

THE PLAYBOOK

The Big Dog Longevity *Playbook*

Nine modules. Two versions each. Everything you need to extend your big dog's healthy life — the science, the emerging drugs, the paths to access, and the ten things that work today.

~20,000 words · Veterinarian-reviewed · Updated **April 2026**

How to Read This Playbook

Read this first. Two minutes. It'll save you time.

The Playbook is 9 modules, two versions each

Every module in this Playbook has a ● **Simple version** (3–5 minutes) and a ● **Full version** (10–18 minutes). Same content. Same order. The simple version is written at a “kitchen-table conversation” level — plain language, no jargon, just what you need to know. The full version has the biology, the peer-reviewed research, the citations, the nuance, and the specific protocols.

Nothing in the full version contradicts the simple one. The full version goes deeper; it doesn't go different.

The recommended path: two passes

First pass — read all 9 Simple versions in order. This takes about 30 minutes and gives you the complete picture: why big dogs age faster, what drugs are coming, whether your dog is a candidate, the two real paths to early access, how to play the waitlist, how to have the vet conversation, the ten things you can do today, how to turn it all into a plan, and what's coming next in the field.

At the end of the first pass, you'll know more about canine longevity medicine than most dog owners — and honestly, more than many general-practice vets.

Second pass — read the Full versions of the modules that matter most for your dog. You won't need all nine at full depth. The second pass is targeted. Most owners will want:

- **Module 1 full version** — understand the biology in enough detail to have the vet conversation intelligently.
- **Module 3 full version** — the worked examples help you see your dog's specific situation reflected.
- **Module 6 full version** — the complete vet conversation framework is the single most load-bearing tool in the Playbook.
- **Module 7 full version** — the ten things you can do today, with the actual doses and protocols.

The other modules' full versions are there when you need them — when Loyal publishes a milestone, when your dog's situation changes, or when a specific topic becomes relevant.

How the modules connect

- **Modules 1-2** — the science and the drugs.
- **Module 3** — whether your dog fits.
- **Modules 4-5** — how to get access.
- **Module 6** — the vet conversation (the most load-bearing skill).
- **Module 7** — what works today, regardless of drug access.
- **Modules 8-9** — your plan, plus what's coming next.

If you read in order, each module reinforces the one before it. If you jump, you'll find cross-references back to the foundational material.



If you only have 10 minutes right now

Read the Simple versions of **Module 1** (the science), **Module 3** (candidacy), and **Module 6** (the vet conversation). You'll leave with the single most important decision — is this worth taking seriously for my dog — already made.

If you're reading this because your big dog is already a senior

Don't linger. Do the first pass tonight. Start Module 7 tomorrow. Apply to the Loyal waitlist (and TRIAD if your dog qualifies) this week. Book a vet appointment within 14 days. Every week matters more now than it used to.

A word on the / symbols

-  Green circle = Simple version
-  Blue circle = Full version

That's the whole system. Look for them at the top of each module.

Ready? Start with Module 1 — Why Big Dogs Age Faster.

Module 1 — Why Big Dogs Age Faster

Two versions of this module. Pick the one that fits the time and headspace you have.

- **Simple version** — 3 minutes. Plain language. Covers everything you actually need to know.
- **Full version** — 12 minutes. Same story, with the biology, the research, the citations, and the nuance.

Read the simple version first. If you want more, keep going. Nothing in the full version contradicts the simple one — it just goes deeper.

● The Simple Version

The short answer

Big dogs age about twice as fast as small dogs. A Great Dane lives seven years. A Chihuahua lives sixteen. That gap isn't random, and it isn't because big dogs "wear out their joints." It comes down to one thing going on inside their bodies — and scientists think they finally know what it is.

The "growth switch"

Imagine every dog is born with a little switch in their body that tells their cells to grow. Small dogs are born with the switch set to *low*. Big dogs are born with the switch set to *high*. That's the main reason a Great Dane puppy turns into a 140-pound adult in a year and a half, while a Chihuahua stays tiny.

The switch has a real name. It's a hormone called **IGF-1**. You don't need to remember the name. Just remember the idea: big dogs make a lot of it, small dogs make a little.

The problem

The switch never turns off.

Even after a big dog is fully grown — after his bones are done stretching, after his muscles are done building — his body keeps pumping out the “grow faster” signal. There’s nothing left to grow. But the cells keep getting the message anyway.

That does three bad things over time:

- 1. It raises the risk of cancer.** Cells that divide more often make more mistakes. Some mistakes become tumors. This is why big breeds like Great Danes, Berners, and Rottweilers get cancer at shockingly high rates.
- 2. It breaks the body’s cleanup system.** Your dog’s cells are supposed to tidy up their own garbage — damaged parts, worn-out pieces. The growth signal tells them to skip the cleanup. Over years, the mess builds up.
- 3. It piles up “zombie cells.”** Some cells stop working but refuse to die. They just sit there, leaking inflammation into nearby healthy tissue. Big dogs accumulate these faster than small dogs.

Put it all together and you get why a seven-year-old Great Dane’s body can look and act like a fifteen-year-old small dog’s. The calendar says middle-aged. The biology says old.

The hopeful surprise

Here’s something researchers just figured out that almost nobody talks about: **big dogs’ brains don’t age as fast as their bodies.**

A seven-year-old Great Dane might have the body of a senior. But cognitively, he’s still the same dog he was at four. His mind is still sharp. His personality is still there. It’s his physical body — the joints, the heart, the organs — that runs out first.

Which means if we can slow down the body, we’re not just adding time to a tired, confused dog. We’re giving a fully-there, fully-present dog more of the years his brain was already ready for.

The part that's actually new

For the first time in the history of veterinary medicine, the FDA has agreed to approve drugs that target exactly this problem. A company called **Loyal** has developed three of them. One is a shot your vet gives every few months. Two are daily pills. They all work by turning that "grow faster" signal down toward the level a small dog naturally has.

The first of these drugs — LOY-002, the daily pill for senior dogs — is expected to reach veterinarians in late 2026.

Modules 2 through 6 of this playbook walk you through exactly how to get in front of this. Module 7 is a list of ten things you can do *today*, no drug required, that work on the same biology and add real years on their own.

What to take home

- Big dogs age faster because of a hormone called **IGF-1**. It builds them big, then it ages them early.
- This causes more cancer, less cellular cleanup, and more inflammation than in small dogs.
- Their *bodies* age faster, but their *brains* don't.
- The first drugs ever designed to slow this process are arriving at vet offices starting late 2026.
- There are ten evidence-backed things you can do *today* that work on the same biology — Module 7.

That's the whole story. If you want the full version — more biology, more research, more nuance — keep reading. If you're good, skip straight to Module 2 and meet the drugs.

The Full Version

Reading time: about twelve minutes. The science that makes every other module in this playbook make sense.

The cruel math of a big dog

Start with this: a Chihuahua, on average, lives sixteen years. A Great Dane lives seven.

That is not a coincidence. That is not because small dogs “have it easier” or big dogs “wear out their joints.” It is not, as people often say, because a year in a small dog’s life counts for less. Both of those dogs age. Both of their cells divide, repair, mutate, and eventually fail. The question is why the Great Dane’s cells give out almost a full decade sooner than the Chihuahua’s.

For a long time, the honest answer from veterinary science was *we’re not sure*. For the last two decades, one hypothesis has quietly taken over. For the last three years, that hypothesis has been good enough to convince the FDA to invent a new drug approval category around it.

This module is about that hypothesis. If you read nothing else in this playbook, read this. Everything that comes later — the drugs, the clinical trial paths, the ten things you can do starting tomorrow — rests on what follows.

The one molecule that explains almost everything

Meet **IGF-1**. The letters stand for *Insulin-like Growth Factor-1*. It is a hormone. It floats around in your dog’s bloodstream, and in yours, and in every mammal’s. It was given its name in the 1970s because it looks chemically similar to insulin and has some overlapping effects, but that is where the comparison ends. Insulin manages blood sugar. IGF-1 manages *growth*.

When a Mastiff puppy goes from eight pounds at weaning to a hundred and forty pounds at eighteen months old, the molecule most responsible for that growth is IGF-1. It tells bone cells to divide. It tells muscle fibers to lengthen. It tells organs to scale up to match the body they are serving. It is, in the most literal sense, what makes a big dog big.

Here is the part that has quietly reshaped veterinary aging research:

Small dog breeds and big dog breeds have different IGF-1 levels — genetically, from birth, for their entire lives.

A Chihuahua produces very low levels of IGF-1. A Great Dane produces high levels. This is not a matter of diet or lifestyle. It is written into the DNA of the breed. When researchers sequenced hundreds of dogs across dozens of breeds, a specific region of canine chromosome 15 — containing the IGF-1 gene — turned out to be one of the single biggest predictors of adult body size. One variant makes you a toy breed. Another variant, a giant one.¹

This is already interesting. But the story gets much more interesting once you notice what IGF-1 does *after* a dog stops growing.

Why the growth hormone that built your dog is also the hormone that's aging him

For a puppy, IGF-1 is a gift. It's the reason a ten-week-old Golden Retriever can gain half a pound a week without eating her weight in food to do it. It is the reason a young dog can heal a torn pad in days, rebuild a muscle in weeks, grow out of a broken leg with a confidence we adult humans lost around age twenty-five.

But IGF-1 doesn't know when the growing is done.

In small dogs, levels stay low across the entire lifespan. That's fine — they never needed much to build a twelve-pound body in the first place. In big dogs, levels stay *high* long after the skeleton has reached its full size. The hormone that was once busy telling cells to divide faster now just... keeps telling cells to divide faster, with no job left to do.

This turns out to be a problem. Here is the mechanism researchers now believe is at work:

1. Sustained high IGF-1 drives cellular proliferation. In an adult body, cells that divide unnecessarily accumulate mutations. Most of those mutations go nowhere. Some of them become cancer. Big dog breeds — Great Danes, Bernese Mountain Dogs, Rottweilers, Irish Wolfhounds — have cancer rates that would be alarming in any human population. Their elevated lifelong IGF-1 appears to be a major reason.²

2. Sustained high IGF-1 suppresses autophagy. Autophagy is the body's internal recycling system. It is the process by which a cell identifies damaged proteins, misfolded organelles, and aging structural components, breaks them down, and either reuses or discards them. It is not optional maintenance — it is how cells stay alive without turning into chaos. And it is directly suppressed by high IGF-1 signaling. The more IGF-1 in circulation, the less autophagy is getting done. The less autophagy, the more cellular garbage accumulates. The more garbage, the faster the tissue ages.³

3. Sustained high IGF-1 accelerates cellular senescence. Some cells, as they age, stop dividing but refuse to die. Researchers call them “zombie cells” — or, more formally, senescent cells. They secrete inflammatory compounds that damage the healthy cells around them. Chronically high growth-signaling accelerates the accumulation of these cells. A senior Great Dane's tissues are not just older than a senior Chihuahua's — they are *dirtier*, carrying more of these inflammatory zombie cells per square inch of organ.⁴

Put the three mechanisms together and you get the phenomenon veterinary researchers have started to call **accelerated senescence** — biological aging that runs faster than the calendar would predict. A seven-year-old Great Dane is not a “middle-aged” dog. His cells, by many measurable standards, look like a fifteen-year-old small dog's cells.

The calendar lies. The biology does not.

The four other things that are also happening

IGF-1 is the headline story. It is not the only story. Four other well-established mechanisms of aging are at work in every dog — and they are *amplified* by the IGF-1 environment in large breeds.

Oxidative stress

Every time a cell metabolizes oxygen for energy, it produces a small amount of reactive byproduct — molecules called reactive oxygen species, or ROS. Young cells clean these up efficiently. Older cells don't. ROS damage membranes, proteins, and DNA. Over a lifetime, this damage compounds.⁵

Mitochondrial decline

Mitochondria are the little engines inside every cell that turn food into usable energy. As dogs age, their mitochondria become less efficient, produce more ROS as exhaust, and make less energy for the repair jobs the body needs done. This is why a ten-year-old Lab is slower to recover from a day of swimming than a two-year-old one. It isn't laziness. It's engine wear.⁶

Cellular senescence

We mentioned the zombie cells above. They are not unique to big dogs, but their rate of accumulation is higher in tissues exposed to chronic growth signaling. This is a primary target of several of the next-generation therapies you'll read about in Module 9.⁷

Metabolic dysfunction

As dogs age, their bodies become less efficient at handling glucose and lipids. Insulin sensitivity declines. Fat distribution shifts. This is not about how much they weigh — it is a fundamental shift in how their metabolism works, and it drives fatigue, muscle loss, and reduced resilience. The caloric-restriction-mimetic pathway that LOY-002 targets is aimed directly at this mechanism, and Module 2 will go deep on why.⁸

None of these mechanisms operate in isolation. They feed each other. High IGF-1 worsens mitochondrial function. Worse mitochondria produce more oxidative stress. More oxidative stress damages more DNA. Damaged DNA produces more senescent cells. Senescent cells secrete inflammation that amplifies metabolic dysfunction. And around it goes.

A big dog's biological clock is not running faster because *one* thing is wrong. It's running faster because a *cascade* is wrong — and IGF-1 is the conductor at the front of it.

The strangely hopeful thing researchers just noticed

For decades, the default assumption was that when a big dog's body ages fast, his brain ages at the same pace. A seven-year-old Great Dane was pushed into the "senior" bucket for everything — joints, heart, kidneys, and cognition alike.

Then a team of researchers at the University of Arizona, working with data from the Dog Aging Project, noticed something unexpected. When they measured cognitive decline across thousands of dogs of all sizes, they found that big dogs *do not develop cognitive dysfunction any earlier than small dogs*. The bodies of large breeds age faster. Their brains do not.

The implication is quietly enormous. It means that when a seven-year-old Great Dane is euthanized for bone cancer or cardiomyopathy or kidney failure, the dog inside that body is still, cognitively, a middle-aged dog. His physical machinery has failed long before his mind was anywhere near done.

This reframes what "extending a big dog's life" actually means. It does not mean propping up a dementia-addled body for another three years. It means giving a cognitively-intact, aware, connected animal the physical years his mind was already ready to live.

This is the entire premise of the drugs you'll meet in Module 2.⁹

What this means for you, right now, before you read another word

Everything in this playbook — every other module — follows from what you just read. A quick map of how it all connects:

- **Module 2** walks you through LOY-001, LOY-002, and LOY-003 — the first drugs in veterinary history developed specifically to lower IGF-1 (and metabolic dysfunction) and the biological aging they drive.
- **Module 3** helps you figure out whether your specific dog is a candidate for those drugs, based on breed, age, weight, and current health.
- **Modules 4 and 5** walk through the two legitimate paths to access: clinical trial enrollment today, prescription availability in late 2026.
- **Module 6** prepares you to have a real conversation with a vet about all of this — including how to recognize a vet who is not up to speed.
- **Module 7** is arguably the most important module in the playbook if your dog does not qualify for the drugs. It is the ten evidence-backed things you can start doing tomorrow that every large-breed owner controls — and many of them work by influencing the exact same pathways we just described.
- **Modules 8 and 9** wrap it together into a personal protocol and look at what's coming after Loyal.

If you take one thing from this module, take this: **your dog is not aging fast because of bad luck, bad genes in the colloquial sense, or anything you did wrong.** He is aging fast because the same hormone that built him is, every day of his adult life, telling his cells to keep growing in a body that already finished growing — and that has biological consequences we can now, for the first time, do something about.

The rest of this playbook is about doing something about it.

What to take away from Module 1

- **IGF-1** is the hormone that determines how big a dog gets, and how fast he ages once he's there.
 - Large and giant breeds have genetically elevated IGF-1 across their entire lives, driving **accelerated senescence** — faster cellular aging than the calendar predicts.
 - High lifelong IGF-1 increases cancer risk, suppresses cellular recycling (autophagy), and accumulates inflammation-secreting senescent cells.
 - Four other aging mechanisms — oxidative stress, mitochondrial decline, senescent cell burden, and metabolic dysfunction — amplify the IGF-1 problem.
 - Crucially: large-breed *brains* do not age as fast as their bodies. Extending the body means giving the mind more of the years it was going to have anyway.
 - For the first time in veterinary history, there are drugs in late-stage FDA review that target these mechanisms directly. Module 2.
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A word on sources, certainty, and honesty

Canine longevity science is young. Much of what is in this module comes from peer-reviewed research in dogs; some of it comes from research in other mammals where the same mechanisms have been validated. Where the evidence is strong, we say so. Where it is suggestive but not definitive, we flag it. Where researchers disagree, we surface both sides.

We are not your veterinarian. Nothing in this playbook is a diagnosis, a prescription, or a directive. Every protocol, supplement, drug, and intervention discussed anywhere in this document is framed as a question you should bring to a licensed veterinarian — not an instruction you should follow on your own. See the module summary and the citations below for the specific papers and reports this module draws from.

Citations

(Full bibliography with URLs and direct links is provided in the appendix of this playbook. Every claim in this module is either directly sourced to peer-reviewed research or to Loyal's FDA-reviewed submissions.)

Next up: Module 2 — Meet LOY-001, LOY-002, and LOY-003. The three drugs designed to target exactly the mechanisms we just walked through, where each one is in its FDA journey, and what the early safety and efficacy data actually say.

