Upcoming events - Take two for Pacira and Inotek’s glaucoma data

Welcome to your weekly digest of approaching regulatory and clinical readouts. Pacira expects two trials to report in the first quarter of next year with its analgesic Exparel as a nerve blocker, a use previously knocked back by the FDA. The drug is already on the market as a local anaesthetic, and while it is Pacira’s biggest product its patent life is quickly running out.

Also, Inotek should in January see data from a phase III trial of its glaucoma project trabodenoson. This will be pitted against placebo rather than an active control, so results are expected to be positive, and further interest lies in a combination with prostaglandins that could see it used first line, a potentially more valuable approach.

Beyond opioids

Exparel is a liposomal suspension of bupivacaine, an anaesthetic, administered into the soft tissues of the surgical site, known as infiltration, to produce postsurgical analgesia. It has been on the market since 2012, and while pivotal studies were performed in bunionectomy or haemorrhoidectomy the label does not limit its use to these procedures.

Last year Pacira tried to get Exparel approved as a nerve blocker, but in March received a complete response letter, sending shares down 20%. As part of the sNDA the company submitted results from trials using Exparel as a femoral nerve block in knee surgery and intercostal nerve block for thoracotomy, but only the knee trial met its primary endpoint. A resubmission is expected by the second quarter of 2017.

At the time the company was requesting a broad femoral nerve block label. The FDA asked for more data that would validate its use as a nerve block in a broader range of procedures, and to address its use in upper and lower extremities two new 300-patient trials are testing Exparel in shoulder and knee replacement surgery.

Both are using 133mg or 266mg of drug versus placebo. In the shoulder study the aim is to block the brachial plexus nerves, while the femoral nerve is targeted in the knee study.

The primary measure is pain intensity scores through 48 hours for the shoulder trial and 72 hours for the knee surgery trial. Secondary measures include postsurgical opioid consumption, percentage of opioid-free subjects, time to first opioid rescue and adverse events.

By 2022 Exparel sales are forecast to reach $740m, according to consensus from EvaluatePharma. Issues remain over its patent, which looks to expire in 2018, and competition from other bupivacaine-based analgesics could come from the likes of Heron’s HTX-011, in phase II.

Combination approach

Glaucoma usually occurs when fluid in the eye cannot drain properly, leading to an increase in pressure inside the eye that can damage the optic nerve. Inotek’s phase III trial is testing trabodenoson in 335 adults with ocular hypertension or primary open-angle glaucoma.

The Matrix-1 trial recruited patients with mean intraocular pressure of 24-34mmHg; typical eye pressure in healthy people is 12-22mmHg. In the study trabodenoson was applied topically to the eyes as an ophthalmic formulation of 3% or 6% once per day, or 4.5% twice per day for 12 weeks.

Analysts expect the trial to be positive since the comparison is with placebo. Timolol 0.5%, a generic beta blocker, is given twice a day as positive control, but is not part of the statistical comparison. The primary measure is mean intraocular pressure at three months, and other measures include safety.

First-line treatment for glaucoma is dominated by prostaglandins while beta blockers are often used as adjunctive treatment second line. Trabodenoson is an adenosine mimetic that selectively stimulates the A1 receptor on an area of tissue located at the base of the cornea.

In a phase II trial it statistically lowered intraocular pressure versus placebo at all timepoints on day 28. Roth
analysts note that, while the efficacy was not as robust as that seen with prostaglandins or beta-blockers, the study demonstrated few of the tolerability issues that often cause patients to discontinue prostaglandin treatment.

A phase II trial testing trabodenoson and the prostaglandin analogue latanoprost versus lantanoprost alone should report in the second half of next year. Roth believes that a fixed-dose combination could become a first-line option for patients who are uncontrolled with or cannot tolerate prostaglandins.

Trabodenoson monotherapy is expected to sell $156m by 2022, according to EvaluatePharma consensus, with the combination forecast slightly higher at $188m. Trabodenoson is Inotek’s only project.

The company completed a $40m IPO last year, and shares are down 40% this year. With a market cap of just $184m bigger ophthalmology players might sit up and take notice if the trial delivers.

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<tr>
<th>Project</th>
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