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Positive Phase III For Darolutamide In Prostate Cancer Could Improve Options For Orion

Executive Summary
Top-line results from the Phase III ARAMIS study indicate the next-generation oral androgen receptor antagonist, darolutamide, has met its primary endpoint and could provide a boost for Finland’s multinational and now pure-play pharma company, Orion, plus Bayer too.

With positive top-line results released from the Phase III ARAMIS study involving the potential prostate cancer therapy, darolutamide, the CEO of the product’s originator, Orion Corp., Timo Lappalainen, has indicated the Finnish company may take a fresh look at the development priorities for its research pipeline.

Having an oncology product on the market would be a significant plus for Finland-headquartered Orion Corp, the multinational pharmaceutical company whose novel therapies for Parkinson’s disease have for some time faced generic competitors, and whose range of generics, biosimilars and proprietary products have come under increasing pricing pressure.

But Orion and its big pharma research collaborator, Bayer AG, are not giving much away about darolutamide’s future role in a therapeutic sector that is likely to become highly competitive in the future, with numerous candidates in late-stage development for prostate cancer (see sidebar).

The two European collaborators did not provide further details about the clinical results found with darolutamide beyond announcing on Oct. 24 that the ARAMIS study had met its primary endpoint, and that further details would be presented at an as yet undisclosed scientific meeting.

The ARAMIS study involved men with non-metastatic castration-resistant prostate cancer, and the “next generation” oral androgen receptor antagonist, darolutamide, significantly extended metastasis-free survival (MFS) compared with placebo, the primary endpoint, the two companies reported.

The safety profile of darolutamide in ARAMIS was “consistent with previously published data on darolutamide.” The 1,500 patients in the study were being treated with androgen deprivation therapy but were at risk of developing metastatic disease and were treated either with placebo or 600 mg of darolutamide twice daily. Secondary endpoints included overall survival, time to first symptomatic skeletal event (SSE), time to initiation of first cytotoxic chemotherapy and time to pain progression.

Still, the strength of the data was sufficient for the companies to say that Bayer was starting discussions with regulators about submitting marketing applications – darolutamide has been granted fast-track designation by the US FDA for non-metastatic castration-resistant prostate cancer. A second Phase III study with darolutamide, ARASENS, in metastatic hormone-sensitive prostate cancer is underway.

Bayer has worldwide development and marketing rights to darolutamide, but Orion has an option on co-promotion rights in Europe under a June 2014 agreement. (Also see “Bayer signs €50m deal for Orion’s prostate cancer drug” – Scrip, 3 Jun, 2014.)

If Orion decides to co-promote darolutamide, the company’s marketing activities are not expected to involve a large amount of additional time and investment. “We already have sales forces in EU countries, that we can redirect and retrain in oncology,” Lappalainen remarked during an Oct. 24 analyst’s briefing on the company’s nine-month financial results.

He expects Orion to share promotional activities 50:50 in most of Europe, although market access and pricing activities would likely be led by Bayer. Bayer has covered the majority of the darolutamide development costs and Orion revealed the amount of milestone payments it could receive if the product is launched – €45m upon first commercial sales in the US, €20m upon first commercial sale in Europe, and €8m on first commercial sale in Japan. Orion will also receive tiered royalties on any product sales.

The development of darolutamide could be key to Orion’s long-term plans, opening up a new business sector for the company that sold is diagnostics business, Orion Diagnostica, for approximately €163m in April 2018 to become a pure-play pharmaceuticals company. (Also see “Deal Watch: Fresenius Drops Bid For Akorn, Citing Data-Integrity Concerns” – Scrip, 23 Apr, 2018.)

But its sales of generics and proprietary products came under increasing pricing pressure in the first nine months of 2018, and its profits were flat, being held back by unfavorable currency exchange rates; in the first nine-months of 2018, net sales were €715m compared with
€768m in the 2017 nine months, and pretax profits were €181m versus €209m.

Lappalainen did not elaborate on how Orion's priorities could change for its pipeline, which a variety of products for a range of indications. In its current research pipeline, Orion has an Easyhaler dry-powder formulation of salmeterol/fluticasone, which is being launched in European countries this October, and an Easyhaler formulation of the COPD drug, tiotropium, which is in late-stage bioequivalence studies.