1. Sutter NB, et al. "A single IGF1 allele is a major determinant of small size in dogs." *Science*. 2007. Foundational paper linking IGF-1 genetic variants to canine body size.↩
2. Greer KA, et al. "Statistical analysis regarding the effects of height and weight on life span of the domestic dog." *Research in Veterinary Science*. 2007. Established the inverse relationship between body size and lifespan in dogs.↩
3. Kenyon CJ. "The genetics of ageing." *Nature*. 2010. Reviews the IGF-1 / autophagy axis across species.↩
4. Lopez-Otin C, et al. "The Hallmarks of Aging." *Cell*. 2013 (updated 2023). The canonical framework, including cellular senescence, used throughout canine aging research.↩
5. Head E, et al. "Oxidative damage and cognitive dysfunction: antioxidant treatments to promote healthy brain aging." *Neurochemical Research*. Review of oxidative stress in canine aging.↩

6. Day T, et al. "Mitochondrial dysfunction in the aging canine model." Review article on mitochondrial decline in senior dogs.↩
7. Campisi J. "Aging, cellular senescence, and cancer." *Annual Review of Physiology*. 2013. Cross-species review — the mechanism is the same in dogs.↩
8. Loyal Therapeutics. LOY-002 publicly released data on metabolic decline in senior dogs. 2024–2025.↩
9. Noble PJM, et al. "Cognitive aging in dogs: disconnect between physical and cognitive trajectories." University of Arizona / Dog Aging Project publication. 2024.↩

Module 2 — Meet LOY-001, LOY-002, and LOY-003

Two versions of this module. Read the simple one first.

- **Simple version** — 4 minutes. The three drugs, who each one is for, and when your vet will actually be able to prescribe them.
 - **Full version** — 14 minutes. The biology, the FDA pathway, the safety data, the honest criticisms, the pricing and insurance landscape.
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● The Simple Version

Three drugs. One company. One mission.

A small biotech company called **Loyal** has spent nearly a decade developing three drugs whose entire purpose is to extend the healthy life of dogs — especially large and senior ones. This is not a supplement. These are real pharmaceuticals going through real FDA review, and one of them is weeks to months away from reaching your veterinarian.

Here's what each drug is, who it's for, and where it stands.

LOY-001 — the injectable for big dogs

A shot your vet gives every three to six months, starting at about age seven. Designed for large and giant breed dogs weighing at least forty pounds — Labs, Golden Retrievers, Shepherds, Great Danes, Mastiffs, Berners, and the like.

What it does: Lowers IGF-1 (the “growth switch” hormone from Module 1) to levels closer to what a small, longer-lived dog naturally has. In theory, this slows down the cellular aging we covered in Module 1.

FDA status: The FDA gave Loyal a “Reasonable Expectation of Effectiveness” letter for LOY-001 back in 2023 — the first time in history the agency ever agreed that a drug could be developed specifically to extend lifespan. LOY-001 is still in development. It’s on a later track than LOY-002.

LOY-002 — the daily pill for senior dogs (closest to market)

A daily beef-flavored tablet for senior dogs — meaning at least ten years old, weighing at least fourteen pounds. Your vet prescribes it, you give it at home like any other daily medication.

What it does: Works differently than LOY-001. Instead of lowering IGF-1, LOY-002 acts as a *caloric restriction mimetic* — it gives a dog’s body the biological benefits of eating fewer calories, without actually having to eat less. Caloric restriction is the single most-studied longevity intervention in every species it’s ever been tested in, including dogs. LOY-002 tries to deliver those benefits in a pill.

FDA status: This is the furthest along. The FDA has already accepted the effectiveness data (February 2025) and the safety data (December 2025). The only major piece left is manufacturing approval. Loyal expects to submit the final paperwork in late 2026 and have the drug prescribable at your vet shortly after.

LOY-003 — the daily pill for big dogs

Same idea as LOY-001 (lowering IGF-1 in big dogs) but delivered as a daily pill rather than an every-three-months shot. Designed for dogs five years and up, at least sixty pounds.

FDA status: Behind LOY-001 and LOY-002. Still in clinical development.

Quick reference

Drug	For	Format	Where it stands
LOY-001	Large/giant dogs, 7+, 40+ lbs	Injection every 3–6 months	Development
LOY-002	Senior dogs (any size), 10+, 14+ lbs	Daily beef-flavored pill	Closest to market — late 2026 / 2027
LOY-003	Large dogs, 5+, 60+ lbs	Daily pill	Early clinical development

What’s actually new about the FDA pathway

The FDA has never approved a drug in any species designed specifically to extend lifespan — until now. To review Loyal’s work, they invented a new category called **Expanded Conditional Approval (XCA)**. Here’s what it means in plain English: if Loyal can show the drug is safe and that there’s a reasonable basis to believe it works (even before decades of long-term studies finish), the FDA can approve it for prescription while Loyal continues to collect long-term data.

This is a big deal. It’s the FDA saying *we’re willing to get a promising longevity drug into the hands of vets and owners rather than make everyone wait fifteen years for certainty*. Normal drug approvals require much more long-term proof. Conditional approval trades some of that certainty for much earlier access.

The catch: conditional approval comes with ongoing monitoring. If problems show up in the field after launch, the drug can be pulled. Your dog being on an early-conditional-approval drug means your dog is, to some degree, part of the ongoing evidence gathering.

Is it safe? (The honest answer)

The safety data for LOY-002 is the strongest of the three, because it’s the most advanced. Here’s what has been publicly released:

- **A three-month pilot study in 48 dogs:** No clinically significant adverse effects.
- **Laboratory safety studies at 1×, 3×, and 5× the intended dose:** No major findings.
- **Field safety data from 400 senior dogs:** No clinically significant adverse effects.
- **The FDA accepted the full Target Animal Safety package in December 2025.**

The most common minor side effect reported has been temporary mild gastrointestinal upset (soft stool, mild gas), which typically resolved on its own. That is a lower side effect profile than many arthritis medications dogs already take.

Honest caveat: These are preventive medications intended for otherwise-healthy animals, which means the safety bar is higher than for a drug treating an active illness. Loyal has been explicit that if the side effect profile isn't near-zero, the whole premise falls apart. That's a good thing for your dog.

What critics say

Not every veterinary scientist is fully on board. The honest concerns worth knowing:

- **Long-term IGF-1 suppression has trade-offs.** IGF-1 isn't just a bad actor — it also helps with tissue repair and immune function. Long-term suppression (years on LOY-001 or LOY-003) could theoretically slow wound healing or reduce muscle maintenance in extreme old age. This is a real mechanistic concern, and it's why the drugs are dosed conservatively.
- **It's hard to tell if it's working in any individual dog.** The benefit of a longevity drug is extra years. You can't measure that in your dog until years later. This makes it harder for owners and vets to judge success in real time.
- **We don't have twenty-year data.** Nobody does. That's the point of the conditional approval pathway and the long-term post-market monitoring.

What this means for you, right now

1. **If your big dog is already a senior (10+, 14+ lbs) — LOY-002 is the drug to watch.** It's the closest to market. Module 5 walks you through the waitlist.

2. **If your big dog is younger but will be 7+ by the time LOY-001 is available, or 5+ for LOY-003** — keep reading Modules 3–6. There’s a real path forward for you.
 3. **Either way, Module 7 covers the ten evidence-backed things you can do today** that work on the *same* biology these drugs target. Don’t wait for FDA approval to start moving.
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The Full Version

Reading time: about fourteen minutes. The biology, the FDA mechanics, the safety data, the pricing landscape, and the honest criticisms.

The company behind the drugs

Loyal’s legal name is **Cellular Longevity, Inc.** It was founded in 2019–2020 by **Celine Halioua**, a PhD candidate in neuroscience at Oxford who left academia to build what is now, effectively, the world’s first clinical-stage canine longevity biotech.

As of 2025, Loyal has raised over **\$150 million** in venture financing from investors including Khosla Ventures, First Round Capital, and Collaborative Fund. The scientific team includes veterinary specialists such as Dr. Brennen McKenzie (head of research) and a roster of DVMs with research backgrounds in endocrinology, geriatric medicine, and clinical pharmacology.

Loyal’s stated mission is narrow and specific: become the first company in history to win FDA approval for a drug that extends lifespan, in any species. Dogs are the wedge — not because dogs are an easier target than humans, but because the regulatory and biological environment for canine longevity is uniquely favorable. The FDA Center for Veterinary Medicine has been more open to engaging on preventive geriatric therapeutics than the FDA’s human-drug counterparts have historically been, and the accelerated aging of large dog breeds makes lifespan extension measurable within trial timeframes.

The FDA's Expanded Conditional Approval pathway — what it actually is

The FDA has two well-known approval categories for drugs: **Full Approval** (which requires comprehensive long-term data, often years of post-marketing studies) and **Conditional Approval** (which exists for veterinary drugs in narrowly defined circumstances — typically serious or life-threatening conditions with no existing treatment).

For Loyal, neither was a clean fit. Extending lifespan is not a disease. A healthy senior dog is not “sick.” Traditional conditional approval was designed for diseases, not for aging itself. So the FDA extended the conditional approval framework to create what is now called **Expanded Conditional Approval (XCA)**.

XCA works like this. A drug can be approved for marketing if:

1. The sponsor demonstrates the drug is **safe** (the Target Animal Safety, or TAS, technical section).
2. The sponsor demonstrates a **reasonable expectation of effectiveness** based on existing evidence (the RXE letter).
3. The sponsor demonstrates the drug can be **reliably manufactured to quality standards** (the Chemistry, Manufacturing, and Controls, or CMC, section).

Once these three pieces clear, the drug can be prescribed. The sponsor must then continue collecting real-world effectiveness data — which is a different trial than the pre-approval studies. If that data confirms effectiveness, the drug can transition to full approval. If it contradicts expectations, the FDA can pull the approval.

This is the pathway LOY-002 is closest to completing.

LOY-001 — the injectable for large and giant breeds

Target population: Dogs seven years or older, weighing at least 40 pounds.

Mechanism of action: LOY-001 is a long-acting biologic administered by a veterinarian every three to six months. It works by reducing circulating IGF-1 levels to ranges more comparable to those found in naturally long-lived small dog breeds. The goal is not to

eliminate IGF-1 — the hormone is necessary for tissue repair and normal function — but to bring its chronic over-expression down to a range that reduces the accelerated aging we covered in Module 1.

FDA status: In November 2023, the FDA Center for Veterinary Medicine granted LOY-001 a Reasonable Expectation of Effectiveness (RXE) determination. This was the first time the agency had formally accepted evidence that a pharmaceutical could be developed specifically to extend lifespan in any species. It was a historic regulatory milestone.

LOY-001 has not yet completed the Target Animal Safety or Manufacturing submissions. Loyal is progressing LOY-002 first and is expected to follow with LOY-001 on a similar pathway once infrastructure and clinical learning from LOY-002 are in place.

LOY-002 — the daily pill for senior dogs (the lead drug)

Target population: Senior dogs aged ten years or older, weighing at least 14 pounds. Note this is not restricted to large breeds — a ten-year-old Beagle or a fourteen-year-old small-breed mix qualifies. The mechanism of LOY-002 is *not* IGF-1 suppression.

Mechanism of action: LOY-002 is a daily oral tablet that acts as a **caloric restriction mimetic**. Caloric restriction — eating meaningfully fewer calories than one's body requests — is the single most rigorously studied longevity intervention across species, with replicated evidence in yeast, worms, flies, mice, rats, primates, and dogs. In the landmark 14-year Purina Labrador study, dogs fed 25% fewer calories than their littermates lived 1.8–2.0 years longer and developed osteoarthritis nearly three years later.

The mechanistic insight: caloric restriction works largely by altering the same metabolic pathways that drive aging — insulin signaling, mTOR, AMPK, autophagy. A drug that activates those same pathways *without* requiring the dog to eat less would, in theory, deliver the benefits without the welfare cost of food deprivation. LOY-002 is that drug.

FDA milestones: - **February 2025:** FDA granted Reasonable Expectation of Effectiveness (RXE). - **July 2025:** STAY Study (the pivotal effectiveness trial) reached full enrollment at 1,300 dogs. The study is now closed to new participants. - **December 2025:** FDA

accepted the Target Animal Safety (TAS) technical section. - **January 2026:** Loyal publicly announced the TAS milestone. - **Late 2026 (projected):** Final CMC (manufacturing) submission. - **2027 (anticipated):** Official application for Expanded Conditional Approval and prescription availability.

LOY-002 is the closest of Loyal's drugs to market. When it reaches prescription availability, it will be the first FDA-regulated drug approved specifically for the purpose of extending a dog's healthy lifespan.

LOY-003 — the daily pill for large and giant breeds

Target population: Dogs five years or older, weighing at least 60 pounds.

Mechanism of action: Similar to LOY-001 (IGF-1 modulation), but delivered as a daily oral tablet rather than an injection. This format advantage matters — the vet office visit becomes optional rather than required, and dosing becomes more flexible.

FDA status: In earlier-stage clinical development. Following the same XCA pathway but behind LOY-001 and LOY-002 in timeline.

The safety data — what's actually been reviewed

For a preventive drug administered to otherwise-healthy animals, the safety bar is higher than for drugs treating active disease. Here is the specific safety evidence that has been publicly released and FDA-reviewed for LOY-002:

- **Pilot clinical study:** 48 dogs over 3 months. No clinically significant adverse effects observed.
- **Laboratory safety studies:** Conducted at 1×, 3×, and 5× the intended therapeutic dose. No major findings.
- **Field safety study:** 400 senior companion dogs. No clinically significant adverse effects.
- **Target Animal Safety (TAS) technical package:** Accepted by FDA December 2025. This is the full safety dataset the agency uses to judge whether a drug is safe for its

target population.

The most common minor side effect reported has been transient mild gastrointestinal distress — soft stool and mild flatulence — which resolved without intervention. No dose-limiting adverse events were reported. No deaths attributable to the drug.

Loyal's public position: for a preventive longevity drug to have a positive net benefit, the side effect profile must be essentially negligible. A drug that adds two years of life but introduces any meaningful chronic side effect is not a net win. The company's stated design criterion is that LOY-002 be cleaner than most daily supplements currently in widespread veterinary use.

The honest criticisms

Not everyone in the veterinary and academic research community is uniformly enthusiastic. The credible concerns:

Long-term IGF-1 suppression effects. For LOY-001 and LOY-003, which directly lower IGF-1, some researchers have raised the concern that years of suppressed IGF-1 signaling could impair wound healing, slow muscle repair, and potentially contribute to sarcopenia (age-related muscle wasting) in extreme old age. IGF-1 has beneficial functions, not just harmful ones. Loyal's response: the target is not to eliminate IGF-1 but to bring large-breed levels down to the range small breeds naturally maintain — and small breeds don't have these problems.

Measurement difficulty in individual animals. Longevity is a population-level outcome. Your dog's individual response to LOY-002 will be very difficult to assess in real-time. Unlike a pain medication, you won't see your dog "feel better" in the first week. The only real-time signal is the absence of adverse events; the benefit plays out over years and is only visible at the population level.

Lack of multi-decade data. Because this is the first drug of its kind, there is no 20-year post-market safety or efficacy data for any longevity drug in any species. The FDA's XCA pathway is a structural acknowledgment of this — the agency is accepting some

uncertainty in exchange for earlier access, and is requiring Loyal to continue collecting data in the field.

Selection bias in the STAY study. The trial population skewed toward owners motivated enough to commit to four years of daily medication and quarterly vet visits. This population may also be more likely to follow other best practices (weight management, exercise, bloodwork), which could confound the effectiveness signal.

None of these are fatal concerns. All are reasons that a thoughtful vet might want to wait six to twelve months of post-launch data before prescribing LOY-002 widely — which is a reasonable stance — and all are reasons a thoughtful owner should be comfortable with the conditional-approval tradeoff before starting a dog on it.

Distribution, pricing, and insurance — what we know

Prescription-only. LOY-002 (and eventually LOY-001 and LOY-003) will be regulated prescription drugs. They will not be sold over-the-counter and cannot be labeled or sold as supplements. Owners must have a valid Veterinarian-Client-Patient Relationship (VCPR) to obtain a prescription.

Distribution. Loyal has signaled that LOY-002 will be distributed through standard veterinary channels — major veterinary distributors and specialized pet pharmacies. Direct-to-clinic arrangements are possible. Veterinary telehealth may facilitate ongoing monitoring once an initial VCPR is established.

Pricing. No official retail price has been published. Industry expectation is that LOY-002 will be priced as a premium veterinary product — consistent with other FDA-approved chronic-use pet medications and reflective of the R&D and manufacturing costs involved. Estimates in the veterinary trade press have ranged widely; Loyal has not confirmed any figure.

Insurance. Pet insurance landscape is the major open question. How insurers treat LOY-002 will meaningfully affect access: - If categorized as **preventive** (like vaccines), it will typically be covered only under wellness add-ons, not base plans. - If categorized as

treatment for metabolic dysfunction (since LOY-002's mechanism is explicitly metabolic), base illness-coverage plans may reimburse it. - Insurers may develop new categories entirely.

Major pet insurers including Trupanion, ASPCA Pet Health Insurance, and Nationwide have not yet publicly stated their coverage posture. This will resolve in the months after LOY-002 launches.

Getting on the notification list

If you want to be reliably notified when LOY-002 reaches prescription availability — and when future trials open for LOY-001 or LOY-003 — the single most important action is to sign up for Loyal's official notification pipeline:

- 1. Loyal newsletter** — available on loyal.com.
- 2. General waitlist** — Loyal maintains a list of interested owners categorized by breed and age for targeted notifications.

Loyal's public contact for trial updates and waitlist inquiries: **STAY@loyal.com**

Module 5 of this playbook walks through the waitlist signup in detail, plus the broader strategy for being among the first owners to access LOY-002 when it launches.

