**Why Karyopharm Is The Next ‘Disruptor’**

In the case of Karyopharm, the company’s disrupting technologies come with a moat that has been dug after years of preparation---preparation that any would-be competitor must also undergo.  And the great thing about companies such as Karyopharm, investors of the stock don’t have to wonder if competitors clandestinely plan to disrupt the disruptor. A mere look at FDA submissions offers a birds-eye view of potential competition, as well as the time frame in which trouble might arrive.

In the case of Karyopharm, the view reveals nothing on the horizon for many years to come.

Karyopharm launched on Nasdaq in 2013.  Since the public offering, the company has progressed its lead drug Selinexor through FDA trials for approval of novel treatments for:

* Penta-refractory myeloma;
* Multiple myeloma and;
* Diffuse large B-cell lymphoma (DLBCL)

As stated on its website, Karyopharm is an “industry leader” among companies targeting nuclear export dysregulation as a mechanism to treat cancer.”  I disagree. In fact, Karyopharm is the ONLY company on anyone’s radar targeting nuclear export dysregulation (I.e. specifically the XPO1 protein) as a mechanism to treat cancer.

Karyopharm lead and and disruptive drug, Selinexor, has been the talk of oncology before the company began phase I trials of the drug in 2013, the year Karyopharm came public.

The drug’s promising effect upon the inhibition of the eukaryotic protein XPO1, the protein regulating RNA functions and maintenance of cells, is considered by many oncologists as the Holy Grail protein to target for the reestablishment of a normal cell function turned cancerous.

It is generally accepted by oncologists that, if the human body’s normal function to purge cancer precursors and allow regeneration of cell development (apoptosis), today’s “carpet bombing” process of cancer treatment --- as *CNBC* Jim Cramer has described the present state of cancer treatment protocols --- spares patients the process of killing healthy cells along with malignant ones during chemotherapy.

After cancer cells have begun to replicate themselves, the manipulation of the XPO1 protein’s function determines whether cells continue to grow malignantly or healthfully.

With Selinexor on deck at the FDA, Karyopharm is expected to introduce this first-in-class inhibitor of the XPO1 protein as a novel approach to eradicate cancerous tissue.  Selinexor has already cleared safety and efficacy evaluations via FDA trials, and awaits a decision by the FDA for its approval.

At this time, the final and most meaningful step for investors of KPTI to consider comes when Karyopharm gains final regulatory approval (or not) for the commercial sale of Selinexor when FDA officials convene on the [Prescription Drug User Fee Act (PDUFA)](https://u6067039.ct.sendgrid.net/wf/click?upn=-2BaP6i7nDv5AMOe2NFrBoMjcgIk1-2FOpS85n7VNYnAtzq-2FRUTqVYV99nJHI0OwdsdxMps8IgzTtdpBjdzYhoOiJLJwrhvlXZuTutkhUBArcLYB-2FYA-2FU6sgYEbHn6QW7LNN_sG0ANujnwMb5zLR1cU179yhFGvhh-2BVeISbc3mDrNlUwAku8x2JKS3cUu2kgoDMz6s9e93MW4QKLqhvELHx1l4K9S3t57qEIGPAdi60XRGoM6HLadf-2FoYQwMZEJjY3Qs8ptPjenavlPb-2BAlNtFDnEU6CiPKfAl1mpdO-2B3LKbYl76Q9Pq-2B67Adetmgy7F1Cfso8unwgRImMmOMs-2Bt3GWYSYYPa7Ir57piwNb-2B1jvyxAeFP7Mjdjiapi7RrIi83x3CtWbV5jTSwqaR7To7fzrr0-2FQ6bO9csc3Tp2LXeX6bDVlPtTOCa-2FagiisZaZCNKfCvwIPRP7mALA8L1l-2FBoqpjhcfV8q3XbiyiUOtQF2qi63BHe2lsLaBKioA88R5-2FC1N8YZBeiB-2FA1eFgQZUZW3SeSa5FuQLwerQGRu-2Fh1T577pX3pIwBcDol-2FhdHUD33hcS3mKmm6rbzXJpykXkQ2drmTYwsoqrrBSqq8b8fBko4ceF90WPRvsQkFGwpNrAvTdC2e1Q9nBGURH2eLAijLNY2j6Mu2W9mezSgJJz-2BaxMCBDQk-3D) meeting date, scheduled for April 6, 2019.

The day of April 6 might be the day of the catalyst for an extended bull market for KPTI.  Therefore, I have parsed through lots of journals, articles and interviews before presenting in this report the very best sources of opinion about the impact Selinexor is expected to impact the cancer market.

As a spoiler, the impact is truly disruptive.

**III) After Consulting With Oncologist, I Got Hooked On KPTI**

I’ve found one renowned expert in the myeloma field, and another expert whose credentials and involvement in the discussions at medical conferences are extensive.  Both do not represent Karyopharm.

The renowned expert in the field of nuclear medicine at John Theurer Cancer Center, David Siegel M.D., PhD, shed the most insight into the magnitude and significance of the FDA trial results demonstrated by Selinexor.  The other expert, Christian Gasparetto M.D. of Duke Cancer Institute, Duke University, who I quote and link to her interview, expounded my understanding in more detail regarding the role Selinexor has when combined with today’s front-line agents.

As you’ll see, Dr. Siegel practically wrote this entire report for me.  Aside from the brief discussion about the revenue implications of an FDA approval of Selinexor might have for Karyopharm, Dr. Siegel touched upon all the points I want to make in this report about the no. 1 catalyst for what could be a soaring stock price.

