Schmidt – the ideal analgesic
Transcript for The20Idea20Analgesic3F20PF614.mp4

0:00:00 --> 0:00:08
If we go back in time, the use of opioids for therapeutic purposes started perhaps 3,000 years ago,
0:00:08 --> 0:00:12
with opium, from the opium poppy.
0:00:12 --> 0:00:20
And interestingly, that was not used so much for pain relief in those days, as it was for treating
diarrhea or other GI diseases.
0:00:20 --> 0:00:29
But then over a period of time, particularly when the active ingredients were isolated, starting in the
early 1800s,
0:00:29 --> 0:00:38
and then going on into synthetic chemistry, we began to look at efficacy of these opium drive
products in different ways.
0:00:38 --> 0:00:42
Oxycodone is certainly one that we're now pretty familiar with.
0:00:42 --> 0:00:51
But we perhaps to develop a new type of analgesic, we want to design one that does not have
immediate onset.
0:00:51 --> 0:00:57
That would make those who are recreational drug users disappointed because they're not going to
get that immediate high
0:00:57 --> 0:00:59
when they take the product the first time.
0:00:59 --> 0:01:08
So having a compound that is slow to reach its peak blood levels, but perhaps have an extended
duration of action would be a different way to take a look at this.
0:01:08 --> 0:01:16
And I'm going to be talking about PF614 in particular because we've designed it chemically to have
a 12 hour half-life,
0:01:16 --> 0:01:21
not from a formulation, but the chemistry itself determines the half-life of the compound.
0:01:21 --> 0:01:26

And because of the way that it's activated, which I'm going to go into a little bit more in another slide
or two,
0:01:26 --> 0:01:31
it's not going to be easy to get this to activate if you snort it.
0:01:31 --> 0:01:39
Or if you inject it, it's not going to activate it at all because it requires one key enzyme, which is only in
the gastrointestinal tract.
0:01:39 --> 0:01:45
It's activated by trypsin, and that's unique for any class of drug.
0:01:45 --> 0:01:51
But it can be used very effectively with multiple classes of drugs, something we can talk about a little bit more later.
0:01:51 --> 0:01:59
But the advantage for us is that we can then switch on activation by simply taking it orally where
everybody has trypsin.
0:01:59 --> 0:02:05
It's something that's required to metabolize proteins and peptides and other food substances.
0:02:05 --> 0:02:14
So we know that we all have the ability to activate this particular compound.
0:02:14 --> 0:02:16
It's clever chemistry and formulation technology.
0:02:16 --> 0:02:20
We have a way to turn off the activation as well.
0:02:20 --> 0:02:27
Even if the compound is taken orally, and I'll talk to you a little bit more about studies that we've
done clinically that have shown for the first time,
0:02:27 --> 0:02:34
that some of the things we've been talking about preclinically over the past many years, we've
actually now demonstrated in human clinical trials.
0:02:34 --> 0:02:44
One other thing that's unique about this compound is that the compound itself is soluble in water,
but it retains its controlled release characteristics.
0:02:44 --> 0:02:54
It retains its, as you'll see, its abuse resistance when you dissolve it in water, just the same as it
would be if you took it in a capsule or in a pill formulation.
0:02:54 --> 0:03:01

None of the other abuse deterrent formulations can make that chain, that claim, because none of
them are soluble in water.
0:03:01 --> 0:03:13
And if you try to make them into an oral formulation, they're not going to have the controlled release
characteristics that they were designed with.
0:03:13 --> 0:03:27
Another thing that is particularly important, particularly in oncology patients or in geriatric patients,
but also in pediatrics, is whether you have a potential food interaction with the product.
0:03:27 --> 0:03:37
Because this compound is activated in the same way that food is digested, we've not seen that there
has been any significant food effect.
0:03:37 --> 0:03:40
We have the clinical data on that as well.
0:03:40 --> 0:03:50
So the future is now today. Let's talk about the chemical safeguards that we have built into PF614.
0:03:50 --> 0:04:01
I mentioned that this started out with a clever chemistry idea, which is to build a compound that is
complex because it has actually a two-stage activation.
0:04:01 --> 0:04:09
One stage starts with taking off some amino acids that are cleaved by trypsin, then a second part is
a timing sequence.
0:04:09 --> 0:04:13
And then the third part is the release finally of oxycodone.
0:04:13 --> 0:04:16
So all that takes place over a period of time.
0:04:16 --> 0:04:22
What we wanted to do, though, was to make a safer opioid overall.
0:04:22 --> 0:04:33
So we want to have pain relief, that's paramount, but we want to make certain that the compound
can be used in a way that potentially prevents overdose situations.
0:04:33 --> 0:04:49
And that by also lowering the CMax, but having a longer duration of action, patients won't have this
zigzag peak effect, and then lower effect, and then peak effect again, which I think drives them to using more of the analgesic over a period of time.
0:04:49 --> 0:04:57

And then if they just had a drug that comes up to a steady state plasma concentration and maintains
that for a period of time.
0:04:57 --> 0:05:03
And the important thing is using a chemical switch to activate or turn off the compound as needed.