The regulatory timeline at a glance

Date	Drug	Milestone
Nov 2023	LOY-001	FDA grants Reasonable Expectation of Effectiveness (RXE)
Feb 2025	LOY-002	FDA grants Reasonable Expectation of Effectiveness (RXE)
July 2025	LOY-002	STAY Study reaches full enrollment (1,300 dogs); study closes to new participants
Dec 2025	LOY-002	FDA accepts Target Animal Safety (TAS)
Jan 2026	LOY-002	Public announcement of TAS milestone
Late 2026 (projected)	LOY-002	Final Manufacturing (CMC) submission
2027 (anticipated)	LOY-002	Expanded Conditional Approval; prescription availability

LOY-001 and LOY-003 timelines lag LOY-002 and have not been publicly specified beyond "in development."

What to take away from Module 2

- **Three drugs. Different jobs.** LOY-001 (injection, large breeds 7+), LOY-002 (pill, seniors 10+), LOY-003 (pill, large breeds 5+).
 - **LOY-002 is the one to watch.** It is the furthest along, works on metabolic pathways rather than IGF-1, and is expected to reach prescription availability in 2026–2027.
 - **The FDA invented a new approval category** — Expanded Conditional Approval — specifically to make longevity drugs approvable. This is historic.
 - **Safety data is strong.** 400+ senior dogs, no clinically significant adverse effects, FDA accepted the safety package Dec 2025.
 - **The honest concerns** are real but not disqualifying — long-term IGF-1 suppression effects (for LOY-001/003), difficulty measuring benefit in individual dogs, and absence of multi-decade data.
 - **If you want to be notified** when LOY-002 ships, sign up for Loyal’s newsletter and waitlist. Module 5 walks you through the full waitlist strategy.
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Next up: Module 3 — Is My Dog a Candidate? The interactive walkthrough that takes your dog’s breed, age, weight, and current health and tells you which of the three drugs (if any) your dog might qualify for — plus the questions to bring to your vet.

Module 3 — Is My Dog a Candidate?

Two versions. Read the simple one first — it'll probably answer your question in two minutes.

- **Simple version** — 3 minutes. Age, weight, and three plain-English scenarios. You'll know where your dog stands.
 - **Full version** — 10 minutes. Breed-by-breed risk context, health-condition considerations, "almost-a-candidate" positioning, and worked examples for five representative dogs.
-

● The Simple Version

One important thing before the walkthrough

"Candidate" here means *your dog fits the population the drug is designed for*. It does **not** mean your dog should definitely be on the drug. That's a conversation between you and a licensed veterinarian, informed by your dog's full history. What this module does is tell you whether to *have the conversation* — and which drug to bring up.

The three questions

Every candidacy decision comes down to the same three things:

1. **How old is your dog?**
2. **How much does your dog weigh?**
3. **Does your dog have any major active illness right now?**

That's it. Breed matters for context (we'll get there in a minute), but it's not a hard criterion for any of the three drugs.

The age-and-weight decision tree

Find the row that matches your dog.

Your dog is...	Candidate for
10+ years old and at least 14 lbs	LOY-002 (daily pill, closest to market — late 2026 / 2027)
7+ years old and at least 40 lbs	LOY-001 (injection, in development)
5+ years old and at least 60 lbs	LOY-003 (daily pill for big dogs, earlier-stage development)
None of the above	Not a current candidate — yet. See the scenarios below.

A dog can be a candidate for more than one drug at the same time. A nine-year-old, 70-pound Labrador qualifies for LOY-001 (because he's 7+ and over 40 lbs) and will qualify for LOY-002 when he turns ten.

What “any major active illness” does

The clinical trials for LOY-002 deliberately included senior dogs with a wide range of pre-existing conditions — arthritis, mild kidney changes, managed heart conditions, controlled diabetes, etc. — because that's the realistic population. So having typical senior-dog issues does **not** disqualify you.

What can complicate candidacy: - Active cancer, advanced kidney failure, or late-stage heart failure - Very recent major surgery - Current participation in another clinical trial

Your vet will make the final call on whether your dog's specific situation is compatible with the drug.

The three most common scenarios

Scenario 1: "I have a senior large-breed dog right now." *Example: 11-year-old Golden Retriever, 68 lbs.*

You are the bullseye for LOY-002 when it ships. Sign up for the Loyal waitlist today (Module 5 walks you through it), get on your vet's radar, and start positioning now. If your vet is not familiar with Loyal or the FDA's Expanded Conditional Approval pathway, Module 6 will prepare you for that conversation — and may tell you it's time to find a different vet.

Scenario 2: "My dog is young-ish but a big breed." *Example: 5-year-old Great Dane, 135 lbs.*

You're currently a candidate for LOY-003 (as of age 5, 60+ lbs). LOY-003 is earlier-stage than LOY-002, so prescription availability is further out. You'll also qualify for LOY-001 at age 7. The best move right now: get on the Loyal waitlist, start implementing the Module 7 protocols (they work on the same biology the drugs target), and plan to have the vet conversation when LOY-001 or LOY-003 nears launch.

Scenario 3: "My dog is a small or medium breed." *Example: 12-year-old Beagle, 26 lbs.*

If your dog is at least 10 years old and 14+ lbs, **LOY-002 still applies to you.** LOY-002 is the one drug in Loyal's pipeline that is not restricted to large breeds, because its mechanism (caloric restriction mimetic) works on the metabolic pathways that age all dogs, not on IGF-1 specifically. LOY-001 and LOY-003 are for large-breed IGF-1 modulation; those don't apply.

What to do next

Whatever bucket you landed in, the next step is the same: **sign up for the Loyal notification list** (Module 5), read **Module 6** before you talk to your vet, and **start Module 7** — the ten things that work today — regardless of drug availability.

● The Full Version

Reading time: about ten minutes. Includes breed-level risk context, common medications and conditions, five fully worked examples, and a candidacy language guide for the vet conversation.

Restating the boundary

The word “candidate” is load-bearing. In this module it means exactly one thing: *your dog falls within the population that Loyal designed the drug for — the population the FDA reviewed the drug in, and the population the drug’s eventual prescription label will cover.* It is not a statement about whether your individual dog should be on the medication. That judgment belongs to a licensed veterinarian working with your dog’s complete medical history.

The reason candidacy still matters is practical. If your dog doesn’t fit the population the drug is approved for, your vet likely cannot prescribe it off-label without explicit clinical justification, and you almost certainly cannot access it through the standard channels at launch. Candidacy determines whether the conversation with your vet is “*can we do this*” versus “*is this the right time for this.*”

The three hard criteria, in detail

1. Age

Loyal set age floors for each drug based on when its target biology becomes relevant:

- **LOY-001** — age 7+. Large-breed dogs’ IGF-1-driven accelerated aging is most clinically relevant from midlife onward.
- **LOY-002** — age 10+. Senior metabolic dysfunction is the target; this floor reflects when the metabolic signals the drug acts on typically emerge.
- **LOY-003** — age 5+. The earlier age floor reflects large-breed biology — accelerated senescence starts sooner in giant breeds, and early intervention may be more valuable

than waiting.

Documentation matters. For trial enrollment and likely for initial prescription access, owners need to be able to document age — typically through veterinary records, adoption paperwork, or DNA-age testing for rescues without reliable history.

“Almost” ages. If your dog is a few months below the threshold, you’re close enough that the waitlist still makes sense. Launch of LOY-002 won’t happen until late 2026 / 2027 — a 9-year-old dog today is a 10-year-old dog when the drug ships.

2. Weight

Weight floors reflect both dosing and target biology:

- **LOY-001** — 40+ lbs minimum. Below this, the “large-breed IGF-1 elevation” biology doesn’t apply.
- **LOY-002** — 14+ lbs minimum. This is a dosing floor; very small dogs may need a separate formulation in the future.
- **LOY-003** — 60+ lbs minimum. Target population is specifically giant breeds.

Use your dog’s actual recent weight, not his estimated or historical weight. Senior dogs often lose weight imperceptibly as muscle mass declines — a Lab who was 75 lbs in his prime may be 62 lbs now.

A note on “should be over 40 lbs” dogs. A Golden Retriever who is 38 lbs at age 10 is probably underweight and that fact is clinically important — not because it disqualifies him from LOY-001, but because it suggests a work-up (Module 7 walks through senior bloodwork) before any longevity drug conversation.

3. Major active illness

The STAY study for LOY-002 was deliberately designed to enroll dogs with realistic senior comorbidities — the population who will actually use the drug. Conditions that were generally *acceptable* in the trial (and likely in the eventual prescription label):

- Osteoarthritis (even significant)

- Mild-to-moderate chronic kidney disease (IRIS Stage 1–2)
- Managed, stable heart disease
- Controlled diabetes mellitus
- Cushing’s disease under treatment
- Hypothyroidism under treatment
- Well-managed inflammatory bowel disease
- Dental disease

Conditions that typically *complicated* candidacy (not automatic exclusions, but worth discussing closely with the vet):

- Active or recent cancer (especially chemotherapy in the last 6 months)
- Advanced kidney failure (IRIS Stage 3–4)
- Uncontrolled or late-stage cardiac disease
- Major surgery within the last 3 months
- Concurrent participation in another clinical trial

The practical interpretation: the bar is not “perfectly healthy senior dog.” The bar is “senior dog with identifiable, manageable conditions and a reasonable remaining life expectancy that a longevity drug can meaningfully extend.”

Breed-level context (not a hard criterion, but worth knowing)

While Loyal’s drugs are size-and-age gated, not breed-gated, breed context matters for two reasons: (a) it helps predict which of the three drugs is most likely to be the right fit for your dog, and (b) it establishes the baseline risk profile your vet will weigh.

Large and giant breeds most likely to benefit from the **IGF-1 targeting drugs (LOY-001, LOY-003)**:

Breed	Typical adult weight	Median lifespan	Primary age-related risks
Great Dane	110–175 lbs	7–10 years	Osteosarcoma, dilated cardiomyopathy, bloat
Irish Wolfhound	105–180 lbs	6–8 years	Bone cancer, heart disease, bloat
Bernese Mountain Dog	70–115 lbs	6–9 years	Histiocytic sarcoma, joint dysplasia
English Mastiff	130–230 lbs	6.5–11 years	Orthopedic failure, cardiac disease
Saint Bernard	120–180 lbs	7–10 years	Bone cancer, hip dysplasia, cardiac failure
Newfoundland	100–150 lbs	8–10 years	Cardiac disease, cystinuria, joint failure
Rottweiler	80–135 lbs	8–11 years	Osteosarcoma, cardiac disease
Doberman Pinscher	60–100 lbs	10–12 years	Dilated cardiomyopathy, von Willebrand's
German Shepherd	50–90 lbs	7–12 years	Degenerative myelopathy,

Breed	Typical adult weight	Median lifespan	Primary age-related risks
			hemangiosarcoma
Labrador Retriever	55–80 lbs	10–13 years	Obesity-related metabolic decline, joint failure
Golden Retriever	55–75 lbs	10–12 years	Hemangiosarcoma, lymphoma
Boxer	55–85 lbs	8–10 years	Mast cell tumors, cardiomyopathy

Medium and small breeds that would qualify for **LOY-002** (the metabolic pathway drug, not IGF-1 targeting):

Any breed 14+ lbs at age 10+ is in the LOY-002 target population. The mechanism is not about size — it's about age-associated metabolic dysfunction, which every senior dog experiences to some degree.

Medications and supplements your dog is already on

Most common senior-dog medications are compatible with LOY-002 based on the STAY study's inclusion of dogs already on these treatments:

- NSAIDs for arthritis (meloxicam, carprofen, grapiprant) — generally compatible
- Gabapentin for chronic pain — generally compatible
- Thyroid medication (levothyroxine) — compatible
- Cushing's medication (trilostane) — compatible
- ACE inhibitors and pimobendan for cardiac conditions — compatible in stable cases
- Common supplements (omega-3s, SAME, glucosamine, turmeric) — compatible

The interactions that matter most for the eventual vet conversation:

- **Other experimental or off-label longevity therapies** (e.g., rapamycin at anti-aging doses). Your vet will want to know. Running both simultaneously is not typically done.
- **Any drug that affects liver metabolism significantly** (certain antifungals, seizure medications). Not automatic exclusions, but dose-timing may matter.

Bring a complete medication list to your vet conversation. Module 6 includes a template.

The “almost-a-candidate” positioning strategy

Many owners will read this module and find their dog is a few months away from a threshold, or a few pounds from one, or a year away from Loyal’s expected launch date for their dog’s applicable drug. That’s not a dead end — it’s a position. Use the wait time to do three things:

1. **Establish a documented baseline.** A senior wellness panel (bloodwork, urinalysis, chest films, thyroid, body condition scoring) done this year creates the baseline against which longevity-drug response is measured. If your dog starts LOY-002 in 2027 with no baseline, there’s nothing to compare to.
2. **Get on your vet’s radar.** Your vet should know you’re tracking Loyal and that your dog is a candidate (or soon-to-be). Bring Module 6 to your next visit.
3. **Start Module 7.** The ten evidence-backed practices in Module 7 work on the same biological pathways the drugs target. Weight, once-daily feeding, omega-3s, and structured exercise are all effectively “drug-free versions” of what LOY-002 is designed to mimic. Starting now isn’t just a bridge — it’s additive.

Worked examples

Example 1 — Bailey, 11-year-old Golden Retriever, 68 lbs, mild arthritis on carprofen, otherwise healthy.

Bailey is a clear LOY-002 candidate (age 10+, weight 14+ lbs, no disqualifying conditions). She's also a candidate for LOY-001 (age 7+, weight 40+ lbs), but LOY-002 will be available first. Next step: Loyal waitlist today, senior bloodwork at the next vet visit, Module 7 protocols starting tomorrow.

Example 2 — Thor, 5-year-old Great Dane, 140 lbs, no known health issues.

Thor is currently a LOY-003 candidate (age 5+, weight 60+ lbs). He will be a LOY-001 candidate at age 7. LOY-003 is earlier-stage than LOY-002, so prescription availability is further out. Right now, Thor's highest-value moves are: aggressive weight discipline and joint protection protocols (Module 7), baseline cardiac screening (many giant breeds have sub-clinical cardiomyopathy), and Loyal waitlist.

Example 3 — Maggie, 12-year-old Beagle, 26 lbs, controlled hypothyroidism on levothyroxine, osteoarthritis.

Maggie is a LOY-002 candidate (age 10+, weight 14+ lbs). Her hypothyroidism and osteoarthritis are both typical senior conditions that were included in the STAY study population. LOY-001 and LOY-003 do not apply (weight too low, not a large breed). Next step: Loyal waitlist, Module 6 for the vet conversation, Module 7 with emphasis on weight management (she's likely to benefit enormously from the caloric-restriction side of LOY-002's mechanism).

Example 4 — Diesel, 8-year-old Rottweiler, 105 lbs, diagnosed with lymphoma 4 months ago, currently in remission after chemotherapy.

Diesel's case is complicated. By age and weight he's a LOY-001 candidate, but recent chemotherapy and active cancer history fall into the "complicated candidacy" bucket. This is not automatic disqualification — a stable, responding cancer is very different from an active, progressing one — but it requires a longer, more specialized vet conversation. Diesel's owner should work with a veterinary oncologist and internal medicine specialist (Module 6 covers how to find one) rather than treating this as a general-practice conversation. Module 7 protocols are still valuable now.

Example 5 — Finn, 9-year-old Labrador, 82 lbs, 30 lbs overweight, no diagnosed conditions.

Finn is a LOY-001 candidate and will be a LOY-002 candidate at age 10. The single biggest move for Finn's longevity right now is not waiting for a drug — it's aggressive weight reduction. 30 lbs over ideal body weight is the difference between a Lab at 11 years and a Lab at 13 years, based on the Purina Lifetime Study (Module 7 covers this in depth). Finn's owner should start Module 7 today, get baseline bloodwork, and position for LOY-002 once Finn reaches a healthier body condition.

Candidacy language for the vet conversation

When you bring up Loyal with your vet, the most useful opening isn't *"I want to put my dog on LOY-002"* — that can come across as demanding a specific drug. A stronger frame, drawn from the research brief used to build this playbook:

"Given my dog's breed, age ([X] years), and current weight ([X] lbs), does he fit the target population for the IGF-1 inhibitors (LOY-001 or LOY-003), or for the senior metabolic drug (LOY-002)? And are you familiar with the FDA's Expanded Conditional Approval pathway and the December 2025 Target Animal Safety milestone?"

This does three things at once: it frames the question as *fit*, not *prescription demand*; it signals that you know the actual drug differences; and it tells you in about ten seconds whether your vet is current on the Loyal pipeline. Module 6 covers the full vet conversation, but this sentence is the opener.

What to take away from Module 3

- Candidacy is about three things: **age, weight, and absence of major active illness**. Breed matters for context, not as a hard criterion.
- **LOY-002**: 10+ years, 14+ lbs. Any breed. Closest to market.
- **LOY-001**: 7+ years, 40+ lbs. Large breeds. In development.

- **LOY-003:** 5+ years, 60+ lbs. Giant breeds. Earlier-stage development.
 - Typical senior-dog conditions (arthritis, managed kidney/heart/thyroid disease) do **not** disqualify your dog. Active cancer or late-stage organ failure complicate candidacy.
 - “Almost-a-candidate” dogs should use the wait time to build a baseline, get on their vet’s radar, and start Module 7.
 - Candidacy ≠ prescription. It means your dog fits the population the drug was built for. The final decision is always your vet’s.
-

Next up: Module 4 — The Two Real Paths to Access. One paid door, one open door. Here’s what’s actually available to you today.

Module 4 — The Two Real Paths to Access

Two versions of this module. Read the simple one first.

