

**PrP»CЦ PjPμPrPëC‡PSPsPiPs P•P°CíC,PsCíCíPIP°PSPSCЦ P»C-PεP°CĤCíCĤPεPsPiPs
P•P°CíPsP±Cí**

(TAMSIN FORTE)

PyP°PjCfCfP»PSP·PëPS CfPüP»PüPeC,PëPIPPS C- PePsPSPeCrCfPüPSC,PSPs P±P»PsPeCrC"
PiPsCfC,CfPëPSP°PiC,PëC±PSC- α1-P°PrCfPüPSPsCfPüC†PüPiC,PsCfPë, P·PsPeCfPüPjP° α1A

C,P° α1D, C%Ps P·PSP°C...PsPrCЦC,CHCГCЦ Cr PiP»P°PrPeC-PN° PjCrCГPeCГP»P°C,CrCГC-
PiPμCГPμPrPjC-C...CrCГPsPiPsC— P·P°P»PsP·Pë, C€PëPN°PePë CГPμC±PsPiPsPiPs PjC-C...CrCГP°
C- PiCГPsCГC,P°C,PëC±PSPsC— C±P°CГC,PëPSPë CrCГPμC,CГPë. P|Pμ PiCГPëP·PiPsPrPëC,CH
PrPs P·PSPëP¶PμPSPSCЦ C,PsPSCrCГCr PiP»P°PrPePsC— PjCrCГPeCГP»P°C,CrCГPë
PiPμCГPμPrPjC-C...CrCГPsPiPsC— P·P°P»PsP·Pë, C€PëPN°PePë CГPμC±PsPiPsPiPs PjC-C...CrCГP°
C- PiCГPsCГC,P°C,PëC±PSPsC— C±P°CГC,PëPSPë CrCГPμC,CГPë C,P° PiPsP»C-PiC€CГC”
PiPëPrC-P»PμPSPSCЦ CГPμC±C-.

PhPrPSPsC±P°CГPSPs P·PjPμPSC€CГCГC,CHCГCЦ CГPëPjPiC,PsPjPë PsP±CГC,CГCГPeCГC-C—
C,P° PiPsPrCГP°P·PSPμPSPSCЦ, PiPsPiBГ™ CЦP·P°PSC- P· PrPsP±CГPsCЦPeC-CГPSPsCГ
PiC-PiPμCГPiP»P°P·C-C”CГ PiPμCГPμPrPjC-C...CrCГPsPiPsC— P·P°P»PsP·Pë
(CГC,CГCГPrPSPμPSPSCЦ PiPsC±P°C,PeCГ CГPμC±PsPiPëPiCГCГPeP°PSPSCЦ,
PiPsCГP»P°P±P»PμPSPSCЦ CГC,CГCГPjPμPSCЦ CГPμC±C-, PeCГP°PiP°PSPSCЦ PiC-CГP»CЦ
P·P°PeC-PSC±PμPSPSCЦ CГPμC±PsPiPëPiCГCГPeP°PSPSCЦ, PIC-PrC±CГC,C,CЦ
PSPμPiPsPiPSPsPiPs CГPiPsCГPsP¶PSPμPSPSCЦ CГPμC±PsPiPsPiPs PjC-C...CrCГP°, C±P°CГC,C-
PiPsP·PëPiPë PrPs CГPμC±PsPiPëPiCГCГPeP°PSPSCЦ PI PSC-C±PSPëPN° C±P°CГ,
PSPμPIC-PrPeP»P°PrPSC-CГC,CH CГPμC±PsPiPëPiCГCГPeP°PSPSCЦ).

P—PrP°C,PSC-CГC,CH α1A-P°PrCГPμPSPsP±P»PsPeP°C,PsCГC-PI P·PjPμPSC€CГPiP°C,Pë
P°CГC,PμCГC-P°P»CHPSPëPN° C,PëCГPe PiPsPiBГ™ CЦP·P°PSP° P·C- P·PjPμPSC€PμPSPSCЦPj
PiPμCГPëC,,PμCГPëC±PSPsPiPs PsPiPsCГCГ. PÿP°PjCГCГP»PsP·PëPS Cr PrPsP±PsPIC-PN°
PrPsP·C- 0,4 PjPi PSPμ CГPiCГPëC±PëPSCЦC” PeP»C-PSC-C±PSPs P·PSP°C±CГC%PsPiPs
P·PSPëP¶PμPSPSCЦ CГPëCГC,PμPjPSPsPiPs P°CГC,PμCГC-P°P»CHPSPsPiPs C,PëCГPeCГ (PhPÿ)
CЦPe Cr C...PiPsCГPëC... PSP° P°CГC,PμCГC-P°P»CHPSCr PiC-PiPμCГC,PμPSP·C-CГ, C,P°Pe C-
PI PiP°CГC-C”PSC,C-PI C-P· PSPsCГPjP°P»CHPSPëPj PiPsC±P°C,PePsPiPëPj PhPÿ.

PαP°CГPjP°PePsPeC-PSPμC,PëPeP°.

