A. Cohen has voting and investment control over the shares held by the selling stockholder.
- (f) David M. Knott has voting and investment control over the shares held by the selling stockholder.
- (g) James P. Andrew and Stephen J. Carter share voting and investment control over the shares held by the selling stockholder.
- (h) Mitchell P. Kopin, President of Downsview Capital, the General Partner of the selling stockholder, has voting and investment control over the shares held by the selling stockholder.
- (i) K. Leonard Judson and Paul F. Glenn share voting and investment control over the shares held by the selling stockholder.
- (j) Wei-Wu He and Bill Snider share voting and investment control over the shares held by the selling stockholder.
- (k) David M. Knott has voting and investment control over the shares held by the selling stockholder.
- (l) John B. Dimmer and John C. Dimmer share voting and investment control over the shares held by the selling stockholder.
- (m) Larry Kopp has voting and investment control over the shares held by the selling stockholder.
- (n) Brenda M. Hackney has voting and investment control over the shares held by the selling stockholder.
- (o) Robert Villiers has voting and investment control over the shares held by the selling stockholder.
- (p) Robert Villiers has voting and investment control over the shares held by the selling stockholder.

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- (q) Jungbluth Fredy has voting and investment control over the shares held by the selling stockholder.
- (r) Robert Villiers has voting and investment control over the shares held by the selling stockholder.
- (s) Paul Siegel and Sheri Siegel share voting and investment control over the shares held by the selling stockholder.
- (t) Matthew Shefler has voting and investment control over the shares held by the selling stockholder.
- (u) Joshua Silverman has voting and investment control over the shares held by the selling stockholder. Mr. Silverman disclaims beneficial ownership of such shares.
- (v) David M. Knott has voting and investment control over the shares held by the selling stockholder.
- (w) Lillian Hahn and Barry J. Hahn share voting and investment control over the shares held by the selling stockholder.
- (x) Jamie Stahler has voting and investment control over the shares held by the selling stockholder.
- (y) Jeff Ferrell and Henry Klein share voting and investment control over the shares held by the selling stockholder.
- (z) W. Austin Lewis IV has voting and investment control over the shares held by the selling stockholder.
- (aa) Includes 563,296 shares that the selling stockholder has the right to acquire from existing stockholders under certain circumstances pursuant to the terms of pledge agreements between the selling stockholder and such existing stockholders.
- (bb) Dr. Weiser is a director of the Company.
- (cc) Millennium Management, L.L.C., a Delaware limited liability company, is the managing partner of Millennium Partners, L.P., a Cayman Islands exempted limited partnership, and consequently may be deemed to have voting control and investment discretion over securities owned by Millennium Partner, L.P. Israel A. Englander is the managing member of Millennium Management, L.L.C. As a result, Mr. Englander may be deemed to be the beneficial owner of any shares deemed to be beneficially owned by Millennium Management, L.L.C. The foregoing should not be construed in and of itself as an admission by either of Millennium Management, L.L.C. or Mr. Englander as to the beneficial ownership of the shares held by Millennium Partners, L.P.
- (dd) Dennis Mykytyn has voting and investment control over the shares held by the selling stockholder.
- (ee) Ranjan Lal has voting and investment control over the shares held by the selling stockholder.
- (ff) Nicholas B. Kronwall, as trustee of the selling stockholder, has voting and investment control over the shares held by the selling stockholder.
- (gg) Dr. Bernd Borgmeier, Dr. Rupert Hengster, J. Gabriel Irwin, Ferdinand-Alexander Leisten, Stephen Pelletier, Susan M. Scheader, John P. Smalling, Andreas Jockel, Harry Rosenbaum, Ute Becker, Alexander Schullgen, Max vo Frantzius, Peter Balle, Thomas Becker, Julia Brauckman, Otmar Gorges, Detlef Vallender, Johann Will, Andreas Becker, Katja Kirchen, Ralf Klein and Ulrike Sauer share voting and investment control over the shares held by the selling stockholder.
- (hh) Ira Levanthal, as senior managing director, has voting and investment control over the shares held by the selling stockholder.
- (ii) Mai N. Pogue, as investment manager, has voting and investment control over the shares held by the selling stockholder.
- (jj) Edmund Debler and Steve Lisi has voting and investment control over the shares held by the selling stockholder.
- (kk) Hamza Amiri and Abubaker Khouri share voting and investment control over the shares held by the selling stockholder.
- (ll) Jay Moorin and Alain Schreiber share voting and investment control over the shares held by the selling stockholder.
- (mm)Mikael Van Loon and Pete Levin share voting and investment control over the shares held by the selling stockholder.
- (nn) Neil Herskowitz and Elliot Herskowitz share voting and investment control over the shares held by the selling stockholder.
- (oo) David M. Knott has voting and investment control over the shares held by the selling stockholder.
- (pp) Highbridge Capital Management, LLC is the trading manager of Smithfield Fiduciary, LLC and has voting control and investment decision over securities held by Smithfield Fiduciary, LLC. Glenn Dubin

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and Henry Swieca control Highbridge Capital Management, LLC. Each of Highbridge Capital Management, LLC, Glen Dubin and Henry Swieca disclaim beneficial ownership of the securities held by Smithfield Fiduciary, LLC.

- (qq) Morris Wolfson has voting and investment control over the shares held by the selling stockholder.
- (rr) Chris Bonvini has voting and investment control over the shares held by the selling stockholder.
- (ss) Donna Darty has voting and investment control over the shares held by the selling stockholder.
- (tt) Robert J. Weyers and Jeffrey J. Weyers share voting and investment control over the shares held by the selling stockholder.
- (uu) Mr. McInerney is a director of the Company.
- (vv) Christina Berger, Gordana Djurin, Andrea Delgado and Christina Bellman share voting and investment control over the shares held by the selling stockholder.
- (ww) Jacob Gottlieb and Dmitry Balyasny share voting and investment control over the shares held by the selling stockholder.