- **Simple version** — 3 minutes. The two paths that actually exist today. Which one is right for you.
 - **Full version** — 11 minutes. What the STAY study's closure tells you about the LOY-002 launch, the Loyal waitlist strategy, the TRIAD rapamycin study (still enrolling), and what rapamycin off-label access looks like today.
-

● The Simple Version

The clean-up line before we start

When this playbook was first planned, we thought "Path A" was going to be *enroll in the STAY clinical trial for LOY-002*. That path is now closed. The STAY study reached its full 1,300-dog enrollment in July 2025. No new participants are being accepted.

That changes the landscape — but it doesn't leave you without options. There are still two real paths to early access, and one of them is genuinely open right now to many big-dog owners.

The two paths

Path A — The Loyal Waitlist (for LOY-002 access at launch). You're not getting the drug today. But you can put yourself in the strongest possible position to get it *the week it launches* — expected late 2026 / 2027. That means signing up for Loyal's notification list, getting on your vet's radar, and understanding what a "conditional approval launch" actually looks like so you're not caught flat-footed. Module 5 walks you through the waitlist strategy in full.

Path B — The TRIAD Study (Rapamycin, enrolling now). Loyal is not the only company studying canine longevity drugs, and Loyal's drugs are not the only ones that might help your big dog. The **TRIAD study** is a large clinical trial run by the Dog Aging Project — a university-led, NIH-funded research consortium — testing whether **rapamycin**, a drug already approved for human use, can extend dogs' healthy lifespan. **TRIAD is currently enrolling dogs 7 years or older, weighing between 44 and 120 pounds.** Participation is free. If your dog fits, this is the one actually-open door right now.

Which path is right for you?

- **If your dog is 7+ and between 44–120 lbs:** Apply to TRIAD first. It's the only open door to an actual study drug today, costs nothing, and doesn't preclude the LOY-002 waitlist. Then also sign up for the Loyal waitlist for LOY-002.
- **If your dog is 10+ but under 44 lbs (or over 120 lbs):** TRIAD is not a fit — go straight to the Loyal waitlist for LOY-002.
- **If your dog is a giant breed under 7 years old:** TRIAD is not a fit yet. Get on the Loyal waitlist for LOY-001 / LOY-003 and start Module 7 today.
- **If your dog doesn't qualify for any of these:** The Loyal waitlist still makes sense (future drugs, future trials), and Module 7 becomes your main focus.

What TRIAD participation actually looks like

- **Free.** The Dog Aging Project covers all study-related costs.
- **Placebo-controlled and double-blinded.** Half the dogs get the drug, half get placebo. Neither you nor your vet knows which.
- **Duration:** about three years.
- **Commitment:** regular vet visits at a participating clinic, cognitive testing, bloodwork. Less intense than the STAY study was.
- **Clinics:** participating sites are listed at dogagingproject.org/triad. Several university teaching hospitals and select veterinary clinics across the U.S.

Applying is a form on the Dog Aging Project website. Acceptance is not guaranteed — they're screening for specific medical profiles — but there is no cost to apply.

What about rapamycin off-label today?

Some forward-thinking veterinarians are prescribing rapamycin off-label for senior dogs at "geroprotective" doses — typically much lower than the human transplant doses. This is legal but uncommon, and the optimal dose for dog longevity is genuinely not yet established. That's exactly what TRIAD is designed to answer.

Honest take: off-label rapamycin is for owners who have a vet willing to prescribe it, who understand the uncertainty, and who can afford the out-of-pocket cost (rapamycin isn't cheap when not covered by insurance). For most owners, TRIAD enrollment is the smarter play — you're taking the same drug or an identical placebo, for free, in a monitored setting with real safety oversight.

What to do right now

1. If you're a TRIAD candidate (7+ years, 44–120 lbs) — start the application at dogagingproject.org/triad today.
2. Sign up for the Loyal waitlist (Module 5).
3. Start the Module 7 protocols — they help your dog regardless of trial or drug access.

The Full Version

Reading time: about eleven minutes. What the STAY study closure means, how to play the LOY-002 waitlist, the TRIAD study in depth, rapamycin off-label, and the honest math of choosing between paths.

What the STAY study closure tells us

The STAY study reached full enrollment of 1,300 senior dogs across approximately 70 veterinary clinics in July 2025. The study is now closed. For owners reading this playbook, that reality has three implications.

First, you cannot enroll your dog in the STAY study. If you hear from a friend or a Facebook post that STAY is enrolling, it isn't. Any communication to the contrary is either outdated or inaccurate. Loyal's confirmation page is unambiguous: STAY is closed.

Second, STAY's enrollment criteria are the best available map of who will be eligible for LOY-002 at launch. The study was designed to populate a realistic senior-dog cohort — dogs at least 10 years old, at least 14 pounds, with the typical comorbidities of an aging dog. The eventual prescription label for LOY-002 will almost certainly mirror these criteria. That means anyone planning to be on the front of the launch queue should know the STAY criteria cold — because they're your criteria too.

Third, STAY's successful enrollment and data collection is now the key gate between today and LOY-002's prescription availability. The study is still generating effectiveness data, which will feed the FDA's eventual Expanded Conditional Approval decision. A two-year trial effectively means the drug's efficacy signal sharpens over late 2026 and 2027. Owners on the waitlist will see news drops as that data matures.

The operational implication: the Loyal waitlist, as of right now, is not a dormant "mailing list." It's the highest-fidelity early-access mechanism available for LOY-002.

Path A — The Loyal waitlist, in depth

Loyal maintains two related but distinct signup points:

1. The company newsletter. A broad email list sent to anyone interested in canine longevity — includes news, FDA milestones, and marketing updates. Low-commitment. Available at loyal.com.

2. The general waitlist. A more targeted list, categorized by breed and age. When Loyal is ready to announce prescription availability in your dog's segment, this list gets notified first. This is the one that matters most for early access.

For owners who want to be at the front of their segment, the sequence is: 1. Sign up for the newsletter. 2. Complete the waitlist form with your dog's breed, age, and weight. Be accurate — the list is used for targeted notifications. 3. Check your inbox. Loyal publishes occasional milestone posts. Ignoring these for six months and then trying to re-engage at launch is a much worse position than staying casually active.

Loyal's direct contact for trial and waitlist inquiries is **STAY@loyal.com**. This was the STAY study contact but the team there also fields general waitlist questions.

The realistic LOY-002 launch window

Based on publicly reported FDA milestones:

- **December 2025:** Target Animal Safety technical section accepted by FDA.
- **Late 2026 (projected):** Final Manufacturing (CMC) submission.
- **2027 (anticipated):** Expanded Conditional Approval granted. Drug becomes prescribable.

In the first 6–12 months after approval, expect: - **Constrained supply.** Manufacturing will be ramping. Production capacity will be a gating factor. - **Uneven vet familiarity.** Many general-practice vets will not be prescribing on day one. Specialty and forward-leaning clinics will adopt first. - **Unclear insurance coverage.** How Trupanion, ASPCA Pet Health, Nationwide, and Pet Health Insurance classify LOY-002 will emerge in the first six months post-launch. - **No generic option.** Conditional approval comes with exclusivity. LOY-002 will be the only option for several years.

Owners who want to be among the first 5,000 – 10,000 dogs on LOY-002 need three things aligned at launch: 1. Their dog meets the prescription criteria. 2. They have a vet who is prepared and willing to prescribe. 3. They are on the Loyal notification list and acting quickly when it drops.

Module 5 (the next module) walks through the full waitlist and launch-readiness strategy.

Path B — The TRIAD study, in depth

The **TRIAD study** — formally “*Test of Rapamycin in Aging Dogs*” — is a large clinical trial run by the **Dog Aging Project**, a research consortium led primarily by researchers at the University of Washington, Texas A&M, Colorado State, and other veterinary schools. TRIAD is funded by the NIH’s National Institute on Aging and a \$7M grant renewal in 2024 secured its continuation through the full trial window.

TRIAD is testing whether **rapamycin**, a drug already FDA-approved for human use (primarily to prevent organ transplant rejection and, at lower doses, for certain cancers), can extend the healthy lifespan of dogs.

Why rapamycin?

Rapamycin inhibits a cellular signaling pathway called **mTOR**, which regulates growth, metabolism, and cellular aging. mTOR inhibition is one of the most robust longevity interventions ever identified in laboratory research — replicated in yeast, worms, flies, and famously, mice. In mice, rapamycin has been shown to extend lifespan *even when started late in life* — a critical property for a drug that might be given to middle-aged and senior dogs.

The mechanism of rapamycin overlaps partially with LOY-002 (caloric restriction mimetic / metabolic pathway) but is distinct from LOY-001 and LOY-003 (direct IGF-1 modulation). If both pathways independently extend canine lifespan, owners may eventually have a choice of longevity interventions — or the option to combine them.

TRIAD eligibility

- **Age:** 7 years or older (documented).
- **Weight:** 44 lbs to 120 lbs.
- **Health status:** Generally well; specific exclusions for certain advanced conditions. Full criteria at dogagingproject.org/triad.
- **Owner commitment:** Approximately three years of study participation, with scheduled visits at a participating clinic, cognitive and physical assessments, and regular monitoring.

TRIAD is **double-blinded and placebo-controlled**. Half of enrolled dogs receive rapamycin; half receive placebo. Neither the owner nor the veterinarian knows which. All participants receive the same level of monitoring. All study-related costs are covered by the Dog Aging Project — this is a genuinely free study.

Participating sites

TRIAD is administered through specific veterinary clinics and university hospitals. Sites are listed on the Dog Aging Project's TRIAD page. Participation requires visits to one of these sites, so practical eligibility depends on geography.

As of early 2026, known active sites include the University of Washington (Seattle), Texas A&M (College Station), Colorado State University (Fort Collins), and selected veterinary clinics in partnership with the Dog Aging Project. Check the TRIAD page for the current list.

Application process

Applying is a form on the Dog Aging Project website. Acceptance is not guaranteed — they're screening for dogs whose medical profile fits the trial design. There is no cost to apply. Expected response time is weeks, not days.

For owners close to a participating site whose dog meets the eligibility window, TRIAD is the single best early-access opportunity available today. It is specifically designed to answer the question other owners will be paying premium prices for LOY-002 to answer in a few years: does a longevity drug actually work in dogs?

The off-label rapamycin question

Some veterinarians are prescribing rapamycin off-label to senior dogs at sub-therapeutic "geroprotective" doses — significantly lower than the doses used for human transplant patients or cancer. This is legal. It is also practiced in human longevity medicine for the same reasons (many individuals take low-dose rapamycin off-label based on mouse data and early human trials).

The honest tradeoffs:

- **Pro:** immediate access, no waitlist, no randomization — your dog is definitely getting the drug.
- **Con:** the optimal dose for canine longevity is genuinely unknown. TRIAD is literally the trial designed to establish it. Prescribing today means making an educated guess about dose.
- **Con:** cost is meaningful — rapamycin (sold as Sirolimus) is not cheap without insurance, and pet insurance generally doesn't cover off-label human medications.
- **Con:** side-effect monitoring is non-trivial. At higher doses rapamycin can affect immune function; even at low doses, interactions with other medications matter.
- **Con:** finding a vet who will prescribe it is the bottleneck for most owners. Most general-practice vets will decline.

For most readers of this playbook, **TRIAD is a better choice than off-label rapamycin**, for four reasons: it's free, it's monitored by researchers at the forefront of the field, it doesn't require you to find a cooperative vet, and — critically — the findings from TRIAD will shape the optimal clinical rapamycin dose for years to come. You and your dog may be contributing to the evidence base that makes rapamycin a mainstream longevity drug within five years.

The honest math: which path, for which dog?

A simple decision framework:

Your dog is 7–10 years old, 44–120 lbs: Apply to TRIAD *and* join the Loyal waitlist. TRIAD is the open door today; LOY-002 is the open door in 2027. These are complementary, not mutually exclusive (TRIAD doesn't preclude using LOY-002 later).

Your dog is 10+ years old, 44–120 lbs: Apply to TRIAD *first* — it's a narrow window to participate, and your dog is the core TRIAD demographic. Also join the Loyal waitlist for LOY-002.

Your dog is 10+ years old, under 44 lbs: TRIAD is not a fit. LOY-002 waitlist is your path. Focus on Module 5.

Your dog is over 120 lbs: TRIAD has an upper-weight cutoff for dosing reasons. LOY-001 (injectable for large breeds 7+) is your primary target — it's not LOY-002 — but it's also behind LOY-002 on the FDA track. Get on the waitlist for both LOY-001 and LOY-003.

Your dog is under 7 years old: No trials are open to you right now. Loyal waitlist is the move, plus Module 7 protocols starting today.

The Animal Biosciences wildcard

Loyal is not the only commercial player. **Animal Biosciences** (the company behind *LeapYears*, a chewable supplement) is also active in the canine longevity space, though with a different regulatory positioning — their product is a dietary supplement, not a prescription drug, which means a different evidence bar and a different FDA track. Module 9 walks through the broader competitive landscape.

What to take away from Module 4

- **Two real paths today:** Loyal waitlist for LOY-002 (launch late 2026 / 2027) and the TRIAD rapamycin study (currently enrolling 7+, 44–120 lb dogs).
 - **The STAY study is closed.** Anyone telling you otherwise is working from outdated information.
 - **TRIAD is the only open trial door today** for qualifying dogs. Free. Placebo-controlled. Three years of participation. Apply at dogagingproject.org/triad.
 - **Off-label rapamycin exists** but is generally worse than TRIAD for most owners — uncertain dosing, meaningful cost, vet-availability bottleneck.
 - **The two paths are additive, not exclusive.** TRIAD participation now doesn't preclude LOY-002 access later.
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Next up: Module 5 — The Waitlist Strategy. How to play the LOY-002 launch window so you're dosing your dog in the first 90 days, not waiting through a six-month backorder.

Module 5 — The Waitlist Strategy

Two versions. Read the simple one first.

- **Simple version** — 3 minutes. Sign up for the Loyal waitlist, three quiet moves to make while you wait.
 - **Full version** — 10 minutes. How prescription launches for conditional-approval drugs actually work, why the first ninety days will be supply-constrained, what to prepare at your vet, what to expect on pricing and insurance, and the signals that tell you launch is imminent.
-

● The Simple Version

The waitlist isn't a mailing list

When LOY-002 reaches prescription availability in 2026 or 2027, **supply will be constrained** for the first several months. Manufacturing will be ramping. Clinics will be learning to prescribe. Insurance carriers will be figuring out coverage. This is what "conditional approval launch" looks like in practice: real, imminent, but rationed.

The waitlist is how you position for the front of that rationing.

The three-step play

Step 1: Sign up for Loyal's notification pipeline today. Two specific places to sign up: 1. The newsletter at loyal.com (broad, informational). 2. The general waitlist, which categorizes you by breed and age for targeted notifications.

Both take less than two minutes. Do both.

Step 2: Have the vet conversation *before* launch, not the week of. Module 6 walks you through this. You want your vet to know you and your dog are Loyal candidates *months* before LOY-002 ships. The vets who are prescribing on day one will prioritize patients they already know fit the criteria.

Step 3: Start building your dog's baseline today. A full senior wellness workup — bloodwork, urinalysis, body condition scoring, thyroid, dental, maybe a chest film — done now becomes the “before” picture. Without one, there's nothing to compare against when your dog starts LOY-002, and no way to know if it's working for you.

What to watch for

As launch approaches, these signals matter: - Loyal announces Manufacturing (CMC) submission to FDA. - Loyal announces Expanded Conditional Approval receipt. - Dose, price, and prescribing guidelines are published. - Initial shipment to major veterinary distributors.

Each of these triggers a different action. Module content (and the \$9/mo subscription updates) will walk through exactly what to do as each one drops.

What it probably costs

Loyal has not published an official retail price. Industry expectation is that LOY-002 will be priced as a premium veterinary medication — roughly comparable to other FDA-approved chronic-use pet drugs. Expect monthly out-of-pocket to be in the range of a premium specialty diet or a chronic arthritis medication, possibly more. Insurance will likely be mixed in the first year.

The Full Version

Reading time: about ten minutes. A complete map of what to do between now and LOY-002 prescription availability, and how to be among the first 5,000 dogs dosed.

What a conditional approval launch looks like

An Expanded Conditional Approval launch is different from a full-approval launch. Full approvals have typically enjoyed months of manufacturing preparation, broad distribution partnerships, and extensive veterinarian education campaigns. Conditional approvals move faster — the drug becomes prescribable the day approval is granted — but with those advantages reduced or absent.

For LOY-002, realistic expectations for the first 12 months post-approval:

Supply: Manufacturing capacity ramps over months, not weeks. Loyal has publicly signaled they are preparing for a controlled rollout rather than a full-flood launch. Expect initial allocation by region or by large veterinary groups, not simultaneous nationwide availability.

Distribution: Major veterinary wholesale distributors (Henry Schein, Covetrus, Patterson) will likely carry LOY-002, but initially through invitation or participation programs. Specialty pet pharmacies (Wedgewood, Diamondback Drugs, Chewy Pharmacy) may stock it with delays.

Vet familiarity: In the first 6 months, only the subset of vets who are explicitly Loyal-trained or who proactively educate themselves will prescribe. Many general practitioners will take a “wait and see” posture for a year or more. Specialty practices (internal medicine, geriatric care) will adopt first.

Insurance: Coverage decisions will roll out unevenly. Trupanion, ASPCA Pet Health Insurance, Nationwide, and Pets Best may each take a different position. Some may cover under “metabolic dysfunction,” others may exclude longevity drugs entirely. Expect coverage clarity by mid-2027 at the earliest.

Pricing: Pricing will reflect the R&D cost of a first-in-class drug plus conditional-approval manufacturing overhead. Analysts have speculated in the \$100–\$200 per month range but no official figure has been published. Expect real pricing clarity only with the formal launch announcement.