And comments made by Dr. Gasparetto about Karyopharm phase II STORM study (efficacy) and her opinion of the study sealed the deal for me to delve much deeper into why oncologists are so excited about Selinexor.

After I spent a weekend delving into the data and comparative analysis surrounding Selinexor, I have come to agree with Dr. Siegel and Dr. Gasparetto that this breakthrough drug is expected by them to be a very big deal.

So, what did Dr. Siegel say about Selinexor?

In a [video](https://u6067039.ct.sendgrid.net/wf/click?upn=B3b2QVtR07unCLj8-2FpqBWmaEDmC2uJybIifWmemi1XI-2BR37xV4GnG9V1ZW13sh6-2FdpXHuXFUCH5awC0qpdnQXQ-3D-3D_sG0ANujnwMb5zLR1cU179yhFGvhh-2BVeISbc3mDrNlUwAku8x2JKS3cUu2kgoDMz6s9e93MW4QKLqhvELHx1l4K9S3t57qEIGPAdi60XRGoM6HLadf-2FoYQwMZEJjY3Qs8ptPjenavlPb-2BAlNtFDnEU6CiPKfAl1mpdO-2B3LKbYl76Q9Pq-2B67Adetmgy7F1Cfso8unwgRImMmOMs-2Bt3GWYSYYPa7Ir57piwNb-2B1jvyxAeFP7Mjdjiapi7RrIi83x3CtWbV5jTSwqaR7To7fzrr0-2FQ6bO9csc3Tp2LXeX6bDVlPtTOCa-2FagiisZaZCNKfCvwEPVKLFBlzOKgfcBTVJZ2kkdjKRIWegzL9XGxIi3BB4WWCrv3tehgziUmlO0vZGK28NxRXCLJCxpdTuj-2B7Q6D5fCQMZZcJSdFtOt1WWyCBte8Aa4JhjTMYPG9VLLlWQCpW2hptqKe8NUaezKE0RFAXIj6sYNnaR8ZjEvL-2FN6wGQQ92KkIJC2k3cNgymWegG3s-2BGK-2FT89b1P-2FvSgsoIGA3GJyDTNAnhMh86WhQqdcvNEI-3D), posted Jan. 8, 2018, Dr. Siegel enthusiastically described the breakthrough results of Selinexor in clinical trials, and intimated that those results should easily clear FDA hurdles to commercialization and further improvements for more effective commercial drugs in the coming years.

We’ve had a number of clinical trials going on with Selinexor in the United States, right now.  The first one is, just single agent Selinexor. And even in very, very heavily pre-treated patients, we’re seeing response rates of 20%.  We’ve had drugs approved [by the FDA] with response rates in that kind of range in patients not nearly as heavily pre-treated.

Because of the results that Selinexor had reached by January 2018, the drug had been granted an Orphan Drug Designation in the United States for the indication of multiple myeloma.  In addition, the FDA has granted a Fast Track designation for Selinexor for the treatment of heavily pre-treated patients suffering from multiple myeloma (“MM”). We’ll know whether the drug has been approved for these indications on April 6, the PDUFA date.

I think the wider scope of combinations is going to be where we really figure it out.  And there are clinical trials going on in combination with Velcade, in combination with Revlimid, in combination with carfilzomib, in combination with pomalidomide, all of which have shown very, very exciting results.

More about the combination of drugs tested with Selinexor can be found on the company website, [here](https://u6067039.ct.sendgrid.net/wf/click?upn=B3b2QVtR07unCLj8-2FpqBWtY-2FJfKM6VGqswjYr9EKxeeMRkYgcX6dDWamS89FimwFMQPHifFY7LLKETFguSkFIA-3D-3D_sG0ANujnwMb5zLR1cU179yhFGvhh-2BVeISbc3mDrNlUwAku8x2JKS3cUu2kgoDMz6s9e93MW4QKLqhvELHx1l4K9S3t57qEIGPAdi60XRGoM6HLadf-2FoYQwMZEJjY3Qs8ptPjenavlPb-2BAlNtFDnEU6CiPKfAl1mpdO-2B3LKbYl76Q9Pq-2B67Adetmgy7F1Cfso8unwgRImMmOMs-2Bt3GWYSYYPa7Ir57piwNb-2B1jvyxAeFP7Mjdjiapi7RrIi83x3CtWbV5jTSwqaR7To7fzrr0-2FQ6bO9csc3Tp2LXeX6bDVlPtTOCa-2FagiisZaZCNKfCvwK8YMhIwxlkhq2iM3AxMwhSyd3cz4N7xPYwXG2oIECcJqQuQsuNX95Miig8s1yX2Upkx6cjQDGNLaHr1AH9R5dVKh-2FnGa4XBSo9obIWX4mQb-2BwakIUckuNhF7p7VLE1-2FQUV8Z44g3RhCh-2FZZKsa2NU6H56K8fgL4sOKqypmgrBIp6aD-2BzWxXJODwzRVH8bIzL7zs3JNkaIEsUuBeYmzAW7dPzWVvehP00zdGYC4MY25c-3D).  Early results of Selinexor suggest the drug’s efficacy and tolerance increase when taken in conjunction with today’s commonly prescribed agents.

Theory is, that there are tumor-suppressor proteins that cancers try to get rid of, the first thing cancer tries to do is get rid of these regulatory molecules that prevent the [cancer] cell from proliferating, cause the cell to die.  And tumor-suppressor proteins are critical in that regulatory process.