PhP±CГPsCГP±CГC-CЦ. PÿP°PjCГC-PS PαPsCГC,Pμ CЦPiP»CЦC” CГPsP±PsCГ
C,P°P±P»PμC,PeCГ PiCГPsP»PsPSPiPsPiP°PSPsC— PrC-C— P· PePsPSC,CГPsP»CHPsPiP°PSPëPj
PiPëPIC-P»CHPSPμPSPSCЦPj, C%Ps P·P°P±PμP·PiPμC±CГC” C,CГPëPiP°P»Pμ C,P°
PiPsPIC-P»CHPSPμ PiPëPIC-P»CHPSPμPSPSCЦ C,P°PjCГCГP»PsP·PëPSCr, C%Ps PrP°C”
PμPeCГPiPsP·PëCГC-CГ P·C- CГP»P°P±PePëPjPë PePsP»PëPiP°PSPSCЦPjPë PiCГPsC,CЦPiPsPj 24
PiPsPrPëPS.

PμC-CГP»CЦ PiPμCГPsCГP°P»CHPSPsPiPs PiCГPëPN°PsPjCr PSP°C,C%PμCГPμCГPμ 57 %
C,P°PjCГCГP»PsP·PëPSCr P°P±CГPsCГP±CГC”C,CHCГCЦ PI PePëC€PμC±PSPëPeCГ.
PëPiPëPrPeC-CГC,CH C- CГPsP·PjC-CГ P°P±CГPsCГP±CГC-C— C,P°P±P»PμC,PsPe
PiCГPsP»PsPSPiPsPiP°PSPsC— PrC-C— PSPμ P·PjC-PSCГC”C,CHCГCЦ PiCГPë
PiP¶PëPiP°PSPSC- C—P¶C- C-P· PSPëP·CHPePëPj PiPjC-CГC,PsPj P¶PëCГCГ. PÿC,CrPiC-PSCH
PiCГPjPsPeC,CrPiP°PSPSCЦ PiC-PrPiPëC%CrC”C,CHCГCЦ PSP° 64 % C,P°B 149 % (AUC C,P°
Pÿ_{max} PIC-PrPiPsPIC-PrPSPs) PiCГPë PiCГPëPN°PsPjC- C—P¶C- P· PiPëCГPsPePëPj PiPjC-CГC,PsPj

Р¶ПёСҖСр РїСсСҖС-PIPSCLPSPs Р· РїСҖПёРНёPsPjPsPj PSP°C,C%PµCГРµСҖС†Рµ.

РҗР°РјСГСрР»PsР·PёPS РrРµРјPsPSCГС,СҖСрС” Р»C-PSC-PMPSCL
C,,P°СҖРјР°РёPsPeC-PSPµC,PёPeСр.

РµC-ГРР»CП PsPrPSPsСҖР°Р·PsPIPsPiPs РїСҖПёРНёPsPjСр РҗР°РјСГС-PS РµPsСҖС,Рµ
PSP°C,C%Pµ Рҗ_{max} Р°РёC,PёPIPSsC— СҖРµC†PsPIPёPSPё Ср РїР»Р°Р·РјC- РёСҖPsPIC-
СГРїPsСГС,РµСҖС-РїР°С”C,СҖСГСCП C†РµСҖРµР· 6 РїPsPrPёPS. Рј СҖС-PIPSsPIP°P¶PSPsPjСр
СГС,Р°PSC-, CПРёPёРНё РrPsСГСCПРїР°С”C,СҖСГСCП PSP° C†РµC,PIPµСҖС,PёРНё РrРµPSCҖ
РїСҖПёРНёPsPjСр РїСҖРµРїР°СҖР°С,Ср, РїC-Рё РёPsPSC†РµPSC,СҖР°С†C-С—
СГРїPsСГС,РµСҖС-РїР°С”C,СҖСГСCП C†РµСҖРµР· 4-6 РїPsPrPёPS PSPµР·Р°Р»РµP¶PSPs PIC-Pr
PIP¶PёPIP°PSPSCП C—P¶C-. РµC-Рё РёPsPSC†РµPSC,СҖР°С†C-С— Ср РїР»Р°РјC- РёСҖPsPIC-
РїC-PrPIPёC%СрС”C,СҖСГСCП Р· РїСҖПёР±Р»P»PёР·PSPs 6 PSPI/PjР» РїC-СГРР»CП
РїРµСҖСёPsPiPs РїСҖПёРНёPsPjСр РrPs 11 PSPI/PjР» Ср СҖС-PIPSsPIP°P¶PSPsPjСр СГС,Р°PSC-.

РїРё СҖРµРµР·CрР»СҖC,Р°C, C,СҖПёPIP°Р»PsPiPs PIPёPIC-Р»СҖPSPµPSPSCП,
PSP°PMPSPёP¶C†PёРНё СҖС-PIPµPSCҖ РёPsPSC†РµPSC,СҖР°С†C-С— C,Р°РјСГСрР»PsР·PёPSCр
Ср РїР»Р°РјC- СГС,Р°PSPsPIPёC,СҖ 40 % РјР°РёCГРёPёРјР°Р»CҖP»СҖPSPsC—
РёPsPSC†РµPSC,СҖР°С†C-С— PSPµР·Р°Р»РµP¶PSPs PIC-Pr PIP¶PёPIP°PSPSCП C—P¶C-. B B B B

Р PsР·РїPsPrC-Р». Р—РїБҗ™ CПР·СрPIP°PSPSCП Р· Р±C-Р»РёР°РјРё РїР»Р°РјCРё Бҗ” 99 %.
РҖР±Бҗ™ C”Рј СҖРµPsР·РїPsPrC-Р»Ср PSPµР·PSP°C†PSPёРНёB (РїСҖПёР±Р»P»PёР·PSPs 0,2 Р»/РёРё).