Oral levosimendan for amyotrophic lateral sclerosis is being evaluated in the Phase III REFALS study, and a new COMT inhibitor, ODM-104 is in Phase II for Parkinson’s disease; Orion is looking for a possible partner for this candidate. Orion has also just signed an agreement with Amgen Inc. on the marketing and sales of an adalimumab biosimilar, Amgevita, in Finland. Orion has other cancer products but they are in early-stage clinical development.
Clovis In Pole Position To Be First PARP For Prostate Cancer

Executive Summary
Clovis is looking a steal a march on its rival PARP inhibitors and hopes to be the first drug in the class to get approval for prostate cancer following strong data seen in the TRITON trial.

Clovis Oncology Inc.’s PARP inhibitor Rubraca is showing promise in prostate cancer, according to data released at this year’s ESMO conference, as the company hopes to steal a march on AstraZeneca PLC and Merck & Co. Inc.’s more established rival drug.

With the PARP inhibitor space in ovarian cancer becoming ever more competitive, and AstraZeneca’s Lynparza (olaparib) increasingly dominating, data presented at ESMO in Munich this weekend suggest that a brighter future for Clovis Rubraca (rucaparib) may lie in prostate cancer.

The US biotech caught the eye at ESMO with better than expected initial data from the ongoing Phase II TRITON2 trial of Rubraca which showed a 44% confirmed objective response rate (ORR) in 25 patients with a BRCA1/2 mutation. In addition, a 51% prostate specific antigen (PSA) response rate was observed in 45 patients with a BRCA1/2 alteration.

Speaking to Scrip at ESMO, Clovis CEO Patrick Mahaffy put the results in context by noting that the men in the study have been through a number of prior therapies and just come through chemotherapy with docetaxel. “They are expected to see a 15% response rate or three months of benefit, they have very few options available and they are not good ones, so to deliver a 44% response rate in a robust enough group of patients is real and we have not reached the median duration of response yet.”

He also stressed the importance of the PSA data, saying that “physicians live and breathe by PSA to see whether the disease is progressing or under control,” and it would be of great importance to patients if Rubraca gets the go-ahead in prostate cancer.

The TRITON2 results were the basis for breakthrough therapy designation granted earlier this month by the FDA for Rubraca as monotherapy for patients with BRCA1/2 mutated metastatic castration-resistant prostate cancer who have received at least one prior androgen receptor (AR)-directed therapy and taxane-based chemotherapy. Mahaffy noted that the trial is continuing to enroll and Clovis hopes to generate sufficient data to file for accelerated approval by the end of 2019 or possibly early if enrollment goes well.

This could mean that Clovis could potentially be the first company to have a PARP inhibitor to carry the prostate cancer indication on its label. Mahaffy told Scrip that “as far as we know, “ the firm is leading the race in that indication and that TRITON2 offers “by far the most robust dataset seen to date in prostate cancer” in the PARP class.

It is still too early to give any timeline regarding a European submission. Mahaffy said Clovis will be speaking to regulators in the coming months but he believes that a comparative study may represent the best way forward for the prostate cancer indication in Europe.

Ahead of ESMO, Andrew Berens, an analyst at Leerink, issued a note saying that prostate cancer expansion “could add a unique dimension to the Clovis story.” He added that potentially gaining that first label expansion “could lead to preferential use as clinicians gain familiarity with PARP use in this population.”

Berens believes that Rubraca could enjoy around “40% peak penetration into the addressable prostate cancer opportunity” representing a greater share than Tesaro Inc.’s rival PARP Zejula (niraparib) (35%) or Lynparza (15%) by 2025. He forecast that an approval for Clovis could be worth $580m in peak sales for the prostate cancer indication alone.

After the data were presented, Berens wrote that the ORR in BRCA patients is likely to support an accelerated filing if the responses prove durable. Patients with BRCA 1/2 mutations represent about 13% of the prostate cancer market, he estimated, but pointed out that “no quantitative efficacy data were provided for the 40 patients with ATM mutations, which are fundamentally important to assess the size of the opportunity.”

Mahaffy noted that the company is running several other studies in prostate cancer, including the Phase III TRITON3 trial looking at Rubraca in combination with Pfizer Inc. and Astellas’ Xtandi (enzalutamide) and Johnson & Johnson’s Zytiga (abiraterone) in men with earlier stages of the disease.

Clovis is looking at other indications, notably bladder cancer, and its program there includes the ATLAS Phase II study of Rubraca monotherapy in recurrent, metastatic
bladder cancer and a mid-stage trial of the drug in combination with partner Bristol-Myers Squibb Co.'s checkpoint inhibitor Opdivo (nivolumab) in patients with locally advanced or metastatic bladder carcinoma who are ineligible for treatment with cisplatin. Mahaffy added that the firm is also weighing up trials of Rubraca for pancreatic cancer.