What this molecule does is sort of trap those proteins in the nucleus of the cell, so that the levels rise and you get back some of this function.  And I think it’s an incredibly exciting process.

Dr. Siegel continued his discussion of the breakthrough Karyopharm has achieved via Selinexor with an important medical distinction the drug has reached.  And that all-important distinction is, that Selinexor fulfills an “unmet need” in the field of oncology.

“Unmet need.”  Those specific words mean Selinexor and the drug’s derivative trials (conjoining with other agents) typically gain special consideration at the FDA.  In other words, Selinexor is not a me-too drug, and comes with faster approval opportunities and lower cash-burn rates.

Dr. Siegel continued:

Oncoproteins, proteins that are mutated and go out from the nucleus, while the messenger RNAs that code for their synthesis go out from the nucleus, and these proteins that cause proliferation, that cause all kinds of other processes to go on that we don’t want that can be inhibited, as well.

It’s really a different kind of target than we are used to in oncology, in general, and myeloma, specifically.  And I think, while it has been a somewhat difficult molecule from a toxicity prospective, we’re starting to understand how to deal with some of these toxicities.

And I think the spectrum of activity that we’ve seen is remarkable.

Patients, who clearly have no other alternatives, who have responded to this type of therapy, we now have a new definition for **unmet need** in myeloma.

And now there’s some early data on combining this molecule with other agents, like lenalidomide, carfilzomib, like Velcade, like pomalidomide.  And incredibly, even in patients who are highly refractory to those drugs,when you add Selinexor to it, the responses get reestablished. And the synergies, the combinations are so effective that we can pullback on the doses we’re using so that the drug is much, much better tolerated.

So, I think this is one of the most exciting things.

And I think there will be second and third-generation XPO1 inhibitors and potentially other targets in the nuclear pore.

While it’s not a high-profile drug that people are talking about all the time, I think it’s an incredibly exciting drug.

Speaking to a reporter at the ASH: 2018 conference, Christian Gasparetto M.D. of Duke Cancer Institute, Duke University explained in an [interview](https://u6067039.ct.sendgrid.net/wf/click?upn=B3b2QVtR07unCLj8-2FpqBWmaEDmC2uJybIifWmemi1XKUjKiUayAnd-2BcRvecyfbv7kZn54-2BVutdlEGPOR1ZVXaw-3D-3D_sG0ANujnwMb5zLR1cU179yhFGvhh-2BVeISbc3mDrNlUwAku8x2JKS3cUu2kgoDMz6s9e93MW4QKLqhvELHx1l4K9S3t57qEIGPAdi60XRGoM6HLadf-2FoYQwMZEJjY3Qs8ptPjenavlPb-2BAlNtFDnEU6CiPKfAl1mpdO-2B3LKbYl76Q9Pq-2B67Adetmgy7F1Cfso8unwgRImMmOMs-2Bt3GWYSYYPa7Ir57piwNb-2B1jvyxAeFP7Mjdjiapi7RrIi83x3CtWbV5jTSwqaR7To7fzrr0-2FQ6bO9csc3Tp2LXeX6bDVlPtTOCa-2FagiisZaZCNKfCvw7W1cpgE3iQeDml1hsSBK-2B7rt7tE2b-2FH7R5CY3MHq-2Fymp61hkDfCBUHtSsb6AnVyTqBHQXUTl-2F8JK8SLdLpe4qhYMC2V3swVwsSA3wmQBZETXOF4Y-2FA28ffcUtSMuyZkSx-2B0QXwWXeXBodEf7IZuT7Z2JRoi49rrTgER8G3KFsVG2RUxStfbwO1lxNYi-2BTnWJndFnmCoUGBOfMuRRLhV7-2FSjSgEcDNF8w0dXL61w2we0-3D) the results of the STORM study, the study in which efficacy rates were achieved when Selinexor was taken with dexamethasone.

Overall, the Selinexor/dexamethasone therapy reached a positive response rate of 26.2% among heavily pre-treated patients, “which is amazing to have a signal [this high] in this population of patients,” Dr. Gasparetto said.  See [page 10 & 11](https://u6067039.ct.sendgrid.net/wf/click?upn=B3b2QVtR07unCLj8-2FpqBWkiBvYU0Kr-2FnDiCxRj1BjMRB-2BWbRILf7IlqA3QukaSLD8BaOIxi06acrLa-2FvHLcTOw-3D-3D_sG0ANujnwMb5zLR1cU179yhFGvhh-2BVeISbc3mDrNlUwAku8x2JKS3cUu2kgoDMz6s9e93MW4QKLqhvELHx1l4K9S3t57qEIGPAdi60XRGoM6HLadf-2FoYQwMZEJjY3Qs8ptPjenavlPb-2BAlNtFDnEU6CiPKfAl1mpdO-2B3LKbYl76Q9Pq-2B67Adetmgy7F1Cfso8unwgRImMmOMs-2Bt3GWYSYYPa7Ir57piwNb-2B1jvyxAeFP7Mjdjiapi7RrIi83x3CtWbV5jTSwqaR7To7fzrr0-2FQ6bO9csc3Tp2LXeX6bDVlPtTOCa-2FagiisZaZCNKfCvw9Qs24m-2FfoirEsh-2BfSoWQLCUAvhx1jVTXnnD3bOn4RGwJtXndNgME-2F1Jkm2lDUMJi13tC878T6cFuENaLSCGucpTVVBiLYKAZWtT-2Br6-2FJvnGCmgf2TE66QbjHUC8Ym0naOSa1qQ86A1axSgIEqrpLnRhI84vCKrIhqPAcWoXsdb6F7CVfl3Kr1X0sq-2B6-2FI26UIwiVFWwKqLFyrJu0IdDWyGLRyAaVlzor06Iin13QfiY-3D) of the presentation material at the JP Morgan Healthcare Conference of January 7, 2019.