РҖРµC,Р°Р±PsР»C-Р·Рј. РҗР°РјСГСрР»PsР·PёPSCр РїC-PrСҖPsC...Р»PsСҖПёPr РјР°С”
PSPёР·СҖPёРНё РµC,,РµРёC, РїРµСҖСёPsPiPs РїСҖPsC...PsPrP¶PµPSPSCП, РїPsPIC-Р»СҖPSPs
РјРµC,Р°Р±PsР»C-Р·СрСҖC†PёСГСҖ. Р°C-Р»СҖСёР° C†Р°СГС,PёPSP° Р°РёC,PёPIPSsC—
СҖРµC†PsPIPёPSPё РїСҖПёСГСрC,PSCП Рї РёСҖPsPIC- Ср PSPµР·РјC-PSPµPSPsPjСр
PIPёРїР»CПР·C-. РҖРµC,Р°Р±PsР»C-Р·СрС”C,СҖСГСCП Ср РїРµC†C-PSC†C-.
Р РµР·CрР»СҖC,Рё in vitro РїPsРёР°Р·CрСҖСҖ,СҖ, C%Ps CYP3A4 C- C,Р°РёPsP¶ CYP2D6
PIPёР»СҖC†Р°СҖ,СҖСГСCП Ср РјРµC,Р°Р±PsР»C-Р·Рј, C-PSCёC- C-Р·PsC,,РµСҖРјPµPSC,Pё CYP
PSPµР·PSP°C†PSPs PIPР»PёPIP°СҖC,СҖ PSP° C,Р°РјСГСрР»PsР·PёPS.
РµСҖПёРїPSC-C†РµPSPSCП РјРµC,Р°Р±PsР»C-Р·СрСҖC†PёC... C,,РµСҖРјPµPSC,C-PIB CYP3A4
C- CYP2D6 РјPsP¶Рµ РїСҖПёР·PIPµСГС,Pё РrPs РїC-PrPIPёC%PµPSPSCП
РµРёСГРїPsР·PёC†C-С— C,Р°РјСГСрР»PsР·PёPSCр РїC-PrСҖPsC...Р»PsСҖПёPrСр (PrPёPI.
СҖPsР·PrC-Р»Pё B«Р°Р·Р°С”РјPsPrC-CП Р· C-PSCёPёРјРё Р»C-РёР°СҖСГСҖPёPёPё
Р·Р°СГР±P±Р°РјРё C,Р° C-PSCёC- PIPёPrPё PIP°С”РјPsPrC-PMB» C-
B«РҖСГР±P±Р»PёPIPsСГС,C- Р·Р°СГС,PsСГСрPIP°PSPSCПB»).B Р·PsPrРµPS C-Р·
РјРµC,Р°Р±PsР»C-C,C-PI PSPµ C” Р°РёC,PёPIPSC-CёPёРј Р·Р° РrC-СҖC†Ср СҖРµC†PsPIPёPSCр.

РPёPIPµPrРµPSPSCП. РҗР°РјСГСрР»PsР·PёPS C,Р° PMPSPiPs РјРµC,Р°Р±PsР»C-C,Pё
PIPёPIPsPrCП,СҖСГСCП Рї PsСГPSPsPIPSsPjСр PSPёСҖРёР°РјРё, 4-6 % РrPsР·Pё
PIPёPrC-Р»CПC”C,СҖСГСCП Ср PSPµР·РјC-PSPµPSPsPjСр PIPёРїР»CПР·C-. РµРµСҖС-PsPr
PSP°РїC-PIIPёPIPµPrРµPSPSCП C,Р°РјСГСрР»PsР·PёPSCр РїСҖПё PsPrPSPsСҖР°Р·PsPIPsPjСр
РїСҖПёРНёPsPjC- C,Р° Ср СҖС-PIPSsPIP°P¶PSPsPjСр СГС,Р°PSC- СГС,Р°PSPsPIPёC,СҖ 19 C- 15
РїPsPrPёPS PIC-PrРїPsPIC-PrPSPs.B

Р»Р»Р»C-PSC-C†PSC- C...P°СҖР°РёC,РµСҖПёСГС,PёРёPё.

РµPsPeР°Р·Р°PSPSCП.

P>C-PeCfPIP°PSPSCII C,,CfPSPeC†C-PsPSP°P»CHbPSPëC... CḡPsP·P»P°PrC-PI P· P±PsPeCf
PSPëP¶PSC-C... CfPµC‡PsPIPëPIC-PrPSPëC... C€P»CII C...C-PI PïCḡPë
PrPsP±CḡPsCIIPeC-CfPSC-PNḡ PiC-PiPµCḡPiP»P°P·C-C— PïCḡPsCfC,P°C,Pë.

PµCḡPsC,PëPiPsPeP°P·P°PSPSCII.