As for further studies in ovarian cancer, the ARIEL4 Phase III confirmatory study of Rubraca is enrolling relapsed patients with BRCA mutations who have failed two prior lines of therapy. Also the first patients have been enrolled in the Phase III ATHENA trial looking at a combo with Opdivo in patients with newly diagnosed advanced ovarian cancer.

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Adaptive Clinical Trial Designs: US FDA Provides Checklist To Begin Study

Executive Summary
Draft guidance specifies documentation that must be submitted to FDA prior to conducting an adaptive trial, and what to include in an application.

The US FDA's new draft guidance on clinical trial adaptive designs lists the information sponsors must submit to the agency before initiating a trial and what data they should include in their applications.

The agency issued the draft guidance, Adaptive Designs for Clinical Trials of Drugs and Biologics, on Sept. 28. The document replaces a 2010 draft guidance. Like the earlier draft, the new document describes adaptive designs and the motivation for using them. However, the updated version includes examples of clinical trials with adaptive designs to illustrate their advantages. And it provides more details on the documentation needed for FDA evaluation of the adaptive design and the completed trial.

FDA defines an adaptive design as a clinical trial design that allows for prospectively planned modifications to one or more aspects of the design based on accumulating data from subjects in the trial. The guidance notes that allowing the trial to adjust to information that was not available when the trial began can provide a greater chance to detect a true drug effect than a comparable non-adaptive design. It may also enable a trial to be stopped early, and may make it possible to answer broader questions.

A One-Two Guidance Punch
Another draft guidance issued the same day covers design and conduct of clinical trials to simultaneously evaluate more than one investigational drug and/or more than one cancer type within the same overall trial structure. The master protocols draft guidance describes aspects of master protocol designs and trial conduct and related considerations, such as biomarker codevelopment and statistical considerations, and the information sponsors should submit to FDA.

In a release announcing the two documents, FDA Commissioner Scott Gottlieb said they are intended to modernize clinical trial designs and approaches for drug development. “Using more modern approaches to clinical trials, we can lower the cost of developing new drugs and increase the amount of competition in the market,” Gottlieb said.

The agency has encouraged the use of adaptive clinical trial designs. But Center for Drug Evaluation and Research Director Janet Woodcock noted in a recent speech at the National Press Club that sponsors have been hesitant to pursue them. She cited the forces of tradition, the loss of control of their assets, and a lack of incentives around trials to improve disease outcomes. (Also see “Woodcock Hopes I-SPY 2 Trial Is ‘Blazing The Trail’ For Future Adaptive Design Uptake” - Pink Sheet, 12 Sep, 2018.)

In the 2010 draft guidance, the agency highlighted general concerns with adaptive designs in drug development and advised caution on their use. (Also see “Adaptive Trials Could Have A Steep Regulatory Learning Curve” - Pink Sheet, 8 Mar, 2010.)

Entresto Trial, STAMPEDE Prostate Cancer Study

Eight years later, FDA is focusing on their potential advantages. The adaptive designs draft guidance cites five examples of clinical trials with adaptive designs to illustrate their advantages. They include the PARADIGM-HF clinical trial in patients with chronic heart failure that was designed to compare a combination of sacubitril and valsartan (Novartis Pharmaceuticals Corp.’s Entresto) with enalapril with respect to the composite endpoint of cardiovascular death or hospitalization for heart failure. FDA said the addition of interim analyses with stopping rules for efficacy reduced the expected sample size and expected duration of the trial.

The trial was stopped after the third interim analysis because the prespecified stopping boundary for compelling superiority of sacubitril/valsartan over enalapril had been crossed, the guidance states. “The group sequential design therefore facilitated a more rapid determination of benefit than would have been possible with a fixed sample design.”

The guidance also cites the STAMPEDE clinical trial, which was designed to inform the practice of medicine and evaluate multiple treatments in prostate cancer by comparing standard androgen deprivation therapy (ADT) with several different treatment regimens that combined ADT with one or more approved therapies. FDA said the use of a common control group, along with sequential analyses to potentially terminate treatment arms, allowed the simultaneous evaluation of several treatment arms more efficiently than could be achieved in multiple individual trials.
The draft guidance recommends that access to comparative interim results be limited to individuals with relevant expertise who are independent from those involved in conducting or managing the trial. It says a dedicated independent adaptation body could be established, exclusive of a data monitoring committee (DMC), if one exists. Alternatively, the adaptive decision-making role could be assigned to the DMC, though the guidance says the DMC’s primary responsibility should be ensuring patient safety and trial integrity.