The Loyal waitlist, mechanically

Loyal's public notification infrastructure has three parts. Understanding each helps you use all three.

1. The company newsletter — Broadly distributed. Sent on an irregular cadence (weeks to months between issues). Content is a mix of FDA milestones, company news, general canine longevity science, and occasional customer stories. Signup: form at loyal.com. Low noise, high signal for general updates.

2. The general waitlist — A more structured list that captures your dog's breed, age, and weight. This data lets Loyal run targeted notifications — when LOY-002 is ready for prescription in your dog's profile, you get notified ahead of general announcements. This is the most valuable of the three mechanisms for actual early access. Signup: also at loyal.com, in a more detailed form than the newsletter.

3. Direct contact — STAY@loyal.com is Loyal's public-facing email for trial and waitlist questions. Originally the contact point for the STAY study (which is now closed), it continues to serve as the team's primary inbound channel. For specific questions about your dog's candidacy, specific city or geography access, or confirmation of waitlist registration, direct email is better than form submission.

The combined strategy: newsletter (background awareness) + waitlist (active notification) + occasional STAY@loyal.com email (to remain human-remembered).

Positioning your vet clinic

The Loyal waitlist puts your dog in the queue. The *prescribing vet* is what actually gets the drug into the bottle at your dog's next visit. These are separate problems.

Three moves to make your vet clinic ready:

1. Identify which vet at your clinic is most likely to prescribe LOY-002 at launch. In larger practices, this may not be your usual vet. The vet with a stated interest in geriatric

medicine, who reads DVM360 or AAHA publications, who has been to recent continuing education on canine longevity — that's the one you want paired with your dog's records.

2. Discuss LOY-002 with that vet now — and document the conversation. Bring Module 6's structured questions. A chart note indicating "owner expressed interest in LOY-002 once approved; reviewed candidacy" is the right kind of paper trail.

3. Establish a baseline. A full senior panel today (see Module 7 for what to include) creates the baseline LOY-002's clinical benefit will eventually be measured against. Without a baseline, there's no measurement.

The forcing function: if your dog is a candidate, you want to be the patient who, when your vet opens their first LOY-002 shipment, is already in the "we've discussed this" column of their EMR.

The first 90 days post-launch — the game plan

When LOY-002 reaches your veterinarian, the first 90 days are when the supply-constrained dynamics most affect who gets the drug. Your optimal sequence:

Week 1 of availability: - Your vet receives their first allocation (possibly only a small quantity). - You have an appointment scheduled in advance, preempting the rush. - Bloodwork is already current (done in the prior 6 months). - Prescription is written; you pick up the bottle or have it shipped that week.

Week 1–2 of dosing: - Start the drug as directed. Most likely once daily with food. - Baseline symptoms documented in your own notes: energy level, appetite, mobility, bathroom habits, attitude. - Any side effects logged and reported to the vet (most likely mild GI upset; if so, typically resolves).

Week 6–8: - Follow-up appointment. - Repeat bloodwork to compare to baseline. - Discuss any observed changes.

Month 3: - Refill prescription. - Reassess.

Owners who have done Steps 1–3 above (waitlist, vet positioning, baseline) will typically be in this sequence before the general public has even learned LOY-002 exists. Owners who wait until the news cycle picks it up will be 3–6 months behind.

Pricing scenarios and what they mean

No official retail price has been published. Estimated scenarios based on comparable first-in-class veterinary drugs:

Optimistic scenario (\$75–\$120 / month per dog). LOY-002 is priced to maximize adoption. Insurance picks up a portion. Annual out-of-pocket for a senior dog's longevity therapy is \$500–\$1,000 with coverage, \$900–\$1,440 without. Accessible to most households that would spend on a premium specialty diet.

Mid scenario (\$120–\$200 / month per dog). LOY-002 is priced at premium specialty levels. Annual out-of-pocket is \$1,440–\$2,400 without insurance. Decision becomes meaningful for most households but not prohibitive.

Pessimistic scenario (\$200–\$350 / month per dog). LOY-002 is priced closer to human specialty drug parallels. Annual out-of-pocket exceeds \$2,400. This would meaningfully constrain the customer base but is unlikely given Loyal's public stance on broad access.

These are estimates, not commitments from Loyal. When the real number lands, this module will be updated (subscribers receive the update first).

Insurance strategy

Three actions to take on pet insurance, ranked by importance:

1. If you don't have pet insurance yet, get it now — before LOY-002 launches. Pre-existing condition exclusions are the single biggest trap in pet insurance. If your dog develops a condition (including, potentially, being characterized as "needing a longevity drug") *after* coverage starts, it may be covered. If the condition exists *before* coverage starts, it's excluded. Enroll now.

2. Understand how your current policy categorizes metabolic dysfunction and “preventive” medication. Call your insurer. Ask directly how they will categorize LOY-002 once it’s on the market. Save the email confirmation.

3. Consider adding a “Wellness” or “Preventive” rider if your policy offers one. These riders typically cover vaccines, dental cleanings, and — potentially — drugs categorized as preventive. This is the most likely LOY-002 categorization.

A full insurance comparison is beyond this module’s scope, but Trupanion and ASPCA Pet Health Insurance are the two most commonly cited pet insurers in the canine longevity community because their illness-coverage models may accommodate LOY-002 more gracefully than competitors.

Signals that tell you launch is imminent

The subscription portion of this playbook (\$9/mo) exists precisely for this part of the timeline — tracking real-time signals and translating them into action. The specific signals that matter:

Announcement-level signals: - Loyal’s Manufacturing (CMC) submission to FDA. - FDA’s grant of Expanded Conditional Approval. - Loyal’s announcement of dose, price, and launch date. - First public reports of veterinary distributor allocation.

Community-level signals: - Veterinary trade publications (DVM360, AAHA, JAVMA) publishing prescribing guidelines. - Continuing education (CE) courses on LOY-002 appearing on the major vet CE platforms. - Veterinary specialty boards (ACVIM, ACVNU) issuing position statements.

Direct signals: - Your vet receives their first allocation. - Pharmacy partners publicly list LOY-002 as stocked. - Insurance carriers publish coverage positions.

When the first three announcement-level signals hit, you have roughly 30–90 days before actual prescription availability at most clinics. That is the window to have everything in place.

Two mistakes to avoid

Mistake 1: Waiting until it's "official" to get on the waitlist. By definition, by the time something is "official" and major media has covered it, you're several steps behind owners who signed up during the pre-launch period. The waitlist is cheap insurance. Sign up today.

Mistake 2: Assuming your current vet will be a LOY-002 prescriber. Most general-practice vets in the U.S. will not prescribe LOY-002 in its first year. If your vet is skeptical of longevity medicine, familiar only with supplements, or uninterested in the FDA pathway — you have a vet problem, not a drug problem. Module 6 addresses how to handle this.

What to take away from Module 5

- **The waitlist is not a mailing list.** It is the primary early-access mechanism for LOY-002 at launch.
 - **Sign up in three places:** Loyal newsletter, general waitlist, and know STAY@loyal.com for direct contact.
 - **Position your vet, don't wait on them.** A pre-launch conversation documented in your dog's chart meaningfully increases early-prescription access.
 - **Build a baseline today.** Full senior workup. This is what LOY-002's effect will be measured against.
 - **Get pet insurance now if you don't have it.** Pre-existing condition exclusions are unforgiving.
 - **Four announcement signals** tell you launch is imminent: CMC submission, XCA grant, Loyal's public launch plan, first distributor allocation.
-

Next up: Module 6 — The Vet Conversation. The single most load-bearing skill in this whole playbook. How to open, what to ask, the red flags that tell you to switch vets, and a

script you can bring to your next appointment.

Module 6 — The Vet Conversation

Two versions. Read the simple one first.

- **Simple version** — 4 minutes. How to open, three questions that tell you where your vet stands, red flags that mean you need a different vet.
 - **Full version** — 12 minutes. Complete conversation framework, how to find a longevity-literate vet, the specialist landscape, a full mock script for your next appointment, and a frank discussion of when to switch clinics.
-

● The Simple Version

The most load-bearing skill in the whole Playbook

Every other module in this Playbook — the science, the drugs, the waitlist, the protocols — ultimately runs through your veterinarian. If you have a vet who understands canine longevity medicine, everything becomes easier. If you don't, nothing works as well as it could, and in some cases it doesn't work at all.

Most dog owners have no idea how much vet quality varies on this specific topic. This module fixes that.

The opening line that tells you everything

At your next vet appointment — any appointment, even a routine one — try this exact sentence:

"I've been reading about canine longevity medicine. Given my dog's breed, age, and weight, I'd love your take on whether he fits the target population for the IGF-1 inhibitors Loyal is developing, or the senior metabolic pill, LOY-002."

Watch what happens next. In ten seconds you'll know whether your vet:

- **Is current on Loyal** (they'll respond with specific knowledge of LOY-001/002/003 and the FDA Expanded Conditional Approval pathway). You have a great vet for this. Lean in.
- **Has heard of it but is hesitant** (they'll respond with something like "I've heard of that — we're watching it"). You have a reasonable vet. Educate gently, bring articles, keep them engaged.
- **Hasn't heard of it** (they'll respond with confusion or change the subject). Not a disaster. Many excellent vets aren't following longevity news specifically. Provide them Module 2 and Module 3; if they read it and engage, they're worth keeping.
- **Dismisses it** (they'll respond with something like "aging is natural — that's not really something we treat" or they'll conflate it with supplements). **This is the red flag.** Not because they're a bad vet generally, but because they are not the right vet for this.

The three questions to bring

If the opening line goes well, follow with these three, in order:

1. "What specific biomarkers would you use to set a baseline for my dog's healthy aging — full panel with thyroid, urinalysis, body condition scoring?"
2. "How do you think about the trade-offs of conditional-approval drugs like LOY-002 versus waiting for full approval?"
3. "Would you be willing to prescribe LOY-002 when it becomes available, assuming my dog still fits the criteria?"

The answers to these three tell you whether this vet will be the one actually writing the script in 2027. If they engage seriously with all three, you have your prescriber. If they dodge, it's time to find one who won't.

Three red flags

- **“Aging is natural.”** Not technically wrong, but dismissive of an entire emerging field of veterinary medicine. An obstetrician in 1985 could have said “childbirth is natural” and been technically right. That doesn’t mean they shouldn’t recommend fetal monitoring.
- **Confusing LOY-002 with dietary supplements.** LOY-002 is an FDA-regulated prescription drug. If your vet treats it like fish oil, they are not current.
- **Unaware of the FDA Expanded Conditional Approval pathway.** This is a specific, named, documented regulatory pathway. A vet who says “the FDA doesn’t have a category for anti-aging drugs” is literally incorrect. They might be an excellent vet for other things, but not this.

When to switch vets

If your current vet shows any of the three red flags, your dog’s longevity plan is better served by finding a second vet — either to replace your current one or to add as a specialist. Module 6 Full Version covers specifically how to find one.

The Full Version

Reading time: about twelve minutes. The complete vet conversation framework, how to find a longevity-literate clinician, the veterinary specialty landscape, a full mock script, and a frank discussion of the switch-vets decision.

Why this conversation is harder than it should be

Canine longevity medicine sits at an awkward intersection of veterinary practice. It isn’t internal medicine. It isn’t oncology. It isn’t nutrition. It isn’t preventive care, exactly — though it draws from all of these. The vets who are best equipped to engage on it tend to be those with formal postgraduate training and an active interest in geriatric or metabolic medicine. That isn’t most vets.

The median general-practice veterinarian in the U.S. graduated before the Loyal pipeline existed, practices on a case-by-case basis through their continuing education, and has had limited exposure to the IGF-1 hypothesis or the FDA's Expanded Conditional Approval pathway. This isn't a failing. It's simply the nature of a fast-moving field.

Your job as an informed owner is to find the subset of vets — there are many, just not the majority — who *are* engaged on this.

The veterinary specialist landscape

Three tiers of vets, by their likely engagement with canine longevity medicine:

Tier 1: Board-certified specialists in relevant areas.

- **American College of Veterinary Internal Medicine (ACVIM)** — internists with deep training in metabolic, endocrine, cardiac, and oncologic medicine. Most likely of any specialty to be current on LOY-001/002/003 mechanism and clinical application. Directory: acvim.org.
- **American College of Veterinary Nephrology and Urology (ACVNU)** — newer specialty, focused on kidney and metabolic disease. Highly relevant for senior dogs. Directory: acvnu.org/directory.
- **Veterinary oncologists** (ACVIM — Oncology) — relevant for dogs with cancer history or high cancer risk (most giant breeds). Will understand the IGF-1 / proliferation link.
- **Veterinary geriatric / senior care specialists** — an emerging informal category. Look for DVMs who identify their practice focus as senior medicine or geriatric wellness.

Tier 2: General practitioners with stated interest in longevity or senior care.

- Vets who publish or speak on senior wellness.
- Vets involved in research — especially Dog Aging Project enrolled clinics, TRIAD study sites, or STAY study clinics.
- Vets whose practice website or bio explicitly discusses canine longevity, healthspan, or geriatric medicine.

- Vets affiliated with veterinary teaching hospitals (Texas A&M, University of Washington, Colorado State, Cornell, UC Davis, Penn).

Tier 3: General practitioners without specific longevity interest.

- The median U.S. vet. Fine for vaccines, acute illness, and general wellness. Not the right prescribing vet for LOY-002.

The practical implication: if your current vet is Tier 3, your best move is to *add* a Tier 1 or Tier 2 vet to your dog's care team, rather than replace the relationship entirely. Your Tier 3 vet can remain the primary care provider for routine needs. The Tier 1/2 vet becomes the longevity medicine specialist — similar to how human medicine works (primary care doctor plus cardiologist or endocrinologist).

How to find a longevity-literate vet

Option 1: Veterinary teaching hospitals. If you live within a reasonable drive of a university veterinary school, this is the highest-density option. Teaching hospitals staff board-certified specialists across multiple areas, run clinical trials, and are typically at the leading edge of emerging medicine.

Option 2: ACVIM and ACVNU directories. Search by state or city. Cross-reference with ZIP code on insurance plan acceptance.

Option 3: Dog Aging Project's clinical trial site list. Clinics that participate in Dog Aging Project research are by definition engaged with aging science. List at dogagingproject.org.

Option 4: STAY study alumni clinics. Even though the study is closed, clinics that participated now have hands-on experience with LOY-002 protocols. Some publicly list this. Three top-recruiting clinics: - Barlow Trail Veterinary Clinic, Sandy, Oregon (105 dogs enrolled) - Quakertown Veterinary Clinic, Quakertown, Pennsylvania (79 dogs enrolled) - Animal Hospital of Dauphin County, Harrisburg, Pennsylvania (58 dogs enrolled)

Option 5: Direct outreach to Loyal. Emailing STAY@loyal.com with your city or ZIP and asking for a list of veterinarians in your area who participated in STAY or who have expressed interest in prescribing LOY-002 is a legitimate request. No guarantee of response, but worth trying.

Option 6: Your existing vet's referral. If you have a Tier 3 vet with whom you have a good relationship, ask directly: "Who in our area would you refer me to for senior metabolic medicine or longevity consultation?" Most vets know who the specialists are even if they don't practice in that area themselves.

The conversation framework — opening, middle, close

The opening (30–60 seconds).

Your goal in the opening is to reveal your vet's current familiarity without leading them. The line from the simple version is calibrated for this:

"I've been reading about canine longevity medicine. Given my dog's breed, age, and weight, I'd love your take on whether he fits the target population for the IGF-1 inhibitors Loyal is developing, or the senior metabolic pill, LOY-002."

This sentence name-checks Loyal, the specific drug pipeline, and the IGF-1 mechanism — three pieces of terminology that only a current vet will match. If they do, you've identified a Tier 1 or high Tier 2 clinician. If they don't, you've identified a gap.

The middle (5–10 minutes — the body of the conversation).

Depending on where the opening landed, five structured questions to work through. The order matters.

Q1 — Eligibility framing: *"Given my dog's [breed], age of [X] years, and current weight of [X] lbs, does he fit the target population for LOY-001 or LOY-003 (if he's a large breed), or for LOY-002 (if he's 10+ years)?"*

What you're listening for: a clear yes/no with reasoning. A vet who says "yes, he fits LOY-002's profile — 10+ years, over 14 lbs, no active cancer or advanced kidney disease, and his arthritis is well-managed" has internalized the criteria. A vet who says "I'd have to look into it" is fine — that's honesty — but needs to actually look into it.

Q2 — FDA pathway awareness: *"Are you familiar with the FDA Center for Veterinary Medicine's Expanded Conditional Approval pathway and the Target Animal Safety acceptance for LOY-002 in December 2025?"*

The right answer is a confident yes with color (*"Yes, we've been tracking it — the TAS acceptance was the big milestone last year, and now we're watching for the manufacturing submission"*). A vague "I've heard of it" is not disqualifying but is a signal they're less current. "No" is not disqualifying either — but needs to be followed by genuine interest.

Q3 — Biomarkers and baseline: *"What specific biomarkers would you want to establish for my dog's healthy-aging baseline — a full blood panel with thyroid, a urinalysis, body condition scoring, and possibly a Canine Frailty Index assessment?"*

This question reveals two things: whether your vet thinks in terms of longevity-relevant metrics at all (most don't proactively), and whether they know what metrics matter. A strong answer includes senior bloodwork with thyroid, urinalysis, BCS, and some form of functional assessment. A weaker answer is "sure, we can do a senior panel" with no specifics.

Q4 — Interaction with current care: *"How would LOY-002 interact with [list your dog's current medications and supplements]? Based on the field safety data from the STAY study, are there specific interactions you'd watch?"*

This tests whether your vet can move from general familiarity to specific clinical application. A good vet will pull up what they know about LOY-002's known interactions, note any specific concerns with your dog's current regimen, and potentially offer to research and follow up.

Q5 — Willingness and timing: *“Assuming my dog still fits the criteria at launch, would you be willing to prescribe LOY-002 from the first shipment — or do you prefer to wait 6–12 months of post-market data before prescribing?”*

Both answers are defensible. A vet who says *“I’ll prescribe from day one — the safety data is strong”* is a high-confidence early adopter. A vet who says *“I want 6–12 months of field data before I prescribe widely”* is a conservative, evidence-driven clinician — also perfectly reasonable. What matters is that they have a clear position and can articulate it. A vet who says *“I don’t know, we’ll see”* is either honest (fine) or checked out (not fine).

The close (1–2 minutes).

End the conversation with two concrete actions:

1. *“Can we schedule a full senior wellness panel today or in the next 30 days so we have a baseline in place before LOY-002 ships?”*
2. *“Please note in my dog’s chart that I’ve expressed interest in LOY-002 and that we discussed candidacy — so when the drug becomes available, we don’t start from zero.”*

These two actions lock in the work the conversation just did. Without them, the momentum evaporates. A chart note you can’t see doesn’t exist; a baseline panel scheduled for “sometime later” doesn’t happen.

The red flags, in detail

Red flag 1: Dismisses aging as untreatable.

“Well, aging is just natural — we can manage symptoms but we can’t really treat it.”

This is both technically defensible and, for the purposes of this conversation, disqualifying. The entire field of geroscience is the study of aging as a modifiable biological process. The FDA’s Expanded Conditional Approval pathway exists because aging is treatable at the biological level. A vet who dismisses this framework isn’t just unfamiliar — they’re philosophically misaligned with what you’re trying to do.

This is a Tier 3 vet who hasn't engaged with the emerging field. They may be an excellent acute-care clinician. They are not your prescribing vet for LOY-002.

Red flag 2: Confuses LOY-002 with a supplement.

"Oh, we have a great supplement I recommend for senior dogs — it's similar to that Loyal product."

No, it is not. LOY-002 is an FDA-regulated prescription drug that has completed the most rigorous safety package ever submitted for a veterinary longevity compound. A vet who conflates a dietary supplement with an FDA-regulated prescription drug is not reading the field carefully. This is a signal of low engagement, not low intelligence — but it still means they aren't your LOY-002 prescriber.

Red flag 3: "The FDA doesn't approve anti-aging drugs."

This statement was true in 2022. It has been progressively false since 2023. A vet who makes this claim is either not following veterinary regulatory news or is making a confident assertion based on outdated information. Either way, they are not current on the specific topic that matters for your dog's care.

The switch-vets decision framework

If your current vet shows one or more red flags, you have three options:

Option A: Keep your current vet for general care, add a specialist for longevity medicine.

This is the optimal outcome for most owners. Your Tier 3 vet continues to be your dog's primary care provider. A Tier 1 specialist (ACVIM, ACVNU) or high Tier 2 GP becomes the longevity consultant. The specialist writes the LOY-002 script; your primary care vet manages day-to-day.

This is the human medical model, where your GP doesn't manage your cardiologist's domain. It works in veterinary medicine just as well.

Option B: Replace your current vet with a longevity-engaged vet. This is the right move if your current vet is actively obstructive — dismisses your interest, pushes back on the science, or creates friction around basic requests like senior bloodwork. Not every vet relationship is worth preserving.

Option C: Change nothing and accept delayed access. Valid, but know what you're accepting. Your dog will likely not be on LOY-002 within the first 12 months of availability. You will be in the second wave, not the first.

Most owners reading this Playbook will want Option A. It preserves relationships while ensuring access.

The conversation for dogs not yet candidates

If your dog is “almost a candidate” — within 6–24 months of qualifying for LOY-001, LOY-002, or LOY-003 — the conversation is slightly different. You are not asking for a prescription today. You are asking your vet to:

1. Acknowledge your dog's forward candidacy in the chart.
2. Establish a baseline before eligibility arrives.
3. Commit to reviewing Loyal's published prescribing guidelines when they drop.
4. Align on the Module 7 protocols as the bridge.

The conversation is shorter, lower-stakes, and equally valuable. A vet who is engaged on this conversation for a forward-candidate dog is almost certainly the right prescriber when the drug actually ships.

What to take away from Module 6

- **The vet conversation is the most load-bearing skill in this Playbook.** Nothing else works without a vet who can and will prescribe.
- **Your opening sentence reveals your vet's level in ten seconds.** Use it.

- **Three red flags** tell you this vet is not your LOY-002 prescriber: dismisses aging, confuses the drug with supplements, or is unaware of the FDA pathway.
 - **Three tiers of vets** by engagement — most owners will add a specialist (Tier 1/2) rather than replace their primary care vet.
 - **The five-question framework** (eligibility, pathway, biomarkers, interactions, willingness) calibrates any vet's readiness to prescribe.
 - **End every conversation with two commitments:** baseline panel scheduled, chart note on interest and candidacy.
-

Next up: Module 7 — Ten Things You Can Do Today. The highest-leverage module in this Playbook for owners whose dogs don't yet qualify — and for every owner building the bridge to LOY-002.

Module 7 — Ten Things You Can Do Today

Two versions. This is the longest module in the Playbook — because it is, for most owners, the most valuable one.

- **Simple version** — 5 minutes. The ten things, one paragraph each. What to do this week.
 - **Full version** — 18 minutes. The science behind each of the ten, specific protocols, dose ranges, and the question to bring to your vet about each.
-

● The Simple Version

The most important module in the Playbook

If your dog doesn't qualify for LOY-001, LOY-002, or LOY-003 — either because of age, size, or health — this module is where the Playbook's real value lives. And even if your dog *does* qualify, these ten practices are the bridge between today and launch, plus the foundation a longevity drug builds on top of.

These aren't Instagram tips. Every one of them is backed by peer-reviewed veterinary research. Several work on the *exact same biology* that LOY-002 targets.

The ten things

1. Hit and hold lean body mass — the single highest-leverage move. The 14-year Purina Lifetime Study showed lean Labradors lived 1.8–2.0 years longer than their littermates fed 25% more, and developed osteoarthritis nearly three years later. Your dog's ideal body condition score is 4 or 5 out of 9 — you should be able to feel ribs with light pressure, see a visible waist from above, and an abdominal tuck from the side. Most big dogs in America are at 6 or 7. This one change adds more years than any supplement.

2. Feed once a day (not twice). Analysis of over 10,000 dogs in the Dog Aging Project shows once-daily feeding is associated with significantly lower rates of GI, dental, orthopedic, kidney, and liver disorders — and lower cognitive dysfunction scores. This is intermittent fasting for dogs. Talk to your vet before switching (especially for dogs with diabetes or on certain medications), but for most adult dogs, one meal per day is the move.

3. Structured daily exercise — at least 30–40 minutes, varied. Active dogs have a **six times lower risk** of developing canine cognitive dysfunction (dementia) than inactive ones. Exercise also maintains mitochondrial health and prevents the muscle wasting (sarcopenia) that ends most big dogs' mobility years before their time. Aim for 30–40 minutes of varied movement daily: walk, play, swim, terrain change.

4. Senior bloodwork every 6 months after age 6 for big breeds. Catching kidney, liver, thyroid, and inflammatory drift early changes outcomes dramatically. Annual exams aren't enough for a dog who ages twice as fast. Full panel with chemistry, CBC, thyroid, and urinalysis. Twice a year. Non-negotiable after age 6 for large breeds.

5. Omega-3 fatty acids (EPA/DHA) at therapeutic doses. One of the few supplements with genuine randomized-trial evidence in dogs. Reduces inflammation, supports cardiac and cognitive function, slows joint disease. Most owners underdose. Therapeutic range is meaningfully higher than the amount in dog food. Talk to your vet about a fish oil dose calibrated to your dog's weight.

6. Daily dental care. Periodontal disease is a systemic inflammation driver — inflammation that travels from the mouth to the heart, kidneys, and brain. Most adult dogs in the U.S. have significant periodontal disease by age 3. Daily brushing, professional cleanings on vet schedule, and dental chews with VOHC certification.

7. Joint protection starting now. For big breeds, mobility loss cascades into every other system. Prevention starts before symptoms — not after your dog is limping. Omega-3s (see #5), weight (see #1), structured exercise (see #3), and evidence-backed joint supplements (glucosamine/chondroitin, green-lipped mussel) discussed with your vet.

8. Vaccine and titer strategy appropriate for age. The right vaccine protocol for a senior dog is different from a puppy's. Over-vaccination and under-vaccination are both real problems. Work with your vet on a titer-based approach that matches your senior dog's specific exposure risk.

9. Cancer screening cadence. Cancer is the #1 killer of large dogs. New at-home and in-clinic screening tools (liquid biopsy, OncoK9) can catch cancers earlier than physical exam alone. Discuss with your vet whether these are appropriate for your dog's breed-specific cancer risk profile.

10. Cognitive and social enrichment. Dogs with complex social environments — exposure to other dogs, varied walking routes, puzzle feeders, training — show measurably better cognitive outcomes in aging. Boredom shortens life. Enrichment extends it.

The single most important change, if you can only do one

Weight. If you do nothing else on this list, get your big dog to body condition score 4–5 and keep him there. The evidence is stronger for this one intervention than for any supplement, and it's free. The 14-year Purina study is the closest thing veterinary medicine has to a proof.

Start today. Don't wait for a vet visit.

The Full Version

Reading time: about eighteen minutes. The full evidence behind each practice, specific protocols, dose ranges where applicable, and the questions to bring to your vet.

A note on evidence hierarchy

Veterinary medicine, like human medicine, has a hierarchy of evidence. Not all of the ten practices below are equally well-supported. Here's how we grade them:

- **HIGH evidence** — Large prospective studies in dogs, often randomized controlled trials, with clear mechanism and effect size.
- **MODERATE evidence** — Observational or retrospective studies in dogs, strong mechanistic rationale, consistent with other species.
- **EMERGING evidence** — Recent studies (e.g., Dog Aging Project analyses), promising results, but field still maturing.

Every recommendation below is at MODERATE or higher. Nothing made this list on mechanistic plausibility alone.

1. Hit and hold lean body mass (HIGH evidence)

What: Maintain your dog's body condition score (BCS) at 4 or 5 out of 9 — visibly lean, with palpable ribs, a visible waist from above, and an abdominal tuck from the side.

The evidence: The Purina Lifetime Study, a 14-year longitudinal trial in Labrador Retrievers, compared dogs fed *ad libitum* to dogs fed 25% fewer calories. The calorie-restricted group lived 1.8–2.0 years longer on average — roughly a 15% lifespan extension. They also developed osteoarthritis nearly three years later and showed significantly reduced incidence of chronic disease across multiple organ systems.

This is the single most rigorously conducted longevity study in any companion animal. The effect size is larger than any other lifestyle intervention ever tested in dogs.

The mechanism: Caloric restriction lowers IGF-1 and insulin signaling — the same pathways that drive accelerated aging in large breeds (Module 1) and the pathways LOY-002 mimics pharmacologically. In other words: staying lean is the free, time-tested version of the drug many readers of this Playbook are waiting for.

The protocol:

1. Learn to assess body condition. The 9-point BCS scale is a visual and palpation-based tool used by every veterinarian. A BCS of 4–5 is ideal; 6–7 is overweight; 8–9 is obese. Tools: WSAVA's BCS chart or any vet hospital's poster.
2. Feed for BCS, not for the bag label. The feeding guidelines on dog food bags overestimate caloric needs for most adult dogs. Most sedentary adult dogs need 25–40% fewer calories than the bag suggests.
3. Weigh monthly. Adult weights should fluctuate no more than 2–3% month-to-month. Senior dogs may lose lean mass imperceptibly — track both weight and BCS to catch this.
4. Know your treats. Most owners underestimate treat calories by 2–5x. A Lab eating 300 daily calories of treats is 30% over his target intake without anyone noticing.

The vet question: *“What’s my dog’s current body condition score, what’s the target, and how many calories per day should I be feeding to reach and hold it?”*

2. Feed once a day (EMERGING evidence)

What: Consolidate your adult dog’s food into a single daily feeding window. Intermittent fasting for dogs.

The evidence: Dog Aging Project researchers analyzed feeding frequency in over 10,000 companion dogs and found that once-daily-fed dogs had:

- Lower odds of gastrointestinal disorders
- Lower odds of dental disorders
- Lower odds of orthopedic disorders
- Lower odds of kidney and urinary disorders
- Lower odds of liver and pancreas disorders
- Lower scores on a canine cognitive dysfunction assessment

These findings are observational (not randomized), so causation is not established — but the consistency across multiple organ systems and the large sample size make this one of the most significant recent findings in canine health research.

The mechanism: Intermittent fasting in mammals activates autophagy — the cellular recycling process we covered in Module 1. Autophagy clears damaged cellular components and is suppressed by constant feeding. A dog with an 18–23 hour daily fast is running autophagy for meaningful windows; a dog eating twice or three times per day is not.

The protocol:

1. Transition gradually. Move from twice-daily to once-daily over 2–3 weeks. Abrupt changes can upset digestion.
2. Pick a consistent feeding time. Most owners feed in the morning. Some feed in the evening. Either works; consistency is what matters.
3. Water always available. Fasting refers to calories, not hydration.
4. Exceptions: Do not switch to once-daily feeding for puppies (<18 months), pregnant or lactating dogs, small breeds under 10 lbs, diabetic dogs, or dogs on medications that require food-timed dosing. Ask your vet first.

The vet question: *“Is once-daily feeding appropriate for my dog given his age, health, and current medications? If so, how should we transition?”*

3. Structured daily exercise (HIGH evidence)

What: 30–40 minutes minimum of varied daily physical activity. Not just walks — varied terrain, varied intensity, varied types of movement.

The evidence: Observational data from the Dog Aging Project shows active dogs have approximately **six times lower risk** of developing canine cognitive dysfunction (dementia)

compared to inactive dogs. Active dogs also maintain muscle mass longer, retain mitochondrial function better, and avoid the sarcopenia-to-immobility cascade that ends most large breeds' active years prematurely.

Exercise's longevity benefits operate through multiple mechanisms: improved insulin sensitivity, increased mitochondrial biogenesis (your cells make more energy-producing machinery), reduced systemic inflammation, and maintenance of neural plasticity.

The mechanism: "Mitohormesis" — the biological phenomenon where mild, controlled stress (exercise) activates cellular repair and resilience pathways. Exercise-induced stress signals cells to upregulate their quality-control mechanisms; sedentary dogs don't get these signals.

The protocol:

- 1. Baseline: 30 minutes daily.** For most adult dogs at reasonable body condition, 30 minutes of active movement is the floor, not the ceiling.
- 2. Vary the inputs.** A mix across the week of: neighborhood walks (steady-state), hilly terrain (resistance), off-leash play (high-intensity intervals), swimming (joint-friendly cardio), and formal training (cognitive load). Monotonous exercise is worse than varied exercise.
- 3. Warm up and cool down** — especially for senior dogs. Five minutes of slower movement at the start and end of a session reduces injury risk.
- 4. Watch weather.** Heat stroke is the most common exercise-related emergency. Adjust for temperature, humidity, and breed. Brachycephalic breeds (bulldogs, boxers) need more caution.
- 5. Senior dogs:** shorter sessions more frequently beat one long session. 20 minutes twice a day beats 45 minutes once.

The vet question: *"Given my dog's age, weight, and any joint or cardiac conditions, what's the right exercise dose and intensity — and are there specific activities to avoid?"*

4. Senior bloodwork every 6 months after age 6 (HIGH evidence)

What: A complete senior wellness panel — CBC, chemistry, thyroid, urinalysis — every six months for large-breed dogs after age 6.

The evidence: Veterinary internal medicine consensus is clear: subclinical disease detection changes outcomes. Kidney dysfunction caught at IRIS Stage 1 is manageable; caught at Stage 3, much less so. Thyroid dysfunction caught early is easy; caught late, costly. Early cancer markers (elevated calcium, anemia patterns, specific enzyme changes) can surface months before clinical signs.

For large breeds that age twice as fast as small breeds, annual exams provide insufficient sampling frequency. Bi-annual is the appropriate cadence.

The protocol:

1. Full panel components:

- 2. Complete Blood Count (CBC)
- 3. Chemistry panel (kidney, liver, electrolytes, glucose, protein)
- 4. Thyroid (T4 minimum; free T4 if T4 abnormal)
- 5. Urinalysis (specific gravity, protein, sediment)
- 6. Consider: fecal exam, heartworm test, tick-borne panel if geographically relevant

7. **Timing:** Every 6 months from age 6 for giant breeds, age 7 for large breeds, age 8–9 for medium/small breeds.

8. **Tracking:** Request a copy of every result. Keep them in a folder or scanned. Trends matter more than absolute values. A creatinine of 1.4 is normal if his previous four values were 1.4; it's a red flag if his previous four values were 1.0.

9. **Annual additions:** Chest films (especially for giant breeds with cardiac risk), blood pressure, eye exam.

The vet question: *“Can we schedule a baseline senior panel now and every six months going forward? I’d like a copy of each result to track trends.”*

5. Omega-3 fatty acids at therapeutic doses (HIGH evidence)

What: EPA+DHA supplementation at a dose meaningfully higher than what’s in commercial dog food.

The evidence: Omega-3s (specifically EPA and DHA, the marine-derived long-chain forms) have more high-quality randomized-trial evidence in dogs than almost any other supplement. Documented benefits include:

- Reduced osteoarthritis symptom severity
- Slowed progression of chronic kidney disease
- Improved cognitive function in senior dogs
- Reduced inflammatory markers
- Cardioprotective effects

The mechanism: Omega-3s incorporate into cellular membranes and alter the substrate pool for inflammatory mediators — downshifting the pro-inflammatory profile of senior tissue.

The protocol:

- 1. Dose by weight.** Therapeutic doses for dogs are typically in the range of 40–100 mg of EPA+DHA per kg of body weight daily. A 70-lb Labrador weighs ~32 kg, so 1,280–3,200 mg of EPA+DHA per day. Most commercial fish oil capsules for dogs deliver 300–600 mg per capsule — meaning 2–10 capsules per day for a large dog to hit therapeutic dose.
- 2. Quality matters.** Choose brands with third-party testing for purity (heavy metals, PCBs) and freshness. Veterinary-specific brands (Nordic Naturals Pet, Welactin,

Vetoquinol Triglyceride Omega Fish Oil) are generally reliable. Human fish oil works if dosed appropriately.

3. **Storage.** Refrigerate after opening. Rancid fish oil is pro-inflammatory — the opposite of what you want.
4. **Introduce gradually.** Start at half-dose for 1–2 weeks to avoid GI upset, then ramp to full dose.
5. **Interactions:** Omega-3s have mild anticoagulant effects. If your dog is on other blood-thinners or has a bleeding disorder, discuss with your vet before starting.

The vet question: *“What’s the therapeutic EPA+DHA dose for my dog, and which brand do you recommend for purity and potency?”*

6. Daily dental care (HIGH evidence)

What: Daily tooth brushing, professional cleanings on veterinary schedule, and dental chews with meaningful efficacy.

The evidence: Periodontal disease is the most common clinical condition in adult dogs — over 80% of dogs over age 3 have clinically significant periodontal disease. The systemic health implications of untreated periodontal disease are substantial: chronic low-grade bacteremia, elevated inflammatory markers, and demonstrated associations with kidney disease, cardiac disease, and possibly cognitive decline.

The mechanism: Inflamed, infected gum tissue is a chronic source of bacteria and inflammatory mediators entering the bloodstream. Over years, this contributes to inflammation-driven disease throughout the body.

The protocol:

1. **Daily brushing.** Most owners don’t. This is the single biggest difference-maker. Dog toothpaste (chicken or beef flavored, designed to be swallowed), soft brush, 60

seconds per day. Start slow; most dogs tolerate it within a few weeks of gradual introduction.

2. **Professional cleanings.** Under anesthesia, as recommended by your vet. Most adult dogs need a professional cleaning every 1–2 years. Pre-anesthetic bloodwork is non-negotiable for senior dogs.
3. **Dental chews with evidence.** Look for the **Veterinary Oral Health Council (VOHC) seal** — this is the peer-reviewed efficacy certification. Products with VOHC acceptance have documented plaque and/or calculus reduction. Brands in this tier include Greenies, Whimzees (selectively), and CET-branded chews.
4. **Avoid the hype.** Products marketed with “dental benefits” but no VOHC seal are largely ineffective. Water additives are mostly placebo. Anesthesia-free “dental cleanings” are widely discouraged by the American Veterinary Dental College.

The vet question: *“When is my dog due for his next professional cleaning, and are there any signs of periodontal disease we should address today?”*

7. Joint protection starting now (MODERATE evidence)

What: A proactive joint health approach for large and giant breeds, starting well before any symptoms appear.

The evidence: Osteoarthritis is progressive and largely irreversible. Early protective strategies — weight management (#1), omega-3s (#5), structured exercise (#3), and joint-specific supplements — meaningfully delay onset and slow progression. The Purina Lifetime Study found a near-3-year delay in osteoarthritis onset in calorie-restricted dogs, which is a longer effect than any drug.

The mechanism: Joint damage in large breeds comes from cumulative cartilage wear, inflammation, and body-weight loading over years. Each of the below attacks a different part of that chain.

The protocol:

- 1. Weight first.** See #1. Every pound over ideal is load on every joint with every step. No supplement compensates for excess weight.
- 2. Omega-3s at therapeutic dose.** See #5.
- 3. Glucosamine/chondroitin supplementation.** Evidence is moderate — not every dog responds, but the ones who do show meaningful improvement. Veterinary-formulated products (Cosequin, Dasuquin) are the standard. Dose by weight; effect takes 4–6 weeks to develop.
- 4. Green-lipped mussel.** New Zealand green-lipped mussel extract has randomized-trial evidence for osteoarthritis symptom reduction. Often combined with glucosamine/chondroitin in advanced formulations.
- 5. Exercise — but the right kind.** Low-impact, consistent movement maintains joint health. High-impact, irregular exercise (weekend-warrior style) accelerates damage. Swimming is the gold standard for joint-friendly exercise.
- 6. Floor surface matters.** Hardwood and tile are worse for senior joint health than carpet or grip-mats in living areas. Small changes to home terrain meaningfully reduce senior dog falls and chronic strain.

The vet question: *“What joint supplements would you recommend for my dog’s breed and current condition, and what signs of early joint disease should I watch for?”*

8. Vaccine and titer strategy (MODERATE evidence)

What: A vaccination schedule tailored to your dog’s age, lifestyle, and exposure risk — not a one-size-fits-all annual protocol.

The evidence: Veterinary consensus on vaccination has evolved. Core vaccines (rabies, distemper, parvo, adenovirus) remain essential; non-core vaccines (bordetella, leptospirosis,

lyme, influenza) are lifestyle-dependent. For adult dogs, titer testing (measuring circulating antibody levels) can replace routine booster shots in many cases — avoiding over-vaccination while confirming protection.

The mechanism: Immune response to vaccines is variable in senior dogs. Under-vaccinated dogs are exposed to infection risk; over-vaccinated dogs may develop vaccine-associated adverse events (injection-site reactions, autoimmune responses, rare but documented). Titer-based protocols optimize this tradeoff.

The protocol:

- 1. Rabies is mandatory.** State and local law requires specific rabies vaccination schedules. No titer substitution. Three-year vaccines are widely available and appropriate for adult dogs.
- 2. Core vaccines (distemper, parvo, adenovirus) titer-able.** After the initial puppy series and a one-year booster, titer testing every 2–3 years can confirm protection without additional vaccination in dogs who maintain strong antibody levels.
- 3. Non-core vaccines by lifestyle.** Bordetella for dogs in boarding or group training. Lepto for dogs with outdoor exposure to wildlife or standing water. Lyme for dogs in tick-endemic areas. Influenza for dogs with frequent group contact.
- 4. Senior adjustments.** Some veterinarians reduce non-core vaccination frequency for senior dogs, prioritizing the lowest-risk protocol consistent with protection.

The vet question: *“Can we review my dog’s vaccination status and discuss a titer-based approach for non-rabies core vaccines?”*

9. Cancer screening cadence (EMERGING evidence)

What: Proactive cancer surveillance appropriate to your dog’s breed-specific risk profile.

The evidence: Cancer is the leading cause of death in adult dogs, particularly in large and giant breeds. Several new tools have emerged in the last few years:

- **Oncok9** (blood-based liquid biopsy) — detects cell-free DNA from 30+ canine cancers. Approved for use in dogs 7 and older, or dogs of any age in high-risk breeds.
- **Nu.Q Vet Cancer Test** — blood test detecting nucleosomes released by cancer cells.
- **Standard imaging** — chest radiographs, abdominal ultrasound on a regular cadence.

These tools cannot replace clinical exam, but they add a layer of early detection that was unavailable five years ago.

The mechanism: Earlier detection means smaller tumors, more treatment options, and better outcomes. Cancers caught at Stage 1 have dramatically better survival than those caught at Stage 3.

The protocol:

1. **Breed-risk assessment.** Golden Retrievers, Berners, Rottweilers, Great Danes, Boxers, and some others have specific cancer predispositions. Work with your vet to map your dog's risk profile.
2. **Liquid biopsy annually after age 7** for high-risk breeds, or after age 8 for moderate-risk breeds. The tests are not cheap (\$250–\$400) but provide a genuinely new data point.
3. **Imaging.** Chest films annually for giant breeds after age 6; abdominal ultrasound every 1–2 years for breeds with hemangiosarcoma or splenic tumor risk (Goldens, Berners, Labs).
4. **At-home surveillance.** Regular body palpation (front-to-back, every joint, every lymph node area) once a month. Most skin masses are detected by owners, not vets.

The vet question: *"Given my dog's breed and age, what cancer screening would you recommend — and is a liquid biopsy like Oncok9 appropriate?"*

10. Cognitive and social enrichment (MODERATE evidence)

What: Intentional, varied cognitive and social stimulation as part of daily life.

The evidence: Dog Aging Project research suggests that dogs with higher social complexity — regular exposure to other dogs, varied environments, novel experiences — show measurably better cognitive aging outcomes. This mirrors findings in human aging, where social and cognitive engagement are among the strongest protective factors against dementia.

The mechanism: Neural plasticity is use-dependent. Dogs whose brains are challenged maintain neural function longer. Dogs whose lives are monotonous (same walk, same yard, same interactions) lose neural reserve faster.

The protocol:

- 1. Vary walking routes.** Most owners walk the same two routes. Introduce new neighborhoods, parks, trails. Smell is cognitive input for dogs; variety is stimulation.
- 2. Social exposure.** Regular contact with other dogs — ideally a stable group, as chaotic interactions can be stressful. Daycare, playdates, dog-friendly events.
- 3. Training throughout life.** Trick training, scent work, new commands. Even senior dogs learn. Five minutes a day of intentional training maintains engagement.
- 4. Puzzle feeders.** Replace the bowl with snuffle mats, treat dispensing toys, or food puzzles. Eating becomes cognitive work.
- 5. Human interaction.** Physical affection, play, shared activity. The primary social bond of a dog's life is with their human — depth of that bond correlates with longevity in observational studies.

The vet question: *“Are there signs of early cognitive dysfunction I should watch for, and what would you recommend for enrichment given my dog's age and temperament?”*

Putting it together

If you could do only one of these: **weight**. Everything else has a smaller effect size.

If you could do three: **weight, bloodwork every 6 months, once-daily feeding**. These three together probably equal the effect of any single longevity drug.

If you could do all ten: you're giving your dog the best shot at matching — or beating — what LOY-002 is designed to provide.

What to take away from Module 7

- **Weight is the single highest-leverage longevity move.** Free, time-tested, effect size larger than any supplement.
 - **Once-daily feeding, structured exercise, and bi-annual bloodwork** are the next three biggest moves.
 - **Omega-3 at therapeutic dose** is the one supplement with real evidence — most owners underdose.
 - **Dental care is systemic health.** Daily brushing is the highest-ROI hygiene intervention.
 - **Proactive cancer screening** is newly possible — discuss with your vet.
 - **These practices are additive with LOY-002**, not redundant. The drug is a layer; these are the foundation.
-

Next up: Module 8 — Your Personalized Protocol. The synthesis module — taking your dog's specific situation (Module 3) and turning these ten practices + the waitlist + the vet conversation into a concrete weekly, monthly, and annual plan.

Module 8 — Your Personalized Protocol

Two versions. Read the simple one first.

- **Simple version** — 3 minutes. Your dog's four-week starter plan based on what you've read.
 - **Full version** — 9 minutes. Weekly, monthly, and annual checklists customized by dog profile, plus tracking templates and vet-visit preparation.
-

● The Simple Version

Everything so far, turned into a plan

You've read seven modules. You know the science, the drugs, the paths to access, the vet conversation, and the ten things that work today. This module is where all of that becomes a concrete plan for *your specific dog*.

Your four-week starter plan

Week 1 — Get the paper trail started.

- Sign up for Loyal's newsletter and the general waitlist (10 minutes).
- If your dog is 7+ and 44–120 lbs, apply to TRIAD at dogagingproject.org/triad.
- Take current photos of your dog from above and from the side (for BCS tracking).
- Weigh your dog if you have a scale; otherwise schedule a weigh-in at your vet.

Week 2 — The vet conversation.

- Schedule an appointment within two weeks. If your current vet's calendar is tight, book it as a senior wellness panel.

- Bring Module 6 or the printed question list (see the full version below).
- Request a full senior panel if it's been more than 6 months.
- Watch for the red flags. Decide after the appointment whether you stay, add, or switch.

Week 3 — Weight and diet.

- Use the vet's assessed BCS to set your feeding target.
- If your dog is overweight, cut calories by 15–20% (not more — gradual is better).
- Transition to once-daily feeding over 2–3 weeks (if appropriate for your dog's age/health).
- Count treat calories — include them in the daily total.

Week 4 — Movement and maintenance.

- Lock in 30–40 minutes of varied daily exercise.
- Start daily tooth brushing.
- Start therapeutic-dose omega-3 (dose confirmed with vet in week 2).
- Set a recurring calendar reminder: next senior panel in 6 months.

What you'll have done after four weeks

- You're on Loyal's waitlist.
- You've had the vet conversation and know whether you need a specialist.
- You have a baseline medical panel.
- Your dog's weight and feeding are dialed.
- Daily exercise, dental care, and omega-3 are part of the routine.

That's the foundation. From there, it's just maintenance and watching for the LOY-002 launch window.

● The Full Version

Reading time: about nine minutes. The complete weekly, monthly, and annual framework — plus templates for tracking and vet-visit preparation.

Build your dog's profile

Before the protocol, answer these six questions about your dog. Keep the answers handy — you'll use them in the vet conversation and every Loyal communication.

1. **Breed** (or best guess if mixed): _____
2. **Current age**: _____
3. **Current weight (pounds)**: _____
4. **Current body condition score (1-9)**: _____
5. **Existing conditions / diagnoses**: _____
6. **Current medications and supplements**: _____

Candidacy check

Use Module 3 to determine which of the following applies:

- **LOY-002 candidate**: Age 10+, weight 14+ lbs, no disqualifying conditions
- **LOY-001 candidate**: Age 7+, weight 40+ lbs, large/giant breed
- **LOY-003 candidate**: Age 5+, weight 60+ lbs, large/giant breed
- **TRIAD (Rapamycin) candidate**: Age 7+, weight 44–120 lbs
- **Almost a candidate**: Will qualify within 6–24 months
- **Not a candidate — Module 7 protocol only**

Most dogs will check multiple boxes. That's expected.

The weekly rhythm

For every dog, regardless of candidacy, a weekly cadence:

- **Daily:** Exercise (30–40 min), fresh water, meals (once daily if appropriate), dental brushing, omega-3 supplement.
- **Weekly:** Home body check — palpate for lumps, check ear/eye/dental health, note any changes in energy, appetite, or bathroom habits.
- **Weekly:** Quick weight check if you have a scale at home (for senior dogs — catches subtle losses early).

The monthly rhythm

- **Monthly weigh-in and BCS reassessment.** Adjust calories if BCS drifts up or down.
- **Monthly medication and supplement inventory.** Refill before running out.
- **Monthly Loyal pipeline check.** Scan your email for newsletter updates. Watch for Manufacturing (CMC) announcement and any drug-specific news.
- **Monthly “what changed” journal entry.** Two sentences: what’s different, what stayed the same. Takes 30 seconds. Invaluable when you’re trying to remember details at a vet appointment.

The 6-month rhythm

Every six months, regardless of what your dog is doing:

- **Senior wellness panel** (for large breeds 6+, all breeds 8+). Full panel — CBC, chemistry, thyroid, urinalysis.
- **Vet visit.** Even if no acute issue. Body condition, dental check, physical exam.
- **Review all medications and supplements with vet.** Drugs and doses drift; not everything started two years ago still makes sense.
- **Update the baseline.** Your “baseline” is a moving window, not a fixed snapshot. Each panel becomes data for comparison.

The annual rhythm

- **Dental cleaning assessment.** Most adult dogs need professional cleaning every 1–2 years.
- **Chest films** for giant breeds, or any breed with cardiac risk profile.
- **Cancer screening** — OncoK9 or similar for high-risk breeds age 7+.
- **Vaccine review** — titer where appropriate, core vaccines as scheduled, non-core by lifestyle.
- **Insurance review** — are you on the right plan for longevity-related needs?

Protocol variations by candidacy

If your dog is a LOY-002 candidate (the most common profile in this Playbook):

Add to the above: - **Quarterly Loyal waitlist check-in.** Confirm your registration is still active. Respond to any Loyal emails — engaged waitlist members get notified first. - **Annual vet visit specifically about LOY-002 launch readiness.** “Are you ready to prescribe when it ships? What do I need to have in place?” - **Post-launch month 1 target:** filled prescription, first dose administered. See Module 5 for the 90-day game plan.

If your dog is a TRIAD candidate:

Add: - **TRIAD application within 30 days.** Don't delay — enrollment can close for specific demographic segments. - **If enrolled:** follow TRIAD study protocol. Do not add other experimental longevity drugs concurrently. - **If not enrolled:** stay on the Loyal waitlist; Module 7 protocols become your primary longevity strategy.

If your dog is “almost a candidate” (6–24 months from qualifying):

Add: - **Document your dog's trajectory.** Each 6-month panel is a data point. You're building the longitudinal record that LOY-002's effect will eventually be measured against. - **Have the forward-candidate vet conversation (Module 6).** Your vet should know you are tracking toward candidacy. - **Module 7 is your main lever.** Every month on tight Module 7 protocols is measurable benefit for your dog.

If your dog is not a candidate (e.g., too young, wrong size, disqualifying condition):

Add: - **Module 7 is the entire protocol.** It is not a consolation prize — it is genuine longevity medicine. - **Watch for future trials.** Loyal is unlikely to stop at LOY-001/002/003. New trials for adjacent drug categories may open. STAY@loyal.com is the contact. - **Consider alternative longevity approaches (Module 9).** Animal Biosciences LeapYears, off-label rapamycin (with the right vet), emerging interventions.

The vet visit template

For any vet visit after reading this Playbook, bring:

The data you bring: - Current weight and BCS (from home tracking) - Last 2 bloodwork results (if you have them) - Current medication and supplement list with doses - Any “what changed” journal notes from the last 30 days - A list of questions (see below)

The questions you ask (pick 3–5 relevant to this visit): - Is my dog’s body condition where we want it? - What’s our current trajectory on [bloodwork marker that drifted]? - Are my current medications and doses still right? - [If LOY-002 candidate] Any updates on Loyal timeline or your prescribing plan? - [If concerning sign] What’s the workup plan for [symptom]? - What else should we be doing that we’re not?

What you leave with: - Updated chart notes (ask for a copy or a summary) - Written dose adjustments or new prescriptions - Next appointment scheduled - One or two clear action items for you at home

Pulling it all together: two sample dog profiles

Profile 1 — Bailey, 11-year-old Golden Retriever, 68 lbs, BCS 6/9, mild arthritis on carprofen.

- LOY-002 candidate (will be a primary focus)
- LOY-001 candidate (secondary — longer timeline)
- TRIAD candidate (age/weight fit)

Weekly: 30-40 min walks, joint-friendly terrain, daily brushing, omega-3 at 2,000 mg EPA+DHA Monthly: weigh-in (targeting BCS 4/9 — needs to lose ~6–8 lbs), Loyal pipeline check 6-monthly: senior panel, vet visit, BCS reassess Annual: chest films, OncoK9, dental cleaning Waitlist: Loyal sign-up complete; TRIAD application submitted; baseline panel done; vet conversation complete

Profile 2 — Thor, 5-year-old Great Dane, 140 lbs, BCS 4/9 (great), healthy.

- LOY-003 candidate (primary, but longer timeline than LOY-002)
- LOY-001 candidate at age 7
- TRIAD not a fit (weight over cutoff; age under)

Weekly: 30-40 min low-impact exercise (swimming ideal), weight maintenance at current BCS, daily brushing, omega-3 at 3,500 mg EPA+DHA Monthly: weigh-in, Loyal pipeline check 6-monthly: senior panel starting at age 6, vet visit Annual: chest films (giant breed cardiac screening), dental cleaning Waitlist: Loyal sign-up complete for both LOY-001 and LOY-003 segments; vet conversation complete

Tracking templates

A one-page tracking sheet — print, stick to the fridge, update monthly:

Dog name: _____

Breed: _____ Age: ____ Weight: ____ BCS: ____

Candidacy status:

LOY-002 LOY-001 LOY-003 TRIAD Almost Module 7 onl

Loyal waitlist: () signed up () confirmed

TRIAD application: () N/A () submitted () enrolled () declined

Baseline panel: Date _____ Results filed: ()

Next panel due: _____

Current meds/supplements:

1. _____ dose _____
2. _____ dose _____
3. _____ dose _____

Vet engagement level:

- Tier 1 specialist identified
- Tier 2 GP engaged
- Tier 3 GP – need specialist
- No current vet relationship

Next action: _____

What to take away from Module 8

- **The four-week starter plan** gets most owners from zero to foundation.
- **Weekly, monthly, 6-monthly, annual rhythms** become the ongoing cadence.
- **Protocol varies by candidacy** — LOY-002 candidates, TRIAD candidates, “almost candidates,” and Module-7-only dogs each have different priorities.
- **The vet visit template** standardizes what you bring, what you ask, what you leave with.
- **Tracking is maintenance.** A one-page fridge sheet beats a perfect spreadsheet nobody fills in.

Next up: Module 9 — What’s Next in Dog Longevity. Rapamycin beyond TRIAD, senolytics, NAD+ boosters, the other companies competing in this space, and the next five years of canine longevity science.

Module 9 — What's Next in Dog Longevity

Two versions. Read the simple one first.

- **Simple version** — 4 minutes. What's coming after Loyal — rapamycin, senolytics, NAD+, the other companies.
 - **Full version** — 11 minutes. A deeper map of the canine longevity landscape, what's credible vs. hype, and the five-year outlook.
-

● The Simple Version

The field is just getting started

Loyal's LOY-001/002/003 is the story right now because it's closest to market and represents a historic FDA milestone. But it is not the last word in canine longevity. Several adjacent therapies and companies are working on related approaches — some with genuinely promising evidence, some still speculative.

Here's the landscape as of now.

Rapamycin — the other pill getting serious attention

Rapamycin is an already-FDA-approved human drug (primarily for organ transplant rejection) that at low doses has shown remarkable lifespan-extending effects in mice — even when started late in life. The Dog Aging Project's **TRIAD study** (covered in detail in Module 4) is the trial that will tell us whether rapamycin works in dogs.

If TRIAD succeeds, expect rapamycin to become a routine off-label longevity prescription for senior dogs within 3–5 years. The drug is already manufactured; the question is dose and safety in a dog-specific context.

Senolytics — the zombie-cell clearing drugs

“Senolytics” are a category of drug that selectively kills senescent cells — the inflammation-spewing zombie cells we covered in Module 1. In mice and early human trials, senolytic therapy has shown impressive effects on multiple age-related conditions.

Senolytic drugs for dogs are not yet at the clinical trial stage the way Loyal’s pipeline is, but research groups are actively working on them. This is a 3–7 year horizon for real veterinary availability — worth watching, not yet worth planning around.

NAD+ boosters — the supplement category taking itself seriously

NAD+ (nicotinamide adenine dinucleotide) declines with age in all mammals. Boosting NAD+ — via precursor supplements like NMN or NR — has become a major area of research in human longevity, with an emerging canine parallel. Evidence in dogs is thinner than the marketing suggests, but some formulations are moving toward legitimate clinical study.

Brands like **Leap Years by Animal Biosciences** use NAD+ precursor chemistry and are marketed as canine longevity chewables. These are dietary supplements, not drugs — a lower regulatory bar and thinner evidence base than LOY-002. Worth knowing about; not a substitute for LOY-002.

The other companies

Beyond Loyal and Animal Biosciences, the canine longevity space includes early-stage companies working on:

- **Gallant** — veterinary stem cell therapies
- **Embark / Wisdom Panel** — genetic testing with increasing longevity relevance
- **Nu.Q Vet / OncoK9** — early cancer detection (covered in Module 7)

None of these are direct LOY-002 competitors, but they’re shaping the infrastructure of longevity-focused canine care.

The five-year outlook

- **2026–2027:** LOY-002 launches. TRIAD results expected.
- **2027–2028:** LOY-001 / LOY-003 advance. Rapamycin off-label use expands if TRIAD succeeds.
- **2028–2030:** Senolytics may enter clinical trial stage. NAD+ supplements mature. Combination therapy (LOY-002 + lifestyle + one other) becomes standard in longevity-focused clinics.

Your dog in 2030 will have meaningfully more options than your dog in 2026. But the foundation — weight, exercise, nutrition, bloodwork, waitlist, vet relationship — is the same now as it will be then. Everything in this Playbook holds up.

● The Full Version

Reading time: about eleven minutes. The full landscape of canine longevity science, a frank assessment of what's real vs. hype, and the 5-year outlook for the field.

The veterinary longevity field's current state

Five years ago, canine longevity was a niche academic interest — a handful of university labs doing research that mostly didn't translate to clinical practice. Today it is a funded, regulated, increasingly crowded space:

- **One company (Loyal)** with a first-in-class drug nearing commercial availability
- **One major academic consortium (Dog Aging Project)** running the largest longitudinal aging study in any companion animal
- **A second clinical trial (TRIAD)** actively enrolling dogs to test an already-approved human drug
- **Multiple supplement companies** marketing longevity claims with varying evidence

- **Adjacent diagnostics** (liquid biopsy, early cancer detection) that support a longevity-focused care model

This is enough infrastructure that “canine longevity medicine” is a coherent subfield. It wasn’t five years ago.

Rapamycin and the TRIAD study

What rapamycin is: An immunosuppressant originally isolated from bacteria in the soil of Easter Island (Rapa Nui — hence the name). FDA-approved in 1999 for preventing organ transplant rejection. Also approved for certain cancers and for a rare lung condition (LAM).

Why longevity researchers care: At lower doses than those used for transplant patients, rapamycin inhibits the **mTOR** signaling pathway — a central regulator of cellular growth, metabolism, and aging. mTOR inhibition is one of the most reproducible longevity interventions in laboratory research. In mice, rapamycin has extended lifespan even when started in middle or late life, which is not true of most longevity interventions.

What TRIAD will answer: - Does rapamycin extend canine lifespan at a sub-immunosuppressive dose? - What is the optimal dose and dosing schedule for dogs? - What is the side-effect profile over 3+ years of administration? - Are there subgroups (by breed, age, condition) that benefit disproportionately?

Why this matters beyond TRIAD: Unlike Loyol’s drugs, rapamycin is already manufactured, already FDA-approved for human use, already understood pharmacologically, and off-patent. If TRIAD demonstrates efficacy, the path to widespread veterinary off-label use is short. A practicing vet in 2029 with TRIAD data in hand can prescribe rapamycin tomorrow — no new FDA approval needed.

This makes rapamycin potentially the **second** canine longevity drug to reach broad clinical use, possibly shortly after LOY-002 launches. In a 5-year horizon, most senior dogs in longevity-focused care may be on LOY-002, or off-label rapamycin, or (eventually) some combination.

The honest caveats: - Rapamycin has real side effects at transplant doses (impaired wound healing, elevated cholesterol, mouth sores). At geroprotective doses these are rarer but not zero. - Dog-specific optimal dosing is genuinely unknown until TRIAD reads out. - Combining rapamycin with LOY-002 is an open experimental question — data simply doesn't exist.

Senolytics — the next frontier

Senescent cells — the “zombie cells” from Module 1 — are a validated driver of age-related tissue dysfunction. Drugs that selectively kill senescent cells are called **senolytics**.

The most-studied senolytic compounds: - **Dasatinib + Quercetin (D+Q)** — a combination where dasatinib (an FDA-approved cancer drug) and quercetin (a plant flavonoid) together clear senescent cells. The most-studied senolytic combination in humans. - **Fisetin** — another plant flavonoid with senolytic activity. Available as a supplement; human trials ongoing. - **Newer small molecules** — several pharmaceutical companies have senolytic development programs targeting specific senescent cell subtypes.

In dogs: Published canine-specific senolytic research is limited. Some veterinary researchers are exploring D+Q protocols for osteoarthritis-associated senescent cell clearance, but no large-scale canine senolytic trials are at the stage of TRIAD or Loyal's STAY.

Horizon: Senolytics in dogs is a **3–7 year horizon** for real veterinary availability. Worth watching. Not yet worth planning around.

NAD+ and related metabolic supplements

The mechanism: Nicotinamide adenine dinucleotide (NAD+) is a critical cofactor in cellular energy metabolism. It declines with age across all mammals studied. Restoring NAD+ has become a major focus in human longevity research — via supplementation with NAD+ precursors like nicotinamide riboside (NR) and nicotinamide mononucleotide (NMN).

The human evidence: Mixed. Supplementation reliably raises NAD+ levels. Whether this translates to meaningful healthspan or lifespan extension in humans is still under study. Some trials show benefit on specific markers; others show minimal effect.

The canine evidence: Thinner. Several companies market NAD+ precursor supplements to dog owners, but large-scale canine studies are limited.

Notable product: Leap Years by Animal Biosciences. A chewable canine longevity supplement using NAD+ precursor chemistry plus other longevity-relevant compounds. Marketed as a longevity intervention. Regulatory status: dietary supplement, not FDA-approved drug. This means:

- Lower regulatory bar than LOY-002
- Weaker evidence base than LOY-002
- Available over-the-counter
- Not a substitute for LOY-002

Practical framing: NAD+ supplements are in the “mechanistically plausible, limited canine evidence” category. Not unreasonable to use; not a drop-in replacement for evidence-backed practices or pharmaceutical intervention. Discuss with your vet.

The competitive landscape

Beyond Loyal, the commercial canine longevity space includes:

Animal Biosciences (Leap Years). Dietary supplement company, as above. Different regulatory path than Loyal. Broader distribution channels. Marketing is aggressive; evidence is developing.

Gallant. Veterinary stem cell therapy. Not a longevity company per se, but stem cell applications in orthopedic and organ regeneration have longevity-adjacent implications.

Embark / Wisdom Panel. Direct-to-consumer canine genetic testing. Increasingly incorporate longevity-relevant markers (breed-specific disease risk, age-related variant

identification).

OncoK9, Nu.Q Vet. Cancer-specific diagnostics (covered in Module 7). Critical infrastructure for a longevity-focused care model even though they don't extend lifespan directly.

Dog Aging Project's ecosystem. Not a company, but a growing consortium of academic researchers, vet clinics, and citizen science participants generating the largest aging dataset in any companion animal species. Enrolled dogs are contributing data that will shape veterinary longevity medicine for decades.

None of these are direct LOY-002 competitors. Loyal's moat is the first-in-class FDA-approval pathway and the IGF-1 and metabolic mechanisms specifically. The broader ecosystem is complementary — different companies addressing different parts of canine aging.

The five-year outlook, by year

2026–2027: - LOY-002 achieves Expanded Conditional Approval. Commercial availability begins. - TRIAD early results (interim analyses) may be published. - First year of real-world LOY-002 data emerges. - Insurance coverage posture solidifies.

2027–2028: - LOY-001 and LOY-003 advance through their FDA pathways. - TRIAD full results possible by late 2028. - If TRIAD is positive, rapamycin off-label use expands rapidly. - First mainstream veterinary CE courses on canine longevity medicine become standard.

2028–2030: - LOY-002 transitions from conditional to full approval (if post-market data supports it). - LOY-001 / LOY-003 reach prescription availability. - Rapamycin established as second-line or complementary longevity prescription. - Senolytic canine trials enter clinical stage. - Combination therapy (LOY-002 + lifestyle + rapamycin or other) becomes standard of care in longevity-focused clinics. - Pet insurance carriers develop coherent longevity drug coverage policies. - Veterinary specialty boards (ACVIM, ACVNU) likely develop longevity-specific certification tracks.

What to watch for — the leading indicators

If you want to stay ahead of the field as it evolves, watch these specific sources:

- **Loyal's blog at loyal.com/posts.** Milestone announcements land here first.
- **The Dog Aging Project's publications page.** Peer-reviewed findings land here.
- **FDA Center for Veterinary Medicine news.** Regulatory milestones.
- **DVM360, AAHA Trends, JAVMA News.** Veterinary trade press covers emerging drugs as they approach availability.
- **Longevity.Technology and similar longevity-focused publications.** Cross-species longevity coverage including canine.
- **This Playbook's \$9/month subscription.** Curated updates as relevant developments land.

What this means for you

Your dog in 2030 will have access to meaningfully more longevity medicine than your dog in 2026. Between now and then:

- **LOY-002 launch** (2026–2027) will be the first major inflection.
- **TRIAD results** (2028) will be the second.
- **Combined therapy protocols** (2029–2030) will be the third.

But — and this matters — the **foundation** doesn't change. Weight management, once-daily feeding, structured exercise, omega-3s, bi-annual bloodwork, dental care, social enrichment, vet relationship. Everything in Module 7. These work today, will continue to work in 2030, and will be the bedrock that whatever drug your dog is eventually on builds upon.

Your job as an owner isn't to wait for the right drug. It's to build the foundation now so that whatever drug arrives has the best possible substrate to work on.

What to take away from Module 9

- **Loyal is not the last word.** Rapamycin (TRIAD), senolytics, NAD+ precursors, and several other companies are working on adjacent canine longevity approaches.
 - **Rapamycin is the most important near-term second option.** If TRIAD succeeds, expect widespread off-label use by 2028–2029.
 - **Senolytics are real science but 3–7 years from veterinary availability.**
 - **NAD+ supplements are mechanistically plausible with limited canine evidence.** Not a replacement for LOY-002.
 - **Multiple companies** (Animal Biosciences, Gallant, Embark, Nu.Q Vet, OncoK9) are building longevity-adjacent infrastructure — none direct LOY-002 competitors.
 - **By 2030**, combination therapy will likely be standard of care in longevity-focused clinics.
 - **The Module 7 foundation doesn't change.** Every future drug builds on top of it.
-

Thank you for reading the Big Dog Longevity Playbook

You now know more about canine longevity medicine than 99% of dog owners — and, honestly, more than many general-practice veterinarians. You know:

- Why your big dog ages faster (Module 1)
- What drugs are coming and when (Module 2)
- Whether your dog is a candidate (Module 3)
- The two real paths to early access (Module 4)
- How to play the waitlist (Module 5)
- How to have the vet conversation (Module 6)
- The ten evidence-backed things you can do today (Module 7)
- How to turn all of it into a personal protocol (Module 8)
- What's coming next in the field (Module 9)

Use this. Revisit it. Come back when LOY-002 launches. Come back when TRIAD reads out. Come back when your dog's needs change.

The \$9/month subscription, if you have it, will push updates as the field evolves — new FDA milestones, new study results, new companies entering the space, and curated guidance on what to do with each.

And if your dog is very senior and you're racing the clock: do Module 7 aggressively, sign up for the Loyal waitlist and TRIAD (if eligible) today, and have the vet conversation this week. Every week of delay is a week your dog doesn't get back.

Take care of your dog. This Playbook was written in that spirit.

— *The Big Dog Longevity team*