P°C-PiPµCḡC‡CfC,P»PëPIC-CfC,CH PrPs C,P°PjCfCfP»PsP·PëPSCf
PiC-PrCḡPsC...P»PsCḡPëPrCf, PIPeP»CḡC‡P°CḡC‡Pë PjPµPrPëPeP°PjPµPSC,PsP·PSPs-
C-PSPPrCfPePsPIP°PSPëPNḡ P°PSPiC-PsPSPµPICḡPsC,PëC‡PSPëPNḡ PSP°P±CḡCIIPe,
P°P±Ps PrPs P±CfPrCHb-CIIPePsC— P· PrPsPiPsPjC-P¶PSPëC... CḡPµC‡PsPIPëPS
PïCḡPµPiP°CḡP°C,Cf; PSP°CIIPIPS-CfC,CH PI P°PSP°PjPSPµP·C-
PsCḡC,PsCfC,P°C,PëC‡PSPsC— PiC-PiPsC,PµPSP·C-C—; C,CII P¶PeP°
PiPµC‡C-PSPePsPIP° PSPµPrPsCfC,P°C,PSC-CfC,CHb.

***P'P·P°C" PjPsPrC-CII P· C-PSC€PëPjPë P»C-PeP°CḡCfCHbPePëPjPë P·P°CfPsP±P°PjPë C,P°
C-PSC€C- PIPëPrPë PIP·P°C" PjPsPrC-PNḡ.***

P"PsCfP»C-PrP¶PµPSPSCII PIP·P°C" PjPsPrC-C— PIPëPePsPSCfPIP°P»PëCfCII C,C-P»CHbPePë Cf
PrPsCḡPsCfP»PëC....

PµCḡPë PsPrPSPsC‡P°CfPSPsPjCf P·P°CfC,PsCfCfPIP°PSPSC- C,P°PjCfCfP»PsP·PëPSCf
PiC-PrCḡPsC...P»PsCḡPëPrCf P· P°C,PµPSPsP»PsP»PsPj, PµPSP°P»P°PiCḡPëP»PsPj P°P±Ps
C,PµPsC,,C-P»C-PSPsPj P»C-PeP°CḡCfCHbPePsC— PIP·P°C" PjPsPrC-C— PSPµ
PIC-PrP·PSP°C‡P°P»PsCfCII. PhPrPSPsC‡P°CfPSPµ P·P°CfC,PsCfCfPIP°PSPSCII P·
C‡PëPjPµC,PëPrPëPSPsPj PiC-PrPIPëC%oCfC", P° P· C,,CfCḡPsCfPµPjC-PrPsPj бḡ“ P·PSPëP¶CfC”
PePsPSC‡PµPSC,CḡP°C†C-Cḡ C,P°PjCfCfP»PsP·PëPSCf PI PiP»P°P·PjC- PeCḡPsPIC-, P°P»Pµ
PsCfPeC-P»CHbPePë C†C- CḡC-PIPS-C P·P°P»PëC€P°CḡC,CHbCfCII Cf PjPµP¶P°C... PSPsCḡPjPë,
Cf CfPiPµC†C-P°P»CHbPSC-PNḡ PePsCḡPµPeC†C-C— PrPsP·CfPIP°PSPSCII
C,P°PjCfCfP»PsP·PëPSCf PSPµPjP°C" PSPµPsP±C...C-PrPSPsCfC,C-.

PJ PrPsCfP»C-PrP¶PµPSPSCII C... *in vitro* PrC-P°P·PµPiP°Pj, PïCḡPsPiCḡP°PSPsP»PsP»,
C,CḡPëC...P»PsCḡPjPµC,C-P°P·PëPr, C...P»PsCḡPjP°PrPëPSPsPS, P°PjC-C,CḡPëPiC,PëP»C-PS,
PrPëPeP»PsC,,PµPSP°Pe, PiP»C-P±PµPSPeP»P°PjC-Pr, CfPëPjPIP°CfC,P°C,PëPS C,P°
PIP°CḡC,,P°CḡPëPS PSPµ PIPiP»PëPIP°CḡC,CH PSP° PIC-P»CHbPSCf C,,CḡP°PeC†C-Cḡ
C,P°PjCfCfP»PsP·PëPSCf Cf PiP»P°P·PjC- PeCḡPsPIC- P»CḡPrPëPSPë. PµPsPrC-P±PSPëPj
C‡PëPSPsPj C,P°PjCfCfP»PsP·PëPS PSPµ P·PjC-PSCHC” CḡC-PIPµPSCḡ PIC-P»CHbPSPëC...
C,,CḡP°PeC†C-PNḡ PrC-P°P·PµPiP°PjCf, PïCḡPsPiCḡP°PSPsP»PsP»Cf,
C,CḡPëC...P»PsCḡPjPµC,C-P°P·PëPrCf C,P° C...P»PsCḡPjP°PrPëPSPsPSCf Cf PiP»P°P·PjC-
PeCḡPsPIC- P»CḡPrPëPSPë.

PµCḡPsC,Pµ PrPëPeP»PsC,,PµPSP°Pe C,P° PIP°CḡC,,P°CḡPëPS PjPsP¶CfC,CHb
PiC-PrPIPëC%oCfPIP°C,Pë C€PIPëPrPeC-CfC,CH PµP»C-PjC-PSP°C†C-C—
C,P°PjCfCfP»PsP·PëPSCf.