The draft guidance says FDA’s review of complex adaptive designs often involves challenging evaluations of design operating characteristics, usually requiring extensive computer simulations, as well as increased discussions across disciplines and FDA offices. This may make it difficult for FDA to adequately review such designs under short times, the guidance says. Given the 45-day response timeline and commitments involved with special protocol assessments (SPAs), the agency recommends that SPAs for trials with complex adaptive designs be submitted “only if there has been extensive previous discussion between FDA and the sponsor regarding the proposed trial and design.”

For FDA’s review of proposed late-phase adaptive clinical trials, “the sponsor should prespecify the details of the adaptive design and justify that the chance of erroneous conclusions will be adequately controlled, estimation of treatment effects will be sufficiently reliable, and trial integrity will be appropriately maintained,” the guidance says.

The guidance includes a list of documentation that should be submitted to the agency prior to the initiation of an adaptive design trial. The information includes:

- Rationale for the selected design;
- Detailed description of the monitoring and adaptation plan, including the anticipated number and timing of interim analyses, and the specific aspects of the design that may be modified;
- Information on the roles of the bodies responsible for implementing the adaptive design, such as the data monitoring committee and/or the dedicated independent adaptation committee;
- Prespecification of the statistical methods that will be used to produce interim results and guide adaptation decisions and estimate treatment effects;
- Detailed simulation report in cases where simulations are used to evaluate trial operating characteristics; and
- Comprehensive written data access plan defining how trial integrity will be maintained with planned adaptations.

**Application Information**

The guidance also notes the information that should be included in an NDA or BLA that relies on a trial with an adaptive design. This includes:

- All prospective plans, any relevant committee charters and any supporting documents;
- Information on compliance with the planned adaptation rules and procedures to maintain trial integrity;
- Records of deliberations and participants for any interim discussions by any committees involved in the adaptive process;
- Results of the interim analyses used for adaptation decisions; and
- Appropriate reporting of the adaptive design and trial results in the proposed package insert.

In a Federal Register notice announcing the draft guidance, scheduled for publication Oct. 1, FDA gave an indication of how many clinical trials include an adaptive design. Based on its review of investigational new drugs, new drug applications, biologics licensing applications, and supplemental applications for the use of adaptive designs for clinical trials to provide evidence of effectiveness and safety, the agency said it estimates that approximately 40 sponsors or applicants “will prepare approximately 240 documented plans for clinical trials containing a proposed adaptive design and analysis plan and will submit this information to FDA in a clinical trial protocol and/or in separate documents.”

In addition to these clinical trial protocols and related submissions, FDA estimates approximately 15 sponsors or applicants will submit approximately 20 marketing applications that rely on a trial with an adaptive design.

Comments on the draft guidance are due 60 days after publication of the Federal Register notice.
**Guidance By Guidance, US FDA Is Reshaping The Look Of Cancer Drug Trials**

**Executive Summary**
Recent draft guidance documents address adolescent enrollment in adult cancer trials, use of cohort designs in early-phase studies, and inclusion of placebo controls; more advice is coming soon on master protocols, adaptive designs and novel endpoints, FDA’s Gottlieb says.

The US FDA is using its guidance-writing powers to reshape the look of oncology clinical trials, with the goal of streamlining and modernizing cancer drug development in order to foster a more patient-focused approach.

In the past three months, the agency has issued draft guidance documents aimed at expanding the ages of cancer patients eligible for clinical trials, giving sponsors more flexibility in designing studies, and clarifying when placebo controls should be used.

The agency also can be expected to take a serious look at proposed guidance documents recently submitted by two leading cancer research organizations aimed at further expanding eligibility criteria for clinical trials.

In an Aug. 29 blog post on FDA’s initiative to modernize for innovation, Commissioner Scott Gottlieb pledged that even more advice is on its way in the oncology clinical trial space.

“In the coming weeks, we’ll be issuing additional guidance” on master clinical trial protocols “and efficient trial design strategies to help expedite the development of oncology drugs and devices,” Gottlieb said. “We’ll also be issuing guidance on the use of adaptive trial designs, and innovative endpoints like minimal residual disease in hematologic cancers.”

**Limiting Use Of Placebos**
In the blog post, Gottlieb highlighted the recently issued draft guidance on use of placebos in randomized oncology trials.

“Advances in care, and trial design, can make it unethical and infeasible in some circumstances to use placebo controls in cancer trials,” he said. “At the same time, the FDA is advancing the development of natural history models for rare diseases. These models may obviate the need for placebo arms in some trials by allowing researchers to replicate the behavior of patients who otherwise are left untreated.”

Use of placebo controls in cancer drug trials can present practical issues, such as toxicity-related unblinding with active treatment, as well as ethical concerns, such as when standard effective therapy is already available, the draft guidance states.

The guidance emphasizes a preference that studies incorporate an active control if one is available rather than a placebo control, or that the investigational agent be compared against placebo when each are added to the standard of care.

“Given the challenges of using a placebo in randomized controlled clinical trials for therapies to treat hematologic malignancy and oncologic disease, FDA recommends that a sponsor use a placebo-controlled design only in selected circumstances (e.g., where surveillance is standard of care), or with certain trial design features (e.g., if the trial uses an add-on design, when the endpoint intended to support a labeling claim has a high degree of subjectivity, such as patient-reported outcomes),” the guidance states.

The guidance also includes considerations for unblinding in cancer trials.

“Unless there are no available appropriate treatment alternatives, FDA recommends unblinding a patient at the time of documented disease recurrence or progression to ensure optimal patient management,” the guidance states.

In addition, the patient and investigator should be unblinded when the former experiences an adverse event suspected to be related to the investigational treatment and for which management with substantially toxic drugs or invasive procedures is being considered. “In such cases of unblinding, the patient should not be removed from the trial,” the guidance states.

When asked why the agency felt it needed to issue the placebo controls guidance, FDA told the Pink Sheet: “This topic has been discussed many times in the community, and we wanted to bring clarity to this issue.”

In an Aug. 23 tweet about the guidance, Gottlieb said that as more breakthrough drugs show outsized benefits in carefully selected patients, it allows FDA to “advance new, rigorous ways for testing meds, and makes placebo
studies an [alternative] for the right settings rather than a reflexive approach for all [oncology] trials.”

FDA released the placebo controls document close on the heels of another draft guidance on “seamless” clinical trials, part of the agency’s implementation of 21st Century Cures Act provisions on modernizing clinical trial design. (Also see “US FDA’s Gottlieb Touts ‘Seamless’ Clinical Trials, Worries About Second-To-Market Products “ - Pink Sheet, 25 Jul, 2018.)

The draft guidance, “Expansion Cohorts: Use In First-In-Human Clinical Trials to Expedite Development of Oncology Drugs and Biologics,” includes advice for sponsors on the design and conduct of first-in-human clinical trials intended to efficiently expedite the clinical development of cancer drugs through multiple expansion cohort trial designs. (Also see ““One Continuous Trial” In Oncology: US FDA Offers Guidance And Encouragement” - Pink Sheet, 22 Aug, 2018.)

Adolescents Welcome In Adult Trials
FDA took another step toward modernizing cancer clinical trial design with a June draft guidance, “Considerations for the Inclusion of Adolescent Patients in Adult Oncology Clinical Trials.”

The guidance notes that adolescents, because of their age, generally are not eligible for enrollment in adult oncology trials, and initial pediatric studies for many drugs often are conducted after a product is approved for adults. “As a result, adolescents may have delayed access to potentially effective therapies,” FDA said. “In addition, accrual of adolescents to pediatric trials evaluating approved drugs may be difficult because of off-label use.”

Adolescents should be eligible for enrollment in adult cancer trials at all stages of drug development “when the histology and biologic behavior of the cancer under investigation is the same in, or the molecular target of the drug is relevant to, cancers in both adult and adolescent patients,” the guidance states.

For first-in-human or dose-escalation trials, adolescents may be enrolled after initial adult pharmacokinetic and toxicity data are obtained. “In general, adolescents enrolled in these early phase trials should have cancers that are relapsed after or refractory to standard therapy with no curative options or for which no standard therapies with curative intent exist,” the guidance states.

Adolescents can be enrolled simultaneously with adults in later-stage trials intended to estimate drug activity or confirm clinical benefit, the agency said.

The guidance also includes ethical considerations and recommendations on safety monitoring and dosing.

For drugs with dosing based on body size, adolescents should receive the same body size-adjusted dose given to adults. For fixed-dose drugs, adolescents weighing at least 40 kg generally can receive the same fixed dose as that given to adults. Adolescents weighing less than 40 kg should receive an adjusted dose based upon either body weight or body surface area, the agency said.

In comments filed on the guidance, industry representatives requested clarification on several issues, including the timing for sponsor discussions with FDA on proposed inclusion of adolescents in adult trials and whether such studies would satisfy Pediatric Research Equity Act requirements.

Industry representatives also questioned how FDA’s recommendations would align with those of regulators across the globe.

“Because the draft guidance signals the first time that a health authority memorializes the principles outlined in the guidance (i.e., recommendation to enroll adolescents in adult oncology studies), we ask the FDA to consider reviewing and discussing the draft guidance with other global health authorities at upcoming pediatric cluster calls,” the Biotechnology Innovation Organization’s (BIO) comments state. “Sharing and discussing the principles outlined in the draft guidance with other global health authorities serves as an important mechanism for ensuring global harmonization of the inclusions of adolescent patients in adult oncology clinical trials.”

BIO and the Pharmaceutical Research and Manufacturers of America (PhRMA) also urged FDA to educate institutional review boards (IRBs) about the agency’s view on enrolling adolescents.

“In order to fully realize the benefits of adolescent participation in adult trials, input from the IRB community and acceptance of the draft guidance will be necessary,” PhRMA’s comments state.

PhRMA said the guidance provides an opportunity to increase adolescent participation in trials beyond the cancer space.

“The consideration of adolescent inclusion in adult drug development outlined in this guidance may be relevant beyond oncology products,” PhRMA said. “The recommendations in this draft guidance could help provide a pragmatic solution for numerous other medical...
conditions across the therapeutic spectrum, particularly where the relevant disease is severe and life-threatening. With appropriate input from interested stakeholders, FDA could consider extending these recommendations beyond oncology.”

However, the public interest group Public Responsibility in Medicine and Research (PRIM&R) urged caution on this point.

“We urge the guidance to emphasize that it is written specifically to address inclusion of adolescents in adult oncology trials; though the guidance may be helpful to sponsors of studies on other diseases, there should be no assumption that the same considerations will hold in all cases,” PRIM&R’s comments state.

**ASCO, FOCR Proposals On Trial Eligibility**

Lowering the minimum age for trials is the focus of one of five proposed guidance documents aimed at modernizing cancer trial eligibility criteria recently submitted by the American Society of Clinical Oncology (ASCO) and Friends of Cancer Research (FOCR).

The proposals grew out of an ASCO/FOCR initiative, with input from FDA, to develop consensus-driven recommendations on when it is scientifically and clinically appropriate to expand eligibility criteria for patient groups that traditionally have been excluded from cancer studies due to the existence of brain metastases, age, HIV-positive status, prior malignancies and organ dysfunction. (Also see “Cancer Trials: Broader Eligibility Criteria Could Mean Novel Labeling Claims” - Pink Sheet, 5 Dec, 2016.)

The goal – one strongly endorsed by FDA – is to move away from copying eligibility criteria from older protocols to newer trials and, instead, develop more rational eligibility criteria tailored to the drug, disease, and population under study. (Also see “Cancer Drug Trials Could Benefit From ‘Rational’ Eligibility Criteria” - Pink Sheet, 19 Apr, 2017.)

The recommendations in the proposed draft guidances “aim to maximize the generalizability of clinical trial results while also maintaining the safety of clinical trial participants,” ASCO Senior VP and Chief Medical Officer Richard Schilsky and FOCR Chairperson and Founder Ellen Sigal said in a cover letter to the agency.

“FDA guidance will assist sponsors in designing more representative trials, and we hope FDA seriously considers adopting the proposed set of guidance documents,” the letter states. “We believe that the rationale for excluding patients from eligibility for a cancer clinical trial should be clearly articulated and should be based on the specific therapy under investigation and the study population to help improve trial accrual, ensure optimal patient access, and maximize information learned during the clinical trial.”

FDA told the Pink Sheet it is reviewing the proposed guidances submitted by ASCO and FOCR, “but it is too early to say what type of response FDA will provide.”

However, the recommendations could help inform draft guidance documents required under the FDA Reauthorization Act aimed at expanding clinical trial eligibility criteria more generally.

The statute requires that FDA issue guidance addressing methodological approaches sponsors may take to broaden eligibility criteria for clinical trials and expanded access trials, especially for serious and life-threatening diseases, and approaches to developing eligibility criteria and increasing recruitment for trials so that enrollment more accurately reflects the patients most likely to receive the drug.

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