When combined with low-dose dexamethasone, Selinexor reached a 79% positive response rate, “which is an incredible response,” she said.  And added:

…with about one-third of patients achieving, actually, what we call a ‘very good partial response’, where we have at least a 90% reduction of the myeloma, a pretty deep response.  If we take into account even the minor response, the overall response was up to 88%. So, an incredible response for this population of patients [the worst patients of all myeloma cases].

Time of response for those patients among the best response to treatment was one month.  Patients with minor responses, the amount of time needed for response to treatment is approximately seven months.

Dr. Gasparetto concluded that, because of these “incredible” results, the approval of Selinexor in combination with low-dose dexamethasone should be approved and available to patients “very soon --- I hope.”

The XPO1 protein.  For a moment, allow me to delve a little into this critical protein of the human body.  It is this protein and its successful manipulation that has gained Karyopharm special consideration at the FDA.

Without lengthening this report beyond my presentation of conclusions drawn about Selinexor by experts in oncology, I refer readers to the company’s presentation report at the JP Morgan Healthcare Conference of January 2019.  In the report, page 6, you’ll find a graphic and more information about the XPO1 protein; how it functions; and why it’s an important target protein in the science of oncology.

An addition report from [*Science Direct*](https://u6067039.ct.sendgrid.net/wf/click?upn=B3b2QVtR07unCLj8-2FpqBWsVz87QjCPohsEejAVxM2r1fBb7LIbGVIyyG68bpKo9jhROMipc0UfcGJhlGiNMGRMr-2F-2FBVCl9ZdZjARN49TJOY-3D_sG0ANujnwMb5zLR1cU179yhFGvhh-2BVeISbc3mDrNlUwAku8x2JKS3cUu2kgoDMz6s9e93MW4QKLqhvELHx1l4K9S3t57qEIGPAdi60XRGoM6HLadf-2FoYQwMZEJjY3Qs8ptPjenavlPb-2BAlNtFDnEU6CiPKfAl1mpdO-2B3LKbYl76Q9Pq-2B67Adetmgy7F1Cfso8unwgRImMmOMs-2Bt3GWYSYYPa7Ir57piwNb-2B1jvyxAeFP7Mjdjiapi7RrIi83x3CtWbV5jTSwqaR7To7fzrr0-2FQ6bO9csc3Tp2LXeX6bDVlPtTOCa-2FagiisZaZCNKfCvw6AUjR6mobq0C-2BZXu0ghNQzan-2FCviNraC1XNx-2B8uNQJl1oTCJH9Rqr-2BfRP8s04L2muA8UXj-2FRIHELsJ481JihVpeZa0SfYjaq3E2xCZScOH6mrIVDuUhg0b16Nc5hPnWhimGA2dhFvhREkaT5Q8YoTQTL35gisgQAij3DLliLJHcbUPh-2Bfm9StJ2ukfaVblLwbfaC8brnIciP0MaUYUZw7wxCJM4A7A3BJPKThUr7Jgo-3D) discusses the XPO1 protein and the implications Selinexor, and Eltanexor --- the company’s second-generation drug --- of improving tolerability and survival rates.  From this report, investors should take away one thing, which is, that a successful outcome at the FDA for Selinexor, and a successful outcome of second-generation drug: Eltanexor, are believed by oncologists to be the beginning to similar treatment protocols and improved survival rates among patients afflicted with other cancers.

That is why I think KPTI might be a stock worth due diligence from the perspective of a long-term holding time period, in addition to the play coming up April 6.

In the report, *Science Direct* discusses the small molecule inhibitors of XPO1, and the implications of Eltanexor (and subsequent generations) as the potential next drug positively impacting the top line of Karyopharm for many years to come.

*Science Direct* states:

Eltanexor, a second-generation SINE [selective inhibitor of nuclear export] compound with minimal blood–brain barrier penetration and improved tolerability profile in preclinical studies, is currently in phase I clinical studies.  Significant antitumor activity of SINE compounds has been reported in preclinical studies of solid organ malignancies such as pancreatic cancer, breast cancer, lung cancer, renal cancer, and melanoma, as well as hematologic malignancies such as acute myeloid leukemia, chronic lymphocytic leukemia, and mantle cell lymphoma, which have been reviewed previously.  In the present review, we have focused on the effects of SINE compounds in MM [multiple myeloma].

Now you’ve been briefed about Selinexor and its history.

At this point, I’ve demonstrated the value proposition of holding the stock for a short and long haul, with the long haul as my preference, at this time.

But what about Karyopharm competition?

As I’ve stated, there is no competition anywhere on the horizon for a competing drug that alters the mechanism of the XPO1 protein in any way close to the biotechnologies of Selinexor.  But what about alternative approaches to the treatment of myeloma?

**IV) Why CAR T-Cell Therapy Is No Threat To Karyopharm**

Some investors might balk at KPTI and its lead drug because of all the fanfare surrounding CAR T-Cell therapy.  Well, that’s look at that therapy.

And after I lay out the insanity associated with the financial implications of this treatment protocol, you’ll drop your fear of CAR T-Cell therapy as a competing force like handling a hot poker.