PhPrPSPsC‡P°CfPSPµ P·P°CfC,PsCfCfPIP°PSPSCII C,P°PjCfCfP»PsP·PëPSCf
PiC-PrCḡPsC...P»PsCḡPëPrCf C-P· CfPëP»CHbPSPëPjPë C-PSPiC-P±C-C,PsCḡP°PjPë CYP3A4

PjPsP¶Pµ PīCḡPēP·PIPµCíC,Pē PrPs P·P±C-P»CHC€PµPSPSCı PIPiP»PēPICí
C,P°PjCíCíP»PsP·PēPSCí PiC-PrCḡPsC...P»PsCḡPēPrCí. PhPrPSPsC‡P°CíPSPµ
P·P°CíC,PSCíCíPIP°PSPSCı P·PePµC,PSPePsPSP°P·PsP»PsPj (PIC-PrPsPjPēPNē
CíPēP»CHPSPēPNē C-PSPiC-P±C-C,PSCḡ CYP3A4) PīCḡPēP·PIPsPrPēP»Ps PrPs
P·P±C-P»CHC€PµPSPSCı AUC C- PŸ_{max} PrPs 2,8 C- 2,2 PIC-PrPiPsPIC-PrPSPs.

PŸP°PjCíCíP»PsP·PēPSCí PiC-PrCḡPsC...P»PsCḡPēPr PSPµ CíP»C-Pr PīCḡPēP·PSP°C‡P°C,Pē Cí
PePsPjP±C-PSP°C‡C-C— C-P· CíPēP»CHPSPēPjPē C-PSPiC-P±C-C,PSCḡP°PjPē CYP3A4 Cí
PīP°C‡C-C”PSC,C-PI P· PSPēP·CHPePēPj PjPµC,P°P±PsP»C-P·PjPsPj CYP2D6.

PŸP°PjCíCíP»PsP·PēPSCí PiC-PrCḡPsC...P»PsCḡPēPr CíP»C-Pr P·P°CíC,PSCíPsPICíPIP°C,Pē P·
PsP±PµCḡPµP¶PSC-CíC,Cḡ Cí PePsPjP±C-PSP°C‡C-C— C-P· CíPēP»CHPSPēPjPē C-
PīPsPjC-CḡPSPēPjPē C-PSPiC-P±C-C,PSCḡP°PjPē CYP3A4.

PhPrPSPsC‡P°CíPSPµ P·P°CíC,PSCíCíPIP°PSPSCı C,P°PjCíCíP»PsP·PēPSCí
PiC-PrCḡPsC...P»PsCḡPēPrCí C- PīP°CḡPsPeCíPµC,PēPSCí (CíPēP»CHPSPēPNē
C-PSPiC-P±C-C,PSCḡ PŸYP2D6) PīCḡPēP·PIPsPrPēP»Ps PrPs P·P±C-P»CHC€PµPSPSCı AUC C-
PŸ_{max} PrPs 1,6 C- 1,3 PIC-PrPiPsPIC-PrPSPs, P°P»Pµ C‡Pµ PSPµ C” PeP»C-PSC-C‡PSPs
P·PSP°C‡CíC%PēPj.

PhPrPSPsC‡P°CíPSPµ P·P°CíC,PSCíCíPIP°PSPSCı P· C-PSC€PēPjPē α1-
P°PrCḡPµPSPsP±P»PsPeP°C,PSCḡP°PjPē PjPsP¶Pµ PīPsCíPēP»CHPIP°C,Pē
PiC-PīPsC,PµPSP·PēPIPSPēPNē PµC,,PµPeC,.

PhCíPsP±P»PēPIPsCíC,C- P·P°CíC,PSCíCíPIP°PSPSCı.

PīPe C- PīCḡPē P·P°CíC,PSCíCíPIP°PSPSC- C-PSC€PēC... α1-
P°PrCḡPµPSPsP±P»PsPeP°C,PSCḡC-PI, PI PsPeCḡPµPjPēC... PIPēPīP°PrPeP°C... PīCḡPē
P·P°CíC,PSCíCíPIP°PSPSC- PīPµCḡPīP°CḡP°C,Cí PjPsP¶P»PēPIPµ P·PSPēP¶PµPSPSCı
P°CḡC,PµCḡC-P°P»CHPSPsPiPs C,PēCíPeCí, C%Ps PjPsP¶Pµ CḡC-PrPePs
PīCḡPēP·PIPsPrPēC,Pē PrPs PIC,CḡP°C,Pē CíPIC-PrPsPjPsCíC,C-. PµCḡPē PīPsCıPIC-
PīPµCḡC€PēC... PsP·PSP°Pe PsCḡC,PSCíC,P°C,PēC‡PSPsC— PiC-PīPsC,PµPSP·C-C—
(P·P°PīP°PjPsCḡPsC‡PµPSPSCı, CíP»P°P±PeC-CíC,Cḡ) PīP°C‡C-C”PSC, PīPsPIPēPSPµPS
PīCḡPēCíC-CíC,Pē P°P±Ps PīCḡPēPNēPSCıC,Pē PiPsCḡPēP·PsPSC,P°P»CHPSPµ
PīPsP»PsP¶PµPSPSCı PrPs P·PSPēPePSPµPSPSCı PIPēC%PµP·PīP°PrP°PSPēC...
CíPēPjPiC,PSPjC-PI.

