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Exhibit 2

Third Point

Third Point LLC
390 Park Avenue
New York, NY 10022
Tel 212 2247400 Fax 224 7401

Via fax and U.S. Mail

September 23, 2005

Mr. David E. Robinson Chairman, President & CEO Ligand Pharmaceuticals, Inc
10275 Science Drive Center San Diego, CA 92121-1117

Dear Mr. Robinson:

Certain entities advised by Third Point LLC ("Third Point") have acquired 7.0 million shares of Ligand Pharmaceuticals ("Ligand" or the "Company") common stock representing an interest of approximately 9.5% in the Company's outstanding stock. We made these purchases after completing an exhaustive due diligence process of the Company's products, pipeline and management effectiveness (the "Investigation"). Based on our Investigation, we have concluded that Ligand shares, currently around \$7.50 per share, trade at approximately half the value of our worst-case estimated value of \$14 per share - as we outline in this letter. We believe this discrepancy is largely due to the overwhelmingly low regard held by the investment community for the management and Board of the Company. When one analyst was queried about the reputation of the senior executives at the Company, he said that you are "the worst CEO in biotech", and another analyst we spoke with attributed the significant valuation disparity between the current stock price and the much higher intrinsic value of the Company to the "David Robinson Discount". I must wonder how in this day and age the Company's Board of Directors has not held you and Paul Maier responsible for your respective failures and shown you both the door long ago - accompanied by a well worn boot planted in the backside. In contrast to your obvious shortcomings as a CEO, the Ligand scientific staff has done a remarkable job developing and gaining approval for an impressive number of compounds and it is they who have generated the significant value in the Company despite your inability to execute on these assets.

Accordingly, it is our view that this management team is unable to derive value

from the Company's assets and therefore we insist that the Board of Directors

immediately retain bankers to evaluate strategic options, including a sale of

the Company. This process should

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commence concurrently with the upcoming revision of the Company's audited

financial statements.

Below we will set forth a sample of the Company's recent Operational and Financial blunders that support our demands that the Company must be sold:

The launch of Avinza in Q2'02 was reportedly one of the worst product launches in history. Your shareholders and "street" analysts were disappointed that the much ballyhooed release generated a mere \$19M in revenues over the first year after launch with the ONLY once a day sustained release opioid in a \$4 billion market. It is our understanding that you only committed some 50 sales people to the release when your main competitor, Purdue Pharmaceuticals used over 800 representatives to sell OxyContin. Your stock price mirrored this marketing debacle, dropping from \$20.50 in March 2002 to a low of \$3.69 in February 2003. Amusingly, during this period you did an interview with Bloomberg in which you predicted sustained profitability for Ligand beginning in the quarter in which you gave the interview (Q2 `02). Incredibly, a mere three weeks later Ligand announced that it would miss second quarter 2002 estimates badly due to previous channel stuffing issues. As for your predictive powers, since then the Company has posted exactly one profitable quarter (still subject to restatement) and zero profitable years.

You then made the decision to allow Organon to detail Avinza starting April 2003. They developed Avinza into a \$170M drug (as approximated by IMS Health) still low for a best in class compound in a \$4 billion market but nonetheless far better than you alone were able to do. As a result, your stock reached a high of \$24.91 on 4/27/04.

Once again, destruction of shareholder value ensued. On May 5, 2004, you missed "street" analysts' Q1'04 estimates by \$0.12, delivering an EPS loss of (\$0.18) versus consensus estimates of (\$0.06). You then missed Q2'04 and Q3'04 estimates by \$0.13 and \$0.08, respectively. On August 3, 2004, Deloitte & Touche resigned as the Company's independent auditor. On March 17, 2005, you announced a delay in the filing of your 2004 10-K. Finally, on March 28, 2005, you announced the failure of PIII pivotal clinical trials for Targretin in non-small cell lung cancer. Over this time, your stock declined from \$24.91 to a low of \$4.69 on April 18, 2005.

On May 20, 2005, the Company announced that it needed to restate consolidated financial statements for FY'02, FY'03, Q1-Q4'03 and Q1-Q3'04. We are puzzled that you have been unable to do so yet. We are further shocked that you have requested three filing extensions (8/1/05, 8/15/05, and 9/2/05) from NASDAQ and, despite being granted an extra month, were unable to meet the deadline. We also understand that you recently cancelled an appearance at the UBS healthcare conference where you were scheduled to appear Monday, September 26th because the financial statements are still not in order.

Valuation

Notwithstanding the sorry state of the Company, the apparent lack of financial controls, the consistently disappointing results and the abysmal investor relations, we estimate that the value of Ligand's assets far outstrip the current enterprise value of the Company, currently valued by the market at approximately \$700 million on a fully-diluted basis. Using a sum of the parts approach to value the Company, Ligand is worth a minimum of \$14/share (\$1.5 billion enterprise value). The analysis is as follows:

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1. Avinza will generate approximately \$170 million in sales for FY'05. With the market suspension of competitor Purdue Pharma's Palladone, a capable Company should be able to grow sales of Avinza considerably. In fact, we strongly believe that you should be able to double sales of Avinza with the appropriate marketing effort. However, using the conservative assumption that Avinza sales remain flat at \$170 million and assigning an average specialty pharmaceutical sales multiple of 4x yields a base case fair value for Avinza of \$680M.
2. Ontak and Targretin, two small cancer products, will generate approximately \$60 million in sales for FY'05. Again, assigning a 4x multiple to these drugs yields a fair value of \$240M for these assets.
3. Ligand owns significant royalties on numerous late stage product candidates, including the following:
 - a. SB-497115 (a thrombopoietin agonist for thrombocytopenia) - 12% royalty; partnered with GlaxoSmithKline
 - b. LY-818 (a PPAR modulator for Type II Diabetes) - low double digit royalty; partnered with Eli Lilly
 - c. GSK-516 (a PPAR modulator for cardiovascular disease/dyslipidemia) - tiered royalty ranging from 12% to 8%; partnered with GlaxoSmithKline
 - d. LY-674 (a PPAR modulator for atherosclerosis/dyslipidemia) -- low double digit royalty; partnered with Eli Lilly
 - e. NSP-989 (a PR agonist for contraception) - low double digit royalties; partnered with Wyeth
 - f. Bazedoxifene (Serum Estrogen Receptor Modulator for post-menopausal osteoporosis) - 3% royalty; partnered with Wyeth
 - g. Bazedoxifene-PREMARIN (Serum Estrogen Receptor Modulator for post-menopausal osteoporosis) - 3% royalty; partnered with Wyeth
 - h. ERA-923 (Serum Estrogen Receptor Modulator for Breast Cancer) - mid single digit royalty; partnered with Wyeth.

We recommend that the Company stop giving its royalty stream away to Royalty Pharma. Many of the Company's drugs represent \$1 billion market opportunities, driving royalty income to Ligand ranging from \$30 million to \$120 million per product. In particular, we are especially excited about your joint effort with GlaxoSmithKline on SB-497115. While we understand the risks inherent in drug development, we would argue that you should be able to generate a minimum of \$120 million in royalty income by 2010. Applying a 10x multiple to \$120 million and discounting back four years at 20%, we arrive at a 1-year fair value of approximately \$550 million for your royalty business. Again, in our opinion this is a worst-case valuation. It assumes success for only ONE of your royalty products, and assumes that product generates only \$1 billion in revenue.

Mr. Robinson, Ligand shares currently trades below the 1993 IPO price of \$13. You claim in your mission statement that you are committed to 'provide a high level of reward for shareholders.' To date, the only high level of reward you have provided is for short sellers. It is time for you to step down from your position and for the Board of Directors to sell the Company to the highest bidder. We have already spoken to investment bankers who would be happy to take the assignment and believe that there are strategic buyers interested in purchasing the Company for a significant premium.

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I would like to remind the Board of Directors of their fiduciary duty to shareholders, not management. Accordingly, should the Board fail to act or to communicate directly with us, we will take steps to replace the members as soon as practicable through the democratic process.

Sincerely,

/s/ Daniel S. Loeb

Daniel S. Loeb
Chief Executive Officer

Cc: Dr. John W. Kozarich
Mr. Michael A. Rocca
Mr. Carl Peck
Mr. John Groom
Mr. Henry F. Blissenbach
Dr. Alexander D. Cross
Mr. Irving S. Johnson

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