CAR T-Cell therapy offered by Gilead and Novartis not only doesn’t achieve impressive enough results to warrant a price tag of between $373,000 and $475,000 per round of treatment protocols, insurers have begun to balk at the 50/50 chance of success, literally, that comes with this outrageous fee.

In response, Novartis has agreed to not charge if the treatment doesn’t show a response within one month of the protocol, which, at first blush, might sound like an attractive proposition.  But after one month positive responses, no assurances can be made of efficacy by the end of the treatment period.

And Gilead has not agreed to such an arrangement.

When compared with the average cancer treatment cost of $163,381 per patient, the high cost of CAR T-Cell therapy becomes a roadblock to treatment for most patients who don’t respond to up to seven front-line therapies.  In these cases, patients don’t experience medication toxicity; but instead, they experience financial toxicity, as insurance providers balk at the price tag of CAR T-Cell therapy taken within a context of response rates.

[*Medscape (Google cached page)*](https://u6067039.ct.sendgrid.net/wf/click?upn=B3b2QVtR07unCLj8-2FpqBWgLsMOp-2BvHAx8ZIwxdm2cvy5A0c1XVTCM0RhQBODfEdwgB9JgICfGRJA7yOtLI3P9HWoByEPTA37rrtSMIxRrv5FlOysWDw7J7SQI1ifFL75iG0iYFekOhH8cCux-2FwsG0ypkc-2FY2vWymv8s69U4Z3DF3sqjrjCQYy3w2JlWdXw9YlezWHk2VKuDq4bNmIro9wA-3D-3D_sG0ANujnwMb5zLR1cU179yhFGvhh-2BVeISbc3mDrNlUwAku8x2JKS3cUu2kgoDMz6s9e93MW4QKLqhvELHx1l4K9S3t57qEIGPAdi60XRGoM6HLadf-2FoYQwMZEJjY3Qs8ptPjenavlPb-2BAlNtFDnEU6CiPKfAl1mpdO-2B3LKbYl76Q9Pq-2B67Adetmgy7F1Cfso8unwgRImMmOMs-2Bt3GWYSYYPa7Ir57piwNb-2B1jvyxAeFP7Mjdjiapi7RrIi83x3CtWbV5jTSwqaR7To7fzrr0-2FQ6bO9csc3Tp2LXeX6bDVlPtTOCa-2FagiisZaZCNKfCvwPNshRKhqVTprirKq2coruIk43BEudme3W3P3S3m9F1FthfKvak6fVnySV1yNacuGnVSFGM8SKJ2aqQmXvTovV-2B26H1fD8Fdbw66sTG-2FZlZcgPrzUCEcBPEw-2BHedhPqSWVMu9WtCzBb2Z2X7uqaLanmni9BLXcwsQslp9cP5xhl1CZxTGebi8077e0-2BEBOkNWO-2FIZGymDZAVBhlcL8Xr6zIfuEdvtpyHiGjieGyLrxGo-3D)explains the ‘rest of the story’ behind the happy headlines about CAR T-Cell therapy:

Two CAR T-cell therapies has now been approved in the United States ― tisagenlecleucel (Kymriah, Novartis), for certain pediatric and young adult patients who have a form of acute lymphoblastic leukemia, and axicabtagene ciloleucel (Yescarta, Kite/Gilead) for adult patients with relapsed/refractory aggressive B-cell non-Hodgkin lymphoma who are ineligible for autologous stem cell transplant.

Both have eye-wateringly high price tags ― $475,000 and $373,000, respectively.

This has been causing problems in getting these products to eligible patients. Snags in reimbursement have been blamed for holding up treatment.

**At the 15 cancer centers in the United States that have been authorized thus far to administer CAR T-cell therapy, only a handful of patients have been treated.  At least 200 others remain on a waiting list**, according to a recent *Bloomberg* [article](https://u6067039.ct.sendgrid.net/wf/click?upn=B3b2QVtR07unCLj8-2FpqBWoxHK4ytgSTtHHMnkzmvKqf8m9xWjE4RJFvUSsH9PpCSLrVIpmW6DVK3-2FAMl-2Bb-2FY1xMFPplMaFeiSJ0Z0k6Dy-2FRT34oM7WTOQiCKlf6C9bW8fqnkXTQAdw9lboz-2BjGHi2CzANZxDUmXcOvYd-2FywdbSI-3D_sG0ANujnwMb5zLR1cU179yhFGvhh-2BVeISbc3mDrNlUwAku8x2JKS3cUu2kgoDMz6s9e93MW4QKLqhvELHx1l4K9S3t57qEIGPAdi60XRGoM6HLadf-2FoYQwMZEJjY3Qs8ptPjenavlPb-2BAlNtFDnEU6CiPKfAl1mpdO-2B3LKbYl76Q9Pq-2B67Adetmgy7F1Cfso8unwgRImMmOMs-2Bt3GWYSYYPa7Ir57piwNb-2B1jvyxAeFP7Mjdjiapi7RrIi83x3CtWbV5jTSwqaR7To7fzrr0-2FQ6bO9csc3Tp2LXeX6bDVlPtTOCa-2FagiisZaZCNKfCvwX0GKcYnVZcOBU2ZYZo5MH8AzxmJOCuZF5cQOqE896dUAvb9KHEWQ07KB5vpEUpyGPVIz6WaDX3Fnk-2BTVm6-2FwSZ-2FZ57oJvGBmMrYxu3Qu-2BJbuIiLxnyfUoSKJSQP8UuzbJl5c4fgFq7riWC99-2BO-2F1gv8CV5ytiLoullyE7mIldb1-2F386i9Btk1th3kt5s-2BHZbSqHDpmgVeqDMYBI4IneXy-2FIPlhdgttFq6Lagqn4cV8w-3D).

"The biggest issue has been insurance, particularly with Medicare and Medicaid," said Michael Bishop, MD, director of the cellular therapy program at the University of Chicago Medicine, Illinois, who was quoted in the article. "There's no billing codes for this. It's been difficult, to be very blunt."

**In addition, related costs can also push up the price of this therapy. For example, treatment carries a high risk for toxicity, which can necessitate management in the intensive care unit. The overall cost of this therapy could reach $1.5 million per patient, one expert estimated.**

Exhibit B



Source: GEA Group

Therefore, insurers who approve CAR T-Cell treatment plans not only face financing a 50/50 chance of survival and a whopping bill, they also take on the additional risk of the occasional $1.5 million liability due to complications from a treatment that costs nearly a half-a-million dollars to begin with.  Are you kidding me?

Medicaid/Medicare are not going to pay these amounts without a fight.  And patients who do fight, don’t live long enough to win any long-shot battle, anyway.

In a press release issued by *HemOnc Today,* Paul G. Richardson M.D. of Dana-Farber Cancer Institute and member of the editorial board at *HemOnc Today* summed up the myeloma treatment quagmire patients with the disease face:

Despite numerous advances in myeloma treatment, currently available therapies are insufficient to address the increasing number of patients with highly resistant, penta-refractory myeloma, [in which] the disease has ultimately become non-responsive to approved therapy.  **There is, therefore, a real urgency for new therapies with novel mechanisms of action for these patients, who have a critical unmet medical need.**

And if CAR T-Cell therapy is so grand, why do all these oncologists talk about “unmet needs” in myeloma treatment in citations included in many of the articles about CAR T-Cell therapy?

Okay, I’ve made my point.  Essentially, in the field of myeloma treatment protocols, it appears Selinexor is the only game in town, as far oncologists and I are concerned.

With the background information contained in this report under your belt, go to the presentation report that was prepared for the JP Morgan Healthcare Conference of January 2019, [here](https://u6067039.ct.sendgrid.net/wf/click?upn=B3b2QVtR07unCLj8-2FpqBWkiBvYU0Kr-2FnDiCxRj1BjMRB-2BWbRILf7IlqA3QukaSLD8BaOIxi06acrLa-2FvHLcTOw-3D-3D_sG0ANujnwMb5zLR1cU179yhFGvhh-2BVeISbc3mDrNlUwAku8x2JKS3cUu2kgoDMz6s9e93MW4QKLqhvELHx1l4K9S3t57qEIGPAdi60XRGoM6HLadf-2FoYQwMZEJjY3Qs8ptPjenavlPb-2BAlNtFDnEU6CiPKfAl1mpdO-2B3LKbYl76Q9Pq-2B67Adetmgy7F1Cfso8unwgRImMmOMs-2Bt3GWYSYYPa7Ir57piwNb-2B1jvyxAeFP7Mjdjiapi7RrIi83x3CtWbV5jTSwqaR7To7fzrr0-2FQ6bO9csc3Tp2LXeX6bDVlPtTOCa-2FagiisZaZCNKfCvwrUjewhzOsb1NsHtr8UXucdia0wLAJVSVI0rPbwxEa3sZV8bTPbQurBxNaHEkJiieytiRbYfDgp-2F2ogRP0hISrrhVxs6YVzYv-2BRhuXPWzZaVwoKYWIwsk02ACOH-2BCmkw1KC90IyGtqRgrXqF4nq3iRiwjDt3uXBEj3Xssx-2FNLIoX2j8BB4HAWyrF2PVhsLrZ-2BDZTrdzqhl83QPK4bSAGri-2F3HihbgK3oJmDz-2Bid6aFr8-3D), and take the time to read through it.  I think the JP Morgan conference report should make more sense to you than delving into the presentation ‘cold’.

**V) Valuation Estimate**

Fortunately, I was able to find annual revenue statistics for Velcade, produced by Amgen subsidiary, Onyx Pharmaceuticals.

Why is Velcade so important? In 2003, Velcade was perched on the exact same catbird seat as Selinexor is perched today. The baseline revenue data from the sale of Velcade was a huge help to me for my revenue and valuation estimates for Karyopharm.

The headline of an informative and downright ‘spooky’ SeekingAlpha post entitled, [Onyx – A “must own” biotech for 2013](https://u6067039.ct.sendgrid.net/wf/click?upn=B3b2QVtR07unCLj8-2FpqBWu0v0Y929UybkuxHSBi8oY4w7YpQ0ykGVV1tDxc18A0q0slI7xYHOysF9pY1n1qRUk1FdUFpK4ccD4IGjPhPC-2BYa4-2FGV6Xz4-2Bm97NKOndEVV_sG0ANujnwMb5zLR1cU179yhFGvhh-2BVeISbc3mDrNlUwAku8x2JKS3cUu2kgoDMz6s9e93MW4QKLqhvELHx1l4K9S3t57qEIGPAdi60XRGoM6HLadf-2FoYQwMZEJjY3Qs8ptPjenavlPb-2BAlNtFDnEU6CiPKfAl1mpdO-2B3LKbYl76Q9Pq-2B67Adetmgy7F1Cfso8unwgRImMmOMs-2Bt3GWYSYYPa7Ir57piwNb-2B1jvyxAeFP7Mjdjiapi7RrIi83x3CtWbV5jTSwqaR7To7fzrr0-2FQ6bO9csc3Tp2LXeX6bDVlPtTOCa-2FagiisZaZCNKfCvwOadTTRD-2BFwoDptgWw0r16s7232BnieBnw3YsxFJQ-2BRs04INzPlsIIWTMbd8iO9Z6nbOKLRvjNi9Q8W9OlOmThN1xOUhWD5j4Log0msrBtnYeJcsgA4UkDVf9C2EYBJJE9eW7kSDpaXKdMR0D7Qvpar1pqqIn4sxxMv5AWptxkXdPv3KoYMYBbaMPpfsXR5c8lpY1L3vwcxpujrJ6RF-2BrMcNmaXGyP-2B9m26KF-2FRWo65k-3D), the author and partner at venture capital firm Pontifax Ltd, [Ohad Hammer](https://u6067039.ct.sendgrid.net/wf/click?upn=B3b2QVtR07unCLj8-2FpqBWoxHK4ytgSTtHHMnkzmvKqdFY0wPwyMESa2YIgi1MGFIloqkeQGOfK26FHJB43G-2FH3eGK2IsDW8n-2BnsS0174BhwSimAIhtvkzsoUoAHDRj0WDnlMEmsj7Q9OagTfn-2B6X24R9m-2B-2Ffme6JKIkDaFLuhIUEiq2pHPMc3FCjQ88k8N99xjd1iN1WaaFrzwlI29OS1VZPAvHmgU-2BPxtZUcBonFVz8BC7-2Fz-2FQCbeIqO-2FJIQ11g_sG0ANujnwMb5zLR1cU179yhFGvhh-2BVeISbc3mDrNlUwAku8x2JKS3cUu2kgoDMz6s9e93MW4QKLqhvELHx1l4K9S3t57qEIGPAdi60XRGoM6HLadf-2FoYQwMZEJjY3Qs8ptPjenavlPb-2BAlNtFDnEU6CiPKfAl1mpdO-2B3LKbYl76Q9Pq-2B67Adetmgy7F1Cfso8unwgRImMmOMs-2Bt3GWYSYYPa7Ir57piwNb-2B1jvyxAeFP7Mjdjiapi7RrIi83x3CtWbV5jTSwqaR7To7fzrr0-2FQ6bO9csc3Tp2LXeX6bDVlPtTOCa-2FagiisZaZCNKfCvw90XfqJ6xCzD7yk-2FObincxAM4aBEL-2B4jOzIOKRdRpJDtzjNMKoMQqV4p4F-2B6e2RwfDzXiv6HX2TA2gNKZNDoOhXOjBPSba4X10SQFIW7HhF3EtUOA1Lbcf2jEhHeVk-2BDEGopNq8cdvi3HRIDDM64N8ErHcOCyiudXZ050dztVHyWyNPb7KirykNH0YQwbhZJp9Efs0qp6SI6GnWlycdmBE1LJJE-2B7oZYCpUNQdf9yn6c-3D), briefly made the same case for Onyx Pharmaceuticals at that time in 2013, as I am today for Karyopharm.  Not only did the post give me the data I needed to run some valuation estimates for KPTI; I could have changed the dates in the post, up those dates six years, changed the name from Onyx to Karyopharm, and a cut-and-paste of the post would have ‘done the trick’ for me.  Also, the market size Hammer referenced had to be adjusted up, too, to today’s larger market size, and voila, done.

Anyway, courtesy of Mr. Hammer, the data he presented was used as a starting point for my revenue estimates for Selinexor.  If you link back to [page 7](https://u6067039.ct.sendgrid.net/wf/click?upn=B3b2QVtR07unCLj8-2FpqBWkiBvYU0Kr-2FnDiCxRj1BjMRB-2BWbRILf7IlqA3QukaSLD8BaOIxi06acrLa-2FvHLcTOw-3D-3D_sG0ANujnwMb5zLR1cU179yhFGvhh-2BVeISbc3mDrNlUwAku8x2JKS3cUu2kgoDMz6s9e93MW4QKLqhvELHx1l4K9S3t57qEIGPAdi60XRGoM6HLadf-2FoYQwMZEJjY3Qs8ptPjenavlPb-2BAlNtFDnEU6CiPKfAl1mpdO-2B3LKbYl76Q9Pq-2B67Adetmgy7F1Cfso8unwgRImMmOMs-2Bt3GWYSYYPa7Ir57piwNb-2B1jvyxAeFP7Mjdjiapi7RrIi83x3CtWbV5jTSwqaR7To7fzrr0-2FQ6bO9csc3Tp2LXeX6bDVlPtTOCa-2FagiisZaZCNKfCvw3eCL4fcSNdS9gnLioZM-2FCadFgkrAyPtD2yX1Mbv4Pjz-2Fjf93WT0Q9yGrVgpj1EXsH-2Bve6jorDgkoIT53UfGk-2BdmlVOmcac33RU9WoZvCBJkg-2FWGRiRxb6-2BIo6p-2B4aazKY1-2BmRWP0kF6uLTDZ4-2FOTvp4pKo-2F3wmAC3L-2BIt6AL7MFZoTQBEYPrh4TmAx5u9AsoTVU-2Bzm500ZBPTGQpEAB-2FmQh82IGQh0r-2Fph2zzQAWRF8-3D) of Karyopharm presentation material, you’ll see the phase III BOSTON study (top bar) that’s about to be published along with an assumed successful New Drug Application (“NDA”), scheduled for early 2020.

Notice the agent used with Selinexor in the BOSTON study awaiting FDA approval in early 2020.  Of course, if you’ve been absorbing this report as I hope you do, the agent is Velcade. Sweet potatoes!  How fortuitous.

Below, is the spreadsheet I created to demonstrate what revenue forecasts for Selinexor, and *only* Selinexor might look like.

The data don’t include revenue that might be expected from the sale of Eltanexor, KPT-9274 and Verdinexor, all of which are expected to treat other indications in the years to come.  And who knows what revenues these drugs might bring in to Karyopharm?

But, because Karyopharm has a deep and wide moat for IPO1 protein inhibitors until the years 2032 (patent rights), at the very earliest, the future appears much brighter for Karyopharm, today, than it was for Onyx at the time of its launch of Velcade, in 2003.

By the way, Onyx was bought by Amgen in 2013 for $125 per share, a 2.66-times net return on each dollar invested in 2009 (4.71 years), the year the company came public.  But I think we can do better with KPTI than a net of 2.66-times in 4.71 years (CAGR 31.75%).

Exhibit C



Source: Raging Bull, Kyle Dennis

Taken from the chart, above, I’ve estimated an initial revenue amount for Selinexor of $726 million, in 2020.

Although Selinexor is scheduled to begin sales in the U.S. at the start of the 2H 2019 (and Q1 2020 in Europe), I made it easy on myself by starting my estimates for the year 2020.

By using the same annual growth rates of Velcade revenue, and adjusting for a $17 billion market for Selinexor from a $3 billion market for Velcade of 15 years ago, I estimate revenue from the sale of only Selinexor at $2.09 billion for 2021.  And I estimate Karyopharm market capitalization of between $6.34 billion and $8.45 billion at the close of 2021.

That estimate range equates to between a 10-bagger and 14-bagger move from today’s $592 million market capitalization.

I know these estimates appear bizarrely high, but that’s where the facts lead me.

* The trial results of Selinexor ‘kick butt’, better than the efficacy and tolerance results shown during the Velcade FDA trials that led to that drug’s NDA in 2003.
* The FDA thinks Selinexor deserves “fast track” designation.
* The distribution network of selling the drug has markedly expanded and improved since 2003.
* Selinexor is scheduled to be sold in the world’s two most wealth continents of the world, where the number of aged patients, especially, as a percentage of the overall populations has soared.  Fifteen more years of baby boomers have reached ages above 50-years old since 2003.
* The timing of the Selinexor entry to the oncology market is superior to the timing of entry of Velcade.

Adding more to this admittedly bizarre valuation estimate, I didn’t include the $2 billion Diffuse Large B-Cell Lymphoma (“DLBCL”) market for Selinexor, another “fast track” indication granted by the FDA.

And I didn’t include other indications for Selinexor, which include another half-a-dozen more cancer markets in the U.S. and Europe.

Therefore, what I present here are really stripped-down revenue estimates, and still come up with a market capitalization for Karyopharm of more than $6 billion.

**VI) Valuation Estimate (Part II); These Data Don’t Lie**

The chart, below, offers you ‘surface validity’ of the reasonableness of my estimates.  You can clear see the dominance of a first-in-class drug (Velcade) as the front-line treatment of multiple myeloma, today.

Why wouldn’t Selinexor repeat?  See my point? Karyopharm has a lock on the patent for the manipulation of the XPO1 protein until 2032, at the earliest.

Let’s get into the chart, and you’ll see what I’m referring to when I state my estimates have “surface validity.”

Exhibit D



Source: Karyopharm Therapeutics

Velcade is represented by the red-color bar.  In the BOSTON phase III study, Selinexor and Velcade are used together to manipulate the XPO1 protein.  And, as I’ve reported, the BOSTON phase III trial is expected to be completed and granted a New Drug Application (“NDA”) in early 2020.

And in the STORM phase II trials, the trials about which Dr. Gasparetto said Selinexor reached an “amazing” and “incredible” signal response rate when taken in combination with the agent dexamethasone.

Dexamethasone is contained in in Darzalex (green-color), Pomalyst (lightest blue-color) and Kyprolis (light-blue). Therefore, arguably, Selinexor will be used with all three of these drugs to boost efficacy and toleration levels. This make sense to me.

And the STOMP phase II trials includes efficacy of Selinexor combined with any one of all agents shown on the chart.  See pages 13, 14 and 15 of the JP Morgan Healthcare Conference presentation materials of January 2019.

Get it?  Do you get why Dr. Siegel and Dr. Gasparetto were so enthusiastic about the explanation of the trial data and unsolicited (I assume) opinion about about the dominant role Selinexor is about to play in oncology now, and in the more than a decade to come?

Therefore, unless the oncology world is shocked by a complete failure of Selinexor at the FDA on April 6, the drug is expected to become the dominate first-line and refractory line treatment protocols for a $17 billion market, at the very least.

And from the facts as I see them, how can any oncologist not prescribe Selinexor in combination with present front-line drug protocols to affect the best chance of recovery as early as possible?

Keep in mind, too, after protocols are established by the American Medical Association (“AMA”) in the U.S., of course, deviating from protocol must be vigorously documented.

It’s rare that physicians deviate from protocol. The ramification could be quite severe, including the revocation of licenses to practice medicine.

And with Karyopharm $330 million of cash/near cash available to carry the company well into Q2 2020 (see page 31 of the JP Morgan Healthcare Conference presentation materials of January 2019), the company has more- than-enough headroom to seize headlines and new investors of the stock in addition to a good portion of the $726 million of additional revenue I expect in 2020.