PµPµCḡPµPr C,PēPj CıPe CḡPsP·PīPsC‡P°C,Pē P»C-PeCíPIP°PSPSCı PīCḡPµPīP°CḡP°C,PSPj
PŸP°PjCíC-PS P»PsCḡC,Pµ, CíP»C-Pr PīCḡPsPNēC,Pē PjPµPrPēC‡PSPµ PsP±CíC,PµP¶PµPSPSCı
P· PjPµC,PSCḡ PIPēCıPIP»PµPSPSCı C-PSC€PēC... CíCíPíCíC,PSC-C...
P·P°C...PIPSCḡCHPIP°PSCḡ, C%Ps PjPsP¶CíC,Cḡ CíPīCḡPēC‡PēPSPēC,Pē C,P°PeC- CíP°PjC-
CíPēPjPiC,PSPjPē, CıPe PrPsP±CḡPsCıPeC-CíPSP° PiC-PīPµCḡPīP»P°P·C-Cı
PīPµCḡPµPrPjC-C...CíCḡPsPIPsC— P·P°P»PsP·Pē. PµPµCḡPµPr PīPsC‡P°C,PePsPj
P»C-PeCíPIP°PSPSCı PSPµPsP±C...C-PrPSPs PīCḡPsPIPµCíC,Pē CḡPµPeC,P°P»CHPSPµ
PsP±CíC,PµP¶PµPSPSCı PīPµCḡPµPrPjC-C...CíCḡPsPIPsC— P·P°P»PsP·Pē C,P° PīCḡPē
PSPµPsP±C...C-PrPSPsCíC,C- bḡ” C,PµCíC, PSP° PIPēP·PSP°C‡PµPSPSCı CḡC-PIPsCı
CíPīPµC‡PēC,,C-C‡PSPsPiPs P°PSC,PēPiPµPSCí PīPµCḡPµPrPjC-C...CíCḡPsPIPsC— P·P°P»PsP·Pē
(PSA) PrPs PīPsC‡P°C,PeCí C,P° C‡PµCḡPµP· PsPrPSP°PePsPIC- PīCḡPsPjC-P¶PePē C‡P°CíCí
PiC-Pr C‡P°Cí P»C-PeCíPIP°PSPSCı.

PSP° C, P°PjCfCfP»PsP·PëPS Cí PïP°C†C-C"°PSC, C-PI P· PSP°CfPIPS C-ClC, Cñ PI
P°PSP°PjPSPµP·C- P°P»PµCñPiC-C— PSP° ClCfP»CHC,, P°PSC-P»P°PjC-PrPë. PŸP»C-Pr
PrPsC, CñPëPjCfPIP°C, PëClCfCf PsP±PµCñPµP¶PSPsClC, C- PïCñPë P·P°ClC, PsClCfPIP°PSPSC-
C, P°PjCfCfP»PsP·PëPSCf PiC-PrCñPsC...P»PsCñPëPrCf PïP°C†C-C"°PSC, P°Pj, Cí ClPePëC...
CñP°PSC-CëPµ PIC-PrP·PSP°C†P°P»P°ClCfCf P°P»PµCñPiC-CfCf PSP°
ClCfP»CHC,, P°PSC-P»P°PjC-PrPë.

*P—P°ClC, PsClCzPIP°PSPSCf C z PïPµCñC-PsPr PIP°PiC-C, PSPsClC, C- P°P±Ps
PiPsPrCzPIP°PSPSCf PiCñCzPrPrCñ.*

PŸP°PjCfC-PS PαPsCñC, Pµ PSPµ PïPsPeP°P·P°PSPëPñ PrP»CfCf P·P°ClC, PsClCfPIP°PSPSCf
P¶C-PSPeP°Pj.

PαPµCñC, PëP»CHPSC-ClC, Cñ

PµC-Pr C†P°ClC PeP»C-PSC-C†PSPëC... PrPsClP»C-PrP¶PµPSCñ C, P°PjCfCfP»PsP·PëPSCf
PïCñPsC, ClPiPsPj PePsCñPsC, PePsPiPs C, P° C, CñPëPIP°P»PsPiPs C†P°ClCfCf
PIC-PrP·PSP°C†P°P»PëClCfCf PïPsCñCfCëPµPSPSCf PµClPeCfP»ClC†C-C—. P'PëPïP°PrPePë
PïPsCñCfCëPµPSPSCf PµClPeCfP»ClC†C-C—, CñPµC, CñPsPiCñP°PrPSPsC—
PµClPeCfP»ClC†C-C— C- PSPµPrPsClC, P°C, PSCñPsC— PµClPeCfP»ClC†C-C—
PIC-PrP·PSP°C†P°P»PëClCfCf Cí PiC-ClP»ClCñPµC"ClC, CñP°C†C-PñPSPsPjCf PïPµCñC-PsPrC-.

*P—PrP°C, PSC-ClC, Cñ PIPïP»PëPIP°C, Pë PSP° CëPIPëPrPeC-ClC, Cñ CñPµP°PeC†C-C— PïCñPë
PePµCñCzPIP°PSPSC- P°PIC, PsC, CñP°PSCfPïPsCñC, PsPj P°P±Ps C-PSCëPëPjPë
PjPµC...P°PSC-P·PjP°PjPë.*

P"°PSCfP»C-PrP¶PµPSPSCf PIPïP»PëPICf PïCñPµPïP°CñP°C, Cí PSP° P·PrP°C, PSC-ClC, Cñ
PePµCñCfPIP°C, Pë C, CñP°PSCfPïPsCñC, PSPëPjPë P·P°ClCfPsP±P°PjPë C- PïCñP°C†CñPIP°C, Pë P·
PjPµC...P°PSC-P·PjP°PjPë PSPµ PïCñPsPIPsPrPëP»PëClCfCf. PñPrPSP°Pe PïP°C†C-C"°PSC, Pë
PïPsPIPëPSPSC- P±CfC, Pë PïCñPsC-PSC,, PsCñPjPsPIP°PSC- PïCñPs PjPsP¶P»PëPIPµ
PIPëPSPëPePSPµPSPSCf P·P°PïP°PjPsCñPsC†PµPSPSCf.

PŸPïPsClC-P± P·P°ClC, PsClCzPIP°PSPSCf C, P° PrPsP·Pë.

P"°P»CfCf PïPµCñPsCñP°P»CHPSPsPiPs P·P°ClC, PsClCfPIP°PSPSCf.

P PµPePsPjPµPSPPrPsPIP°PSP° PïCñPëPñPjP°C, Pë C, P°P±P»PµC, PeCf C%PsPrPµPSPSPs,
PSPµP·P°P»PµP¶PSPs PIC-Pr PIP¶PëPIP°PSPSCf C—P¶C-. PŸP°P±P»PµC, PeCf ClP»C-Pr
PePsPIC, P°C, Pë C†C-P»PsCñ, PSPµ CñPsP·P¶PsPICfCñC†Pë C, P° PSPµ CñPsP·P»P°PjCfCñC†Pë
C—C—, PsClCfC-P»CHPePë C†Pµ P±CfPrPµ PïPµCñPµCëPePsPrP¶P°C, Pë
PïCñPsP»PsPSPiPsPIP°PSPsPjCf PIPëPIC-P»CHPSPµPSPSCñ P°PeC, PëPIPSPsC—
CñPµC†PsPIPëPSPë.

PŸCñPëPIP°P»C-ClC, Cñ P»C-PeCfPIP°PSPSCf PICfC, P°PSPsPIP»CñC"°C, CñClCfCf
C-PSPrPëPIC-PrCfP°P»CHPSPs.

PµP°C†C-C"°PSC, P°Pj C-P· PSPëCñPePsPIPsCñ PSPµPrPsClC, P°C, PSC-ClC, Cñ PSPµ

PiPsC, C7C-P±PSP° PePsC7PμPeC†C-C7 PrPsP·Pë. PμP°C†C-C"PSC, P°Pj C-P·
 PiPμC†C-PSPePsPIPsC7 PSPμPrPsC†C, P°C, PSC-C†C, C7 PiPsPjC-C7PSPsPiPs C, P°
 C†PμC7PμPrPSC7PsPiPs C†C, C†PiPμPSC7 C, C7P¶PePsC†C, C- PePsC7PμPeC†C-C7 PrPsP·Pë
 PSPμ PiPsC, C7C-P±PSP° (PrPëPi. C, P°PePsP¶ C7PsP·PrC-P»
 B«PμC7PsC, PëPiPsPeP°P·P°PSPSC7B»).

B

P"C-C, Pë.

PμC7PμPiP°C7P°C, PSPμ P·P°C†C, PsC†PsPIC†C7C, C7 PrP»C7 P»C-PeC†PIP°PSPSC7
 PrC-C, PμPNë.

P'PμP·PiPμPeC† C, P° PμC,, PμPeC, PëPIPSC-C†C, C7 P·P°C†C, PsC†C†PIP°PSPSC7
 C, P°PjC†C†P»PsP·PëPSC† PrC-C, C7Pj PSPμ PsC†C-PSC7PIP°P»Pë.

PμPμC7PμPrPsP·CzPIP°PSPSC7.

PÿPëPjPiC, PsPjPë.

PμPμC7PμPrPsP·C†PIP°PSPSC7 C, P°PjC†C†P»PsP·PëPSPsPj PiC-PrC7PsC...P»PsC7PëPrPsPj
 PjPsP¶Pμ PiPsC, PμPSC†C-PNëPSPs C†PiC7PëC†PëPSPëC, Pë C, C7P¶PeC†
 PiC-PiPsC, PμPSP·PëPIPSC† PrC-C7. PÿC7P¶PeP° PiC-PiPsC, PμPSP·PëPIPSP° PrC-C7
 PIC-PrP·PSP°C†P°P»P°C†C7 PiC7Pë C7C-P·PSPëC... C†C, C†PiPμPSC7C...
 PiPμC7PμPrPsP·C†PIP°PSPSC7.

P»C-PeC†PIP°PSPSC7.

Pj PIPëPiP°PrPeC† C7P°PiC, PsPIPsPiPs P·PSPëP¶PμPSPSC7 P°C7C, PμC7C-P°P»C7PSPsPiPs
 C, PëC†PeC† PIPSP°C†P»C-PrPsPe PiPμC7PμPrPsP·C†PIP°PSPSC7 C†P»C-Pr PiC7PsPIPsPrPëC, Pë
 PiC-PrC, C7PëPjC†C7C†C† C, PμC7P°PiC-C7, C†PiC7C7PjPsPIP°PSC† PSP°
 PIC-PrPSPsPIP°PμPSPSC7 PSPsC7PjP°P»C7PSPsC— C,, C†PSPeC†C-C— C†PμC7C†PμPIPs-
 C†C†PrPëPSPSPsC— C†PëC†C, PμPjPë, (PSP°PiC7PëPeP»P°Pr, PiP°C†C-C"PSC, PjP°C"
 PiC7PëPNëPSC7C, Pë PiPsC7PëP·PsPSC, P°P»C7PSPμ PiPsP»PsP¶PμPSPSC7). PiPeC%Ps C†PμPNë
 P·P°C...C-Pr PSPμ PrC-C", PiC7PsPIPμC†C, Pë C-PSC,, C†P·C-PNëPSC† C, PμC7P°PiC-C7 C, P°
 PiC7PëP·PSP°C†PëC, Pë PIP°P·PsPiC7PμC†PsC7PSC- P·P°C†PsP±Pë. PkPμPsP±C...C-PrPSPs
 C†P»C-PrPeC†PIP°C, Pë P·P° C,, C†PSPeC†C-C"C7 PSPëC7PsPe C, P° PiC7PsPIPsPrPëC, Pë
 P·P°PiP°P»C7PSC† PiC-PrC, C7PëPjC†C7C†C† C, PμC7P°PiC-C7. P'PSP°C†P»C-PrPsPe
 PIPëC†PsPePsPiPs C†C, C†PiPμPSC7 P·PiB7™ C7P·C†PIP°PSPSC7 C, P°PjC†C†P»PsP·PëPSC† P·
 P±C-P»PeP°PjPë PiP»P°P·PjPë PeC7PsPIC- PiC7PsPIPμPrPμPSPSC7 PiPμPjPsPrC-P°P»C-P·C† C"
 PSP°PIC7C7Pr C†Pë PrPsC†C-P»C7PSPëPj.

P— PjPμC, PsC7 PiC7PëPiPëPSPμPSPSC7 PiPsPrP°P»C7C€PsPiPs
 PIC†PjPsPeC, C†PIP°PSPSC7 PiC7PμPiP°C7P°C, C† PjPsP¶PSP° C€C, C†C†PSPs
 PIPëPeP»PëPeP°C, Pë P±P»C7PIP°PSPSC7. PμC7Pë PiPμC7PμPrPsP·C†PIP°PSPSC-
 P·PSP°C†PSPsC— PeC-P»C7PePsC†C, C- PiC7PμPiP°C7P°C, C† PiP°C†C-C"PSC, C†
 PSPμPsP±C...C-PrPSPs PiC7PsPjPëC, Pë C€P»C†PSPsPe C-P·
 P·P°C†C, PsC†C†PIP°PSPSC7Pj P°PeC, PëPIPsPIP°PSPsPiPs PIC†PiC-P»P»C7 C, P°
 PSPëP·C7PePsPsC†PjPsC, PëC†PSPëC... PiPsC†P»P°P±P»C7PIP°P»C7PSPëC...

3 C₇PsPePë.

PJPjPsPIPë P•P±P_μC₇C-PiP°PSPSC_Π.

P—P±P_μC₇C-PiP°C,Pë Cr PSP_μPrPsC₇C,C₇PiPSPsPjCr PrP»C_Π PrC-C,P_μPN₂ PjC-C₇C₇C-.

P—P°C...PëC%₀P°C,Pë PIC-Pr C₇PIC-C,P»P° C,P° PIPsP»PsPiPë.

P—P±P_μC₇C-PiP°C,Pë PI PsC₇PëPiC-PSP°P»CH₂PSC-PN₂ CrPiP°PePsPIC₇C- PiC₇Pë C,P_μPjPiP_μC₇P°C,C₇C₇C- PSP_μ PIPëC%₀P_μ 25 °P₇ Cr C₇C₇C...PsPjCr PjC-C₇C₇C-.

PJPiP°PePsPIPëP°.

P_μPs 10 C,P°P±P»P_μC,PsPe Cr P±P»C-C₇C,P_μC₇C-; PiPs 3 P±P»C-C₇C,P_μC₇Pë PI PeP°C₇C,PsPSPSC-PN₂ PePsC₇PsP±C₇C-.

P₇P°C,P_μPiPsC₇C-C_Π PIC-PrPiC₇C₇PeC₇.

P—P° C₇P_μC₇P_μPiC,PsPj.

P'PëC₇PsP±PSPëPe.

P₇C-PSC,PsPS P₇C-C₇PiP°PSC-C_Π, P₇.P>./Synthon Hispania, S.L.

P₇C-C₇C₇P_μP•PSP°C...PsPrP₇P_μPSPSC_Π PIPëC₇PsP±PSPëPeP° C,P° P°PrC₇P_μC₇P° PjC-C₇C₇C_Π PiC₇PsPIP°PrP₇P_μPSPSC_Π PN₂PsPiPs PrC-C_ΠP»CH₂PSPsC₇C,C-.

P₇/ P₇P°C₇C,P_μP»P»Ps, B₇- 1, P₇P°PSC, P'PsC- PrP_μ P>P»PsP±C₇P_μPiP°C,, P'P°C₇C₇P_μP»PsPSP°, 08830, P₇C₇PiP°PSC-C